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Professional

Autonomic Dysreflexia and Other Autonomic Dysfunctions Following Spinal Cord Injury

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Key Points

Autonomic dysreflexia (AD) is a potentially life-threatening blood pressure spike that can lead to a hypertensive emergency affecting people with spinal cord injury *at the level of T6 or above* (sometimes as low as T8, though rare).

AD is the result of sympathetic nervous system overactivity in response to a strong sensory stimulus below the level of injury. This stimulus is often something that is noxious or irritating, such as a wound or tight clothing, but it can also be a normal bodily function, most commonly an overly full bladder or bowel.

The main sign of autonomic dysreflexia is a sudden rise in blood pressure. An increase of 20 to 30 mmHg above your patient's normal *systolic blood pressure* is considered to indicate autonomic dysreflexia.

Other signs and symptoms of AD may include: pounding or throbbing headache, profuse sweating, flushing or blotching of the skin above the level of injury.

The identification and removal of the possible trigger and subsequent decrease of afferent stimulation to the spinal cord is the most effective prevention and management strategy in clinical practice.

Evidence of effective management and prevention of AD include:

Botulinum toxin injections into the detrusor muscle or external urethral sphincter seem to be a safe and valuable therapeutic option in individuals with SCI who perform clean intermittent self-catheterization and have incontinence resistant to anticholinergic medications. Its use in the prevention of AD is less well defined.

Capsaicin and its analogue, resiniferatoxin, are effective in the management of AD in people with SCI.

Anticholinergics do not appear to be sufficient for the management of AD in SCI.

Sacral deafferentation may reduce AD during urodynamic investigations.

Urinary bladder surgical augmentations may diminish or resolve episodes of AD.

Lidocaine anal block can limit the AD response in susceptible patients undergoing anorectal procedures.

Topical lidocaine may prevent AD during digital bowel stimulation but does not prevent AD during anorectal procedures.

Adequate anesthesia (spinal or epidural if possible) is needed with vaginal delivery, Caesarean delivery or instrumental delivery.

Anesthesiologists and surgeons working with individuals with SCI must know how to recognize the AD syndrome, how to prevent its occurrence, and how to manage it.

Epidural anesthesia is preferred and effective for most women with AD during labour and delivery.

Anesthesia should be used during surgical procedures in individuals with SCI despite apparent lack of sensation.

Topical anesthetic is not effective for the prevention of AD during FES.

Nifedipine may be useful to prevent or control AD in individuals with SCI; however, serious adverse effects from its use at higher dosages (e.g., 80mg for hypertension in people without SCI).

Nitrates are commonly used in the control of AD in SCI; however, no studies have been done to show their effectiveness or safety in SCI.

Preliminary evidence suggests that captopril is effective for the management of AD in SCI.

There is limited evidence for the use of Terazosin as an agent for control of AD in individuals with SCI.

Prazosin can prophylactically reduce severity and duration of AD episodes in SCI.

It is not known whether Phenoxybenzamine is effective for the management of AD in SCI.

Prostaglandin E2 is effective for reducing BP responses during electroejaculation.

Sildenafil has no effect on AD responses in men with SCI during ejaculation.

Table of Contents

1 Chapter Summary

What is autonomic dysreflexia?

Autonomic dysreflexia (AD) is a potentially life-threatening blood pressure spike that can lead to a hypertensive emergency affecting people with spinal cord injury (SCI) *at the level of T6 or above* (sometimes as low as T8, though rare). Sympathetic neurons within the mid thoracic spinal cord segments control a large group of blood vessels that supply the lower body and many abdominal organs, such as the stomach and intestines. Therefore, higher levels of SCI (T6 and above), as well as complete injuries rather than incomplete, are more likely to lead to the development of AD (Krassioukov et al. 2003; Curt et al. 1997; Mathias & Frankel 1988).

AD is a medical emergency that requires an immediate response. It occurs more often in the chronic phase of SCI, but can happen in the first few months after injury as well. Episodes of autonomic dysreflexia are usually brief and have an identifiable trigger (Teasell et al. 2000; Karlsson, 1999; Mathias & Frankel 1988; Elliott & Krassioukov 2006).

What are the signs and symptoms of autonomic dysreflexia?

The main sign of autonomic dysreflexia is a sudden rise in blood pressure. An increase of 20 to 30 mmHg above your patient's normal *systolic blood pressure* is considered to indicate autonomic dysreflexia. Since the normal blood pressure of a person with SCI is often 15 to 20 mmHg lower than a person without an SCI, blood pressure can be in the range of 'normal' or 'slightly elevated' and still indicate an episode of AD.

Signs and symptoms of autonomic dysreflexia:

- Sudden rise in blood pressure of 20 to 30 mmHg above the person's normal systolic blood pressure (main symptom)
- Change in heart rate – usually a slow heart rate which can sometimes become rapid or irregular
- Pounding or throbbing headache
- Profuse sweating, flushing or blotching of the skin above the level of injury
- Goosebumps or hair standing on end above the level of injury
- Dry and pale skin below the level of injury
- Increased number and severity of muscle spasms
- Metallic taste in the mouth
- Feeling anxious or a feeling of impending doom
- Nasal congestion
- Blurred vision
- Seeing spots
- Nausea
- Difficulty breathing or a feeling of chest tightness

This rise in blood pressure is usually accompanied by other symptoms, which can range from not feeling anything or having mild discomfort and a headache, to a life-threatening emergency where symptoms can be severe. It is important for patients and clinicians to be able to recognize the symptoms of AD so they can act accordingly. Clinicians should also be aware that in some people with SCI, AD could occur without any symptoms, a condition known as a silent or asymptomatic AD (Ekland et al. 2008; Linsenmeyer et al. 1996).

Why does autonomic dysreflexia happen?

AD is the result of sympathetic nervous system overactivity in response to a strong sensory stimulus below the level of injury. This stimulus is often something that is noxious or irritating, such as a wound or tight clothing, but it can also be a normal bodily function, most commonly an overly full bladder or bowel. In response to the stimulus, the sympathetic nervous system signals the arteries to constrict, which increases blood pressure. This increase in blood pressure is followed by reflexive a slowing of the heart rate which can then become irregular. Because of the damage to the spinal cord, the body can not effectively control the blood pressure and restore it to normal levels, resulting in AD.

Triggers of autonomic dysreflexia

Bladder issues

- Urinary tract infection
- Urinary retention
- Blocked catheter
- Overfilled collection bag

Skin issues

- Pressure ulcers
- Extreme heat or cold
- Pressure or pinching of the skin
- Ingrown toenails
- Burns
- Tight clothing
- Any direct irritant below the level of the injury

Bowel issues

- Distention or irritation of the bowel
- Constipation or impaction of the bowel
- Hemorrhoids
- Infection or irritation of the bowel

Sexual activity and reproductive processes

- Overstimulation
- Reproductive activity
- Menstrual cramping
- Labor and delivery

Other causes

- Heterotopic ossification
- Acute abdominal conditions (such as ulcers)
- Fractures

What should I do if my patient has an episode of Autonomic Dysreflexia?

AD is a medical emergency and requires immediate treatment. The most effective treatment strategy is to identify the trigger of the episode and reduce the stimulation that is causing it. The goal of intervention is to alleviate symptoms and avoid the complications associated with uncontrolled hypertension (Vallès et al. 2005; Eltorai et al. 1992; Pine et al. 1991; Yarkony et al. 1986).

If the conservative treatments for AD are not effective in reducing blood pressure and it remains at or above 150 mmHg, drug treatments are used. This involves the use of fast-acting anti-hypertensive drugs to rapidly lower the elevated blood pressure.

What to do if your patient has autonomic dysreflexia

1. Move patient into an upright sitting position
2. Check blood pressure, and re-check every 5 minutes
3. Loosen tight clothing
4. Search for and eliminate the cause of the incident where one can be identified
    a. Check bladder
    b. Check bowel
    c. Check skin
5. Seek medical attention if there is no reduction in blood pressure after following these steps

Source: Consortium for Spinal Cord Medicine, 2001

Which prevention methods are effective?

Preventing an AD episode is far more effective than treating one (Braddom & Rocco 1991). Researchers have done studies on various treatments to determine which are helpful in preventing incidents of AD (Courtois et al. 2012; Krassioukov et al. 2009).

Capsaicin: Studies have shown that administering the chemical compound, Capsaicin, and its more concentrated cousin, Resiniferatoxin, into the bladder by a catheter can decrease the incidence AD during bladder procedures (Igawa et al. 2003; Kim et al. 2003; Giannantoni et al. 2002).

Surgical bladder augmentation: Some early evidence suggests that surgery to augment the bladder may also reduce or resolve episodes of AD (Ke & Kuo, 2010; Perkash, 2007; Sidi et al. 1990; Barton et al. 1986).

Sacral denervation: Sacral deafferentation surgery may reduce bladder-related episodes of AD (Hohenfellner et al. 2001; Kutzenberger, 2007).

Botulinum toxin: Two studies have demonstrated that injections of Botulinum toxin into the muscles of the bladder is effective in reducing episodes of AD (Walter et al. 2020; Huang et al. 2024), which is supported by previous findings (Chen & Kuo 2012; Chen et al. 2008; Kuo, 2008; Schurch et al. 2000; Dykstra et al. 1988).

Anticholinergic and antimuscarinic medications: The use of anticholinergic medications does not appear to be effective in preventing AD during bladder procedures (Giannantoni et al. 1998). One study (Walter et al. 2023) supported the effectiveness of antimuscarinics, specifically fesoterodine, in reducing the frequency and severity of AD episodes.

Lidocaine: A lidocaine anal block has been found to limit the AD response in patients undergoing anorectal procedures (Cosman & Vu 2005). Topical lidocaine may prevent AD during digital bowel stimulation, but not during anorectal procedures (Furusawa et al. 2009; Cosman et al. 2002). Intravesical lidocaine may reduce the incidence and severity of AD during catheter change (Solinsky & Linsenmeyer 2018).

Anesthesia for use during pregnancy and labour: Studies have found that the use of adequate anesthesia (spinal or epidural if possible) is needed with vaginal, Caesarean, or instrumental delivery to prevent AD during labour. Epidural anesthesia is preferred and effective for most women with SCI (Skowronski & Hartman 2008; Cross et al. 1992; Cross et al. 1991; Hughes et al. 1991).

Anesthesia for use during general surgery: Anesthesia should be used during surgery for people with SCI despite the apparent lack of sensation to prevent AD. Anesthesiologists and surgeons working with patients with SCI need to be able to recognize, prevent, and manage AD (Eltorai et al. 1997; Lambert et al. 1982).

Topical anesthesia during functional electrical stimulation (FES) treatment: Studies have found that the application of topical anesthesia is not effective in preventing AD during FES treatment. More research is required to understand how to prevent AD during FES (Matthews et al. 1997).

Stoma surgery: There is preliminary evidence that stoma surgery may reduce the number of incidents of autonomic dysreflexia, if other treatments have failed to improve management of neurogenic bowel (Coggrave et al. 2012).

Where can I find more information?

For more information, please click through the rest of the Autonomic Dysreflexia chapter (https://scireproject.com/evidence/autonomic-dysreflexia/introduction/), refer to the PVA guidelines (Krassioukov et al. 2021; https://pva.org/research-resources/publications/clinical-practice-guidelines/) and consult a physician who specializes in SCI and/or Cardiovascular issues.

2 Introduction

Autonomic dysreflexia (AD) is a clinical emergency that can occur in individuals with spinal cord injury (SCI), commonly in those with an injury at level T6 or above (Mathias & Frankel 1988; Mathias & Frankel 2002; Teasell et al. 2000). An episode of AD is usually characterized by an acute elevation of arterial blood pressure (BP) and bradycardia (slow heart rate), which may be replaced by tachycardia (rapid heart rate) on occasion. Objectively, an increase in systolic BP greater than 20–30mmHg is considered a dysreflexic episode (Teasell et al. 2000). Individuals with cervical and high thoracic SCI have resting arterial BPs that are approximately 15 to 20 mmHg lower than individuals without SCI (Mathias & Bannister 2002; Claydon & Krassioukov, 2006). As such, acute elevation of BP to normal or slightly elevated ranges could indicate AD in this population. Intensity of AD can vary from asymptomatic (Linsenmeyer et al. 1996), to mild discomfort and headache, to a life threatening emergency where systolic blood pressure can reach 300mmHg and symptoms can be severe (Mathias & Bannister 2002). Untreated episodes of AD may have serious consequences, including intracranial hemorrhage, cardiac complications, retinal detachments, seizures, and death (Eltorai et al. 1992; Pine et al. 1991; Vallès et al. 2005; Yarkony et al. 1986). During an episode of AD, a significant increase in visceral sympathetic activity with coronary artery constriction can result in myocardial ischemia, even in the absence of coronary artery disease (Ho & Krassioukov 2010).

It has been observed that higher level of SCIs equate to greater degrees of cardiovascular dysfunctions (Curt et al. 1997; Krassioukov et al. 2003). Another factor affecting the severity of AD is the degree of completeness of SCI as AD is three times more prevalent in people with complete tetraplegia (91% of individuals presenting with signs of AD) compared to those with incomplete tetraplegia (27% of individuals presenting with signs) (Curt et al. 1997). However, it is important to note that although autonomic dysreflexia occurs more often in the chronic stage of spinal cord injury at or above the 6th thoracic segment, there is clinical evidence of early episodes of autonomic dysreflexia within the first days and weeks after the injury (Krassioukov et al. 2003; Silver, 2000).

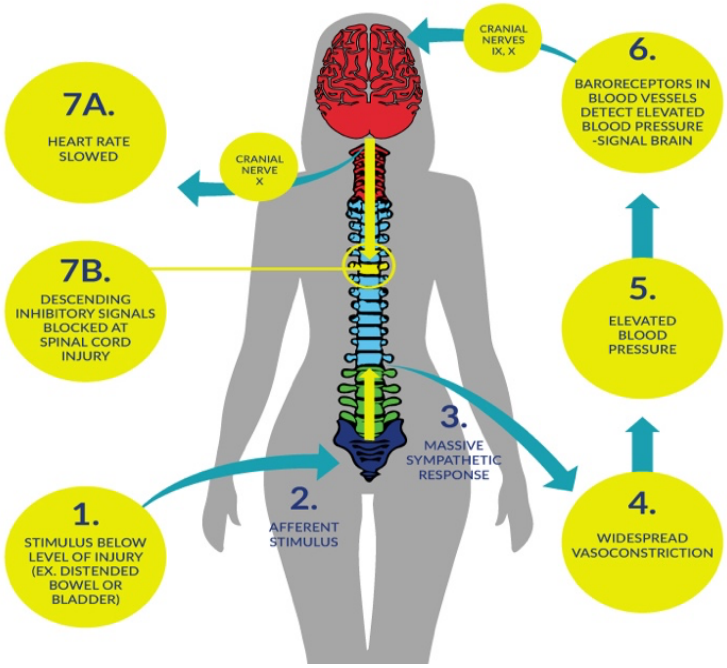


Figure 1. How Autonomic Dysreflexia occurs due to SCI

3 Pathophysiology of Autonomic Dysreflexia

AD is most commonly triggered by urinary bladder issues or colon irritation. However, many other causes have been reported in the literature (Mathias & Frankel 2002; Teasell et al. 2000). AD is caused by a widespread sympathetic response triggered by either noxious or non-noxious stimuli below the level of injury (Krassioukov & Claydon 2006). AD episodes are usually short-lived either due to treatment or inherently self-limiting. However, there are reports of AD triggered by a specific stimulus, which continued to be present days up to weeks (Elliott & Krassioukov 2006).

Numerous mechanisms have been proposed for the development of AD. It is known from animal studies that autonomic instability following SCI results from plastic changes occurring within the spinal cord and peripheral autonomic circuits in both the acute and chronic stages following injury (Krassioukov, 2006; Mathias & Frankel 1988; Mathias & Frankel 2002; Teasell et al. 2000). Currently, unstable blood pressure control following SCI can be attributed to the destruction of the descending vasomotor pathways, resulting in the loss of inhibitory and excitatory supraspinal input to the sympathetic preganglionic neurons (Furlan et al. 2003). Moreover, there is significant animal and human evidence suggesting that plastic changes within the spinal cord (specifically spinal sympathetic neurons and primary afferents) underlies the abnormal cardiovascular control and the development of AD following SCI. Further, altered sensitivity of peripheral alpha-adrenergic receptors (receptors in the sympathetic nervous system) may contribute to AD (Arnold et al. 1995; Karlsson, 1999; Krassioukov et al. 1999; Krassioukov et al. 2002; Osborn et al. 1990).

Table 1a. Signs and Symptoms

- Severe bilateral pounding headache
- Feeling of anxiety/impending doom
- Profuse sweating above the level of injury
- Flushing and piloerection (body hair 'stands on end') above the level of injury
- Dry and pale skin due to vasoconstriction below the level of injury
- Blurred vision
- Nasal congestion
- Cardiac arrhythmias, atrial fibrillation

Table 1b. Characteristics of AD

Author Year Country Score Research Design Sample Size	**Methods**	**Outcome**
Calderón-Juárez et al. 2024 Canada Pre-post Level 4 N=24	**Population:** N=24, 17M, 7F AIS A: 14 AIS B: 7 AIS C: 3 AIS D: 0 **Treatment:** Participants underwent urodynamic studies (UDS) and BP was monitored every 1-2 minutes to identify AD. **Outcome Measures:** BP, finger-photoplethysmography and ECG	1. SBP increased as the UDS progressed, and the highest HR was reached 60 seconds after maximal sBP. 2. The accuracy of the standard deviation of heartbeats (variability in HR) threshold for predicting episodic AD was strong (AUC = 0.811, 95% confidence interval [CI] = 0.688 – 0.934, $p < 0.001$).
Cívicos Sánchez et al. 2021 Spain Pre-post Level 4 N=37	**Population:** N=37, 27M, 10F Mean age: 42.4 years Cervical: 32 Thoracic: 5 ASIA A: 20 ASIA B: 4 ASIA C: 5 ASIA D: 7 ASIA E: 1 **Treatment:** Participants rested in supine position on a tilt table for 40 min while a 30ml blood sample was drawn. After 3 minutes of head-up tilt at 60 degrees, another blood sample was collected. In	1. There was a correlation between the magnitude of maximum sBP and time since SCI ($\rho = 0.52$; $p = 0.004$). 2. AD was typically precipitated in participants with ASIA impairment scores A or B (19/22, 86%), but only in 3 out of 8 (37.5%) patients with ASIA scores of C, D or E ($p = 0.02$). 3. 55% of SCI participants with AD presented neurogenic orthostatic hypotension (NOH) concomitantly, but none of SCI participants without AD had NOH ($p = 0.01$). 4. Participants with AD + NOH had lower levels of noradrenalin

Author Year Country Score Research Design Sample Size	Methods	Outcome
	supine position, 100-400ml of 0.9% saline at 37°C was infused into the patient via urinary catheter. HR, BP, and peripheral resistance was measured **Outcome Measures:** HR, BP, and peripheral resistance	compared to participants without NOH in supine (107.2 ± 170.0 vs. 145.7 ± 116.7 pg/ml, p = 0.143) and upright (173.6 ± 334.8 vs. 318.1 ± 310.3 pg/ml, p = 0.034) positions.
Currie et al. 2019 Canada Pre-post Level 4 N=26	**Population:** N=26, 73% male All participants had AIS score of A or B **Treatment:** BP was measured over a 24-hour period, automatically every 15 min during the day and every 60 min at night. Participants were to manually measure BP during any activity that may trigger AD/OH or anytime they experienced AD/OH symptoms. Baseline daytime values were calculated by averaging three successive automatic measurements after the participant woke up and had transferred to their chair. Baseline nighttime values were determined using the average of the first 3 automatic BP measurements during sleep. **Outcome Measures:** BP, incidences of AD or OH.	1. No AD parameters (e.g., frequency, maximum sBP, maximum change in sBP, longest AD episode) were independently related to arterial stiffness (cfPWV) 2. Although not significantly correlated, there was a mean of 5 AD events per day, with an average maximum sBP of 154 mmHg. The mean maximum change in sBP was 49 mmHg and the longest average AD period was 25 minutes. 3. cfPWV was also positively correlated with the total number of BP events (r = 0.480, P = 0.013).
Huh et al. 2024 Korea Pre-post Level 4 N=29	**Population:** N=29 with cervical SCI, 26M, 3F AIS A: 19 AIS B-D: 10 **Treatment:** Participants recorded BP using beat-by-beat continuous BP measurement. Participants' bladders were filled with normal saline (37°C) up to cystometric capacity. sBP, dBP, MAP an HR were continuously monitored while participant was in supine	1. Restoration time demonstrated strong positive correlations with peak sBP and sBP change, indicating that individuals with a greater increase in sBP are likely to have longer restoration times (r = 0.61, p = 0.000; r = 0.64, p = 0.000, respectively). 2. Restoration time exhibited a strong positive correlation with both peak systolic blood pressure (SBP) and

Author Year Country Score Research Design Sample Size	Methods	Outcome
	position. Restoration time was analysed during and after urination. Restoration time is the duration from the initiation of voiding until BP returns to the pre-filling resting level. **Outcome Measures:** sBP, dBP, MAP, HR, restoration time	SBP change (r = 0.61, p = 0.000; r = 0.64, p = 0.000, respectively). 3. sBP change in beat-to-beat BP measurement was significantly associated with prolonged restoration time (p=0.016) and was found to be the most significant factor for prolonged restoration time.
Walter et al. 2018 Switzerland Pre-post Level 4 N=300	**Population:** N=300, 259M, 41F Tetraplegia: 98 Paraplegia: 202 AIS A: 120 AIS B-D: 180 **Treatment:** All participants underwent a urodynamic investigation while monitoring sBP, dBP, and HR. The bladder was filled with a 37°C mixture of 0.9% sodium chloride solution and contrast medium via a transurethral catheter. **Outcome Measures:** sBP, dBP, HR	1. The presence of neurogenic detrusor overactivity predicted AD during urodynamic investigation (p=0.030).

Discussion

Individuals who have SCI and AD often experience increases in HR along with BP (Calderón-Juárez et al. 2024). Walter et al. (2018) also found neurogenic detrusor overactivity to be predictive of AD during urodynamic investigation.

Furthermore, events of AD commonly occur during urination, where longer restoration times (the time from initiation of voiding until BP returns to resting value) are correlated with higher peak sBP and change in sBP (Huh et al. 2024).

Conclusion

There is level 4 evidence (from one pre-post) (Calderón-Juárez et al. 2024) that sBP increased as urodynamic studies progressed, and the highest HR was reached 60 seconds after maximal sBP.

There is level 4 evidence (from one pre-post) (Cívicos Sánchez et al. 2021) that most individuals with AD presented neurogenic orthostatic hypotension (NOH) concomitantly, but none of SCI participants without AD had NOH.

There is level 4 evidence (from one pre-post) (Currie et al. 2019) that AD parameters are not significantly correlated with arterial stiffness.

There is level 4 evidence (from one pre-post) (Huh et al. 2024) that restoration time is strongly correlated with peak sBP and change in sBP.

There is level 4 evidence (from one pre-post) (Walter et al. 2018) that the presence of neurogenic detrusor overactivity may predict AD during UDS.

3.1 How to Assess - Autonomic Assessment Form

The complexity of the autonomic nervous system and its involvement in almost every system in the body makes selecting appropriate autonomic function tests for individuals with SCI difficult (Krassioukov et al. 2007). It is not clear how many practitioners in SCI care have experience with testing in this area, even if the operational definitions of autonomic dysfunction are defined (Krassioukov et al. 2007). Inattention to autonomic function post-SCI can pose significant risk to a person's neurological function and quality of life (Krassioukov et al. 2007). During the last decade, the assessment of individuals with SCI has improved significantly, though autonomic screening remains somewhat difficult to complete. Previous research has recommended that the assessment of autonomic functions be a part of clinical evaluation of individuals with SCI, in addition to already established motor and sensory assessment (Krassioukov et al. 2007).

The International Standards to Document Remaining Autonomic Function after Spinal Cord Injury (ISAFSCI) was developed by a working group of the American Spinal Injury Association (ASIA) and International Spinal Cord Society (ISCoS) (Wecht et al. 2021; Alexander et al. 2009; Krassioukov et al. 2012). The ISAFSCI is an assessment designed to determine which autonomic functions are intact, impaired or lost following SCI, and the Assessment form consists of 2 major sections – General Autonomic Function, and Lower Urinary Tract, Bowel, and Sexual Function (Krassioukov et al. 2012).

General Autonomic Function

Cardiovascular	Scoring	Condition	Definitions	Score
Heart Rate	**Normal (2)**		61-99 bpm	
		Bradycardia	≤ 60 bpm	
Supine _____bpm	**Altered (1)**	Tachycardia	≥ 100 bpm	
		Arrhythmias §		
Seated _____bpm	**Not Tested (NT): indicate reason other comments:**			
Systolic BP	**Normal (2)**		91-139 mmHg	
		Supine Hypotension	SBP ≤ 90 mmHg	
Supine _____mmHg		Orthostatic Hypotension	Fall ≥ 20 mmHg within 10 minutes*	
	Altered (1)	Neurogenic Shock	within 30 days of injury; heart rate ≤ 60 bpm; SBP ≤ 90 mmHg	
		Autonomic Dysreflexia**	increase in SBP > 20 mmHg above baseline	
Seated _____mmHg		Supine Hypertension	≥ 140 mmHg	
	Not Tested (NT): indicate reason, other comments:			
Diastolic BP	**Normal (2)**		61-89 mmHg	
		Supine Hypotension	≤ 60 mmHg	
Supine _____mmHg	**Altered (1)**	Orthostatic Hypotension	Fall ≥ 10 mmHg within 10 minutes*	
		Supine Hypertension	≥ 90 mmHg	
Seated_____mmHg	**Not Tested (NT): indicate reason other comments:**			

*§ define the arrhythmia; * within 3 minutes, but delayed orthostatic hypotension; within 10 minutes, may be more common in the SCI population. ** self-report "within the past 7-days, unanticipated i.e., not in response to known intervention (e.g., medication).*

Thermoregulation	Scoring	Conditions	Definitions	Score
Core Body Temp**	**Normal (2)**	Normal	36.4-37.6 °C (97.5-99.7 °F)	
		Subnormal	35.1-36.3 °C (95.1-97.4 °F)	
°C *or* °F	**Altered (1)**	Elevated	37.7-37.9°C (99.8-100.3 °F)	
°C *or* °F		Hypothermia	≤35°C (≤95°F)	
°C *or* °F		Hyperthermia	≥38.0°C (≥100.4°F)	
	Not Tested (NT): indicate reason, other comments:			

*** Under ambient conditions: 20-25°C (68-77°F); 30-50% relative humidity; wearing single-layer, indoor garments; after 10-minutes of rest; no acute illness or infection*

continued

Sudomotor*	Scoring	Conditions	Definitions	Score
	Normal (2)	Normal sweating	Sweating on all skin surfaces	
		Indicate the condition(s) met if scored as (1)		
	Altered (1)	Hypohidrosis	Diminished sweating above NLI Diminished sweating below NLI	
		Hyperhidrosis	Excessive sweating above NLI Excessive sweating below NLI	
	Absent (0)	Anhidrosis	No sweating above or below NLI	
	Not Tested (NT): indicate reason, other comments:			

** Record sweating responses to high ambient heat or exercise only. Do not record sweating associated with AD, OH, or mental stress.*

Broncho-pulmonary System	Findings	Conditions	Definition	Score
	Normal (2)			
		Invasive ventilation	24 hours/day	
	Altered (1)	Partial invasive ventilatory support	< 24 hours/day	
		Impaired voluntary respiration not requiring ventilatory support	Continuous Positive Airway Pressure (CPAP) for sleep apnea	
	Not Tested (NT): indicate reason, other comments:			

Forced Vital Capacity (FVC) supine _____ seated _____
abdominal binder: YES_____ NO_____
mL ____; kg ____; mL/kg _____

Total Score General Autonomic Section

Sacral Autonomic Function

Bladder Emptying Method / Frequency / Timing / Voluntarily — Yes _____ No _____

System/Organ	Scoring	Anticipated Function (based on ISNCSCI)	Anticipated Functional Score	Patient Reported Score
Awareness bladder fullness	Normal (2)	Any level injury with normal sensation in the T11-L2 and S3-S5 dermatomes		
	Altered (1)	Any level injury with partial preservation of sensation in the T11-L2 and/or S3-S5 dermatomes		
	Absent (0)	NLI at or above T9 no sensation below		
	Not Tested (NT): indicate reason, other comments			
Ability to prevent bladder leakage	Normal (2)	Individuals with normal sensation and motor function in the S3-S5 dermatomes		
	Altered (1)	Individuals with partial sensation and motor function in the S3-S5 dermatomes		
	Absent (0)	No motor function at the S3-5 dermatomes		
	Not Tested (NT): indicate reason, other comments:			
Bowel Emptying	Method / Frequency / Timing / Voluntarily — Yes _____ No _____			
Awareness of bowel fullness	Normal (2)	Normal sensation and motor function in the S3-S5 dermatomes		
	Altered (1)	Partial preservation of sensation or motor function in the S3-S5 dermatomes		
	Absent (0)	No sensation or motor function in the S3-5 dermatomes		
	Not Tested (NT): indicate reason, other comments:			

continued

System/Organ	Scoring	Anticipated Function (based on ISNCSCI)	Anticipated Functional Score	Patient Reported Score
Ability to prevent bowel leakage	Normal (2)	Individuals with normal sensation and motor function in the S3-S5 dermatomes		
	Altered (1)	Individuals with partial sensation and motor function in the S3-S5 dermatomes		
	Absent (0)	No motor function at the S3-5 dermatomes		
	Not Tested (NT): indicate reason, other comments:			
Psychogenic arousal	Normal (2)	Normal sensation and reflex motor function at T11-L2		
	Altered (1)	Partial sensation and motor reflex function at T11-L2		
	Absent (0)	No sensation or reflex motor function at T11-L2		
	Not Tested (NT): indicate reason, other comments:			
Reflex genital arousal	Normal (2)	Normal sensation and reflex function at S3-5		
	Altered (1)	Partial sensation and/or motor reflex function at S3-S5		
	Absent (0)	No sensation or motor function at S3-S5 and absent sacral reflex		
	Not Tested (NT): indicate reason, other comments:			
Orgasm	Normal (2)	Intact S3-5 sensation and or motor function with any degree of preserved sacral reflexes		
	Altered (1)	No S3-5 sensation or motor function and preserved sacral reflexes		
	Absent (0)	No S3-5 sensation or motor function and absent sacral reflexes		
	Not Tested (NT): indicate reason, other comments:			
Ejaculation	Normal (2)	Normal T11-12 sensation and sacral reflexes		
	Altered (1)	Diminished sensation at T11-12 dermatomes and normal sacral reflexes		
	Absent (0)	No sensation at T11-12 dermatomes and absent sacral reflexes		
	Not Tested (NT): indicate reason, other comments:			

Total Score Sacral Autonomic Section

Figure 2. Autonomic Standards Assessment Form – Available from: https://scireproject.com/wp-content/uploads/2025/03/ISAFSCI-Autonomic-General-and-Sacral-Exam-Worksheets.pdf

4 Systematic Review of Autonomic Dysreflexia

As knowledge is growing in the field of AD management in the SCI population, it is important to regularly review the literature and ensure that the information used both in research and practice is current and evidence based. This section will provide an overview of the current systematic reviews available in the areas related to AD management in the SCI population.

Table 2. Systematic Reviews - Autonomic Dysreflexia

Author Country Date included in the review Total Sample Size Level of Evidence Type of Study Score	**Methods Databases**	**Conclusions**
Gray et al. 2022 Canada Reviewed published articles from 1997 to 2020	**Methods:** A keyword search was conducted for English-language studies published after 1960 investigating the impact of local analgesics in reducing AD. **Databases:** Medline, CINAHL, Central, Cochrane Reviews, PsycINFO, Embase, Web of Science	1. Four RCTs and two quasi-experimental studies met inclusion criteria. All six studies administered lidocaine. Lidocaine was found to have a beneficial effect on AD in three studies, no effect in two studies and a detrimental effect in one study. 2. Three studies reported lower SBP values or AD incidence with use of lidocaine compared to control/placebo and two studies reported no difference in SBP values or AD incidence. 3. One study reported that the use of lidocaine may worsen AD because the absolute maximum SBP was higher in the lidocaine condition compared to the placebo condition.
Liu et al. 2015 Canada Reviewed published articles from 1956 to 2014 N=40 **Level of Evidence:** Methodological quality not assessed	**Methods:** Literature search for English articles, including original articles, practice guidelines, case reports, and literature reviews pertaining to iatrogenic urological triggers of AD following SCI. Studies with no data on AD or changes in blood pressure during urological assessments were excluded. The keywords used during the search were population	1. The included articles were divided into four groups according to the urological procedure: 1) urodynamics and cystometry (n = 21); 2) cystoscopy and transurethral litholapaxy (n = 12); 3) extracorporeal shock-wave lithotripsy (ESWL) (n = 6); and 4) other procedures (n = 2). 2. Incidence of AD ranged from 36.7%-77.8% in urodynamics. AD symptomatic rate ranged from 50%-65%.

Author Country Date included in the review Total Sample Size Level of Evidence Type of Study Score	**Methods Databases**	**Conclusions**
Types of study: Information not provided AMSTAR: 5	search terms that included 'paraplegia', 'tetraplegia', 'quadriplegia', 'spinal cord inj*', 'spinal cord dys*(function)', 'spinal cord dis*' and 'spinal cord lesion', as well as 'autonomic dysreflexia' or 'autonomic hyperreflexia'. Databases**:** PubMed	3. No relationship was found between AD and neurogenic detrusor overactivity or detrusor sphincter dyssynergia. 4. The majority of patients without anesthesia developed AD during cystoscopy, transurethral litholapaxy, and EWSL. 5. Nifedipine was shown to be most effective medication during urodynamics, cystoscopy and ESWL for relief of acute AD and for prevention of AD. 6. Flexible cystoscopy is accepted as an effective alternative to rigid endoscopy in minimizing occurrence of AD 7. Common types of anesthesia used for individuals with SCI include local, subarachnoid, epidural, and general anesthesia. 8. The effectiveness of different anesthesia methods is dependent on blocking nociceptive signals from the lower urinary tract (LUT) below the level of injury.
Krassioukov et al. 2009 Canada Reviewed published articles from 1950 to 2007 N=31 **Level of Evidence:** PEDro scale – RCTs, Modified Downs and Black – non-RCTs	**Methods:** Literature search for English articles, practice guidelines, and review articles evaluating the efficacy of interventions related to autonomic dysreflexia (AD) in the spinal cord injury population. Interventions included non-pharmacologic and pharmacologic (nifedipine, captopril, terazosin, prazosin, phenoxybenzamine, prostaglandin E2, sildenafil, and nitrates) management of AD, as well as preventative strategies to reduce episodes	1. There is strong evidence (level 1 and 2) supporting the use of intravesical resiniferatoxin as well as intersphincteric anal block with lidocaine for the management of AD in SCI patients. 2. There is also evidence that topical lidocaine does not limit or prevent AD in susceptible patients during anorectal procedures and that there is no beneficial effect of topical anesthetic in the prevention of AD during FES. 3. Nifedipine is the only pharmacological agent supported by controlled trials (Level 2) in the prevention of dangerous blood pressure reactions.

Author Country Date included in the review Total Sample Size Level of Evidence Type of Study Score	**Methods Databases**	**Conclusions**
Types of study: 6 RCTs 11 pre-post 5 observational 5 case series 3 prospective controlled 1 case report AMSTAR: 5	and symptoms of AD from common triggers. **Databases:** PubMed/MEDLINE, CINAHL, EMBASE, PsycINFO	4. There is low-level evidence (level 4 and 5) for the effectiveness of botulinum toxin injections into the detrusor muscle and use of intravesical capsaicin and anticholinergics in limiting AD. 5. There is conflicting level 4 evidence regarding the effectiveness of sacral deafferentation in the prevention of AD 6. There is level 5 evidence (clinical consensus) but there are no clinical studies that support the use of nitrates in the acute management of AD. 7. There is conflicting evidence with the use of phenoxybenzamine for AD management. 8. There is level 2 evidence that sildenafil citrate has no effect on blood pressure changes during AD episodes induced by vibrostimulation in men with SCI.
Courtois et al. 2012 Canada Reviewed published articles from 1948 to 2011 N=37 **Level of Evidence:** Methodological quality not assessed **Types of studies:** Information not provided AMSTAR: 2	**Methods:** Literature search for English or French language articles of all levels of evidence that provided scientific evidence on the specific treatment of AD following SCI in human males. The review focused on treatments that could be implemented at home during sexual activities therefore studies on intravenous treatment were generally rejected (with the exception of one). Also excluded were studies that only mentioned a procedural management of AD in their methods without giving specific results. Interventions included non-pharmacologic and	1. 37 papers on the specific treatment of AD showed that nifedipine, prazosin, captopril and clonidine are candidates in the context of sexual activities. 2. Prazosin, has an initial hypotensive effect requiring to begin treatment 12h before intercourse, which makes it less ideal for spontaneous sexual activities. 3. Captopril has an initial hypotensive effect and was only studied in acute AD. Its usefulness in prophylaxis remains to be demonstrated. 4. Clonidine has successfully been used clinically for decades, but never studied in randomized control trials. 5. Nifedipine remains the most widely studied and significant treatment of AD whether in acute or prophylactic conditions. Recent concerns suggest increased cardiovascular risks with sublingual nifedipine in non-SCI populations, but negative long-term

Author Country Date included in the review Total Sample Size Level of Evidence Type of Study Score	Methods Databases	Conclusions
	pharmacologic (nifedipine, prazosin, prostaglandin E_2, sildenafil, captopril, terazosin, doxazosin, phenoxybenzamine) management of AD, as well as preventative strategies to reduce episodes and symptoms of AD from common triggers Outcome measure: seated blood pressure (SBP), incidence of AD. **Databases:** PubMed/MEDLINE	effects have not been reported in the SCI population.

Discussion

We found four systematic reviews examining the effectiveness of AD management interventions.

The systematic review by Liu et al. (2015) explored the incidence of AD during diagnostic procedures of the bladder in people with SCI and found a high incidence rate in urodynamics and that the majority of patients without anesthesia developed AD during cystoscopy, transurethral litholapaxy, and extracorporeal shock wave lithotripsy (EWSL). Nifedipine was shown to be the most effective medication during urodynamics, cystoscopy, and ESWL for relief of acute episodes and prevention of AD.

Nifedipine was the most widely studied and significant treatment of AD whether in acute or prophylactic conditions. Courtois et al. (2012) reviewed the literature on the acute or prophylactic treatment of AD in the context of sexual activities; they found multiple studies with strong evidence that nifedipine was effective for preventing AD during electroejaculation and vibrostimulation.

Gray et al. (2022) found six studies examining the effectiveness of lidocaine on AD, with the majority supporting its use with a beneficial effect on AD during bowel procedures, urological care, or functional electrical stimulation. Similarly, Krassioukov et al. (2009) found strong evidence that intravesical resiniferatoxin and intersphincteric anal block with lidocaine were effective in the prevention of AD episodes. The same authors also found evidence that

nifedipine is useful in the prevention of dangerous blood pressure elevation during diagnostic or therapeutic procedures. However, Krassioukov et al. (2009) concluded that topical lidocaine is not beneficial for the management of AD in the SCI population. Finally, these authors found limited evidence supporting the use of botulinum toxin injections into the detrusor muscle and no support for the use of anticholinergics for AD management.

Although higher quality research assessing the management of AD in the SCI population is needed, Liu et al. (2015) concluded that careful evaluation, increased awareness, and early recognition of possible triggers remains the most effective approach in AD prevention and management for individuals with SCI.

5 Prevention Strategies

The most effective approach to AD is the prevention of occurrence (Braddom & Rocco 1991). This includes careful evaluation of the individual and early recognition of possible triggers that could result in AD. Improved clinician awareness and greater attention to the need to eliminate noxious stimuli in individuals with SCI is a priority. Further, clinicians, family members, and caregivers should be aware that increased afferent stimulation (e.g., via surgery, invasive investigational procedures, labour, and birth) in persons with SCI will increase the risk of developing AD. Fortunately, a variety of procedures and medications can be used to prevent episodes of AD.

As prevention is more effective than treatment, avoiding known triggers of AD episodes with appropriate bladder and bowel routines or pressure sore prevention are the most effective measures for preventing AD. Specific triggers for AD should be identified and eliminated for each individual as much as possible to manage and prevent hypertensive episodes (Krassioukov et al. 2020; Blackmer, 2003; Mathias & Frankel 2002; Teasell et al. 2000). Furthermore, establishing routine blood pressure monitoring and using interventions to prevent UTIs and constipation are crucial steps in averting episodes of life-threatening AD (Krassioukov et al. 2020).

Key Points

The identification of the possible trigger (often bowel, bladder, or skin issues) and a decrease of afferent stimulation to the spinal cord is the most effective prevention strategy in clinical practice.

5.1 Prevention of AD during Bladder Procedures

Urinary bladder irritation or stimulation is a major trigger of AD following SCI (McGuire & Kumar, 1986; Linsenmeyer et al. 1996; Giannantoni et al. 1998; Teasell et al. 2000; Mathias & Frankel 2002). Thus, a bladder management program and continuous urological follow-up are important elements in the medical care of people with SCI (Waites et al. 1993a; Vaidyanathan et al. 1994; Vaidyanathan et al. 2004). An established bladder management program with intermittent catheterization or an indwelling Foley catheter allows people with SCI to plan for bladder emptying when convenient or necessary (Consortium for Spinal Cord Medicine, 2006). A study by Furusawa et al. (2011) found that the highest incidence of symptomatic AD was diagnosed in participants using reflex voiding as a bladder management method, while the lowest incidence of symptomatic AD was seen in participants using continent spontaneous voiding followed by intermittent catheterization.

In the past years, urological follow-up including annual urodynamic evaluations and cystoscopy (depending on the bladder management program) have decreased the frequency of urinary tract infections and the development of renal failure in people with SCI (Waites et al. 1993a; Waites et al. 1993b; DeVivo et al. 1999). However, conservative management is not always successful and alternative strategies (e.g., application of Botulinum toxin, capsaicin, anticholinergics, sacral denervation, and bladder or urethral sphincter surgery) may be needed to decrease afferent stimulation from the bladder to prevent development of AD. In addition, urodynamic procedures and cystoscopy are associated with significant activation of urinary bladder afferents and have the potential to trigger AD (Linsenmeyer et al. 1996; Dykstra et al. 1987; Snow et al. 1978; Chancellor et al. 1993). Therefore, strategies are also required during these procedures to reduce afferent stimulation.

Table 3. Prevention of AD during Bladder Procedures

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Furusawa et al. 2011 Japan Case control Level 3 Level N=571	**Population:** N=571, 466M, 105F, mean age at discharge: 52.3 years AIS A: 168 AIS B: 35 AIS C: 127 AIS D: 241 **Treatment:** Bladder management methods were divided into six categories (continent spontaneous voiding,	1. Of the 196 patients who used continent spontaneous voiding as a bladder management method, 14 experienced AD. 2. 122 patients used intermittent catheterization (IC) and 32 experienced AD. 3. 110 patients used indwelling supra-pubic catheterization and 44 experienced AD.

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	IC, indwelling supra-pubic catheterization, indwelling urethral catheterization, reflex voiding and others), and the incidence of AD while using each one was investigated. **Outcome measures:** Incidence of AD	4. 79 used indwelling urethral catheterisation and 28 experienced AD. 5. 30 used reflex voiding and 13 experienced AD. 6. 34 used another method of bladder management and 10 experienced AD. 7. The highest frequency of symptomatic AD was in reflex voiding. 8. The lowest incidence of symptomatic AD was in patients who used continent spontaneous voiding followed by IC.
Xiong et al. 2015 China Case Series Level 4 N=89	**Population:** 89 SCI cases with bladder stones undergoing cystolitholapaxy 64 males, 25 females Mean (SD) age in years = 35.98 (8.17) Injury level: 57 participants above T6 **Treatment:** 48 with with spinal anesthesia, 26 with general anesthesia, 15 with local anesthesia **Outcome measures:** Presence of AD, stone size and number, length of surgery	1. Of 89 patients, 31 (34.83%) developed AD during the operation. 2. Patients with AD had larger (4.58+/-1.26 cm vs. 3.75+/-1.15cm) and more stones (2.29+/-0.86 vs. 1.74+/-0.81). 3. 83.87% of patients with AD had lesion level at or above T6 vs. 41.38% in non-AD group. 4. Operation time was longer in AD group vs. non-AD group (60.65+/-17.78 min vs. 49.31+/-14.31 min). 5. Incidence rate of AD was highest in patients with local anesthesia (18/20, 90%), followed by general anesthesia (12/27, 44.44%) and spinal anesthesia (1/40, 2.5%).

Discussion

One case series (Xiong et al. 2015) revealed that individuals experiencing AD during cystolitholapaxy had larger bladder stones, a higher number of bladder stones, and longer operation times. Spinal anesthesia may be the most effective way to prevent incidences of AD in cystolitholapaxy procedures as only 2.5% of participants with spinal anesthesia experienced AD. Furthermore, the bladder management method that an individual uses may contribute to the prevalence of AD episodes. A study by Furusawa et al. (2011) found that participants who used reflex voiding experienced the highest incidence of symptomatic AD, while participants who used continent spontaneous voiding followed by intermittent catheterization experienced the least.

Conclusion

There is level 3 evidence (from one case control) (Furusawa et al. 2011) that reflex voiding as a bladder management method resulted in the highest incidence of symptomatic AD while continent spontaneous voiding followed by intermittent catheterization resulted in the lowest.

There is level 4 evidence (from one case series) (Xiong et al. 2015) that spinal anaesthesia may be more effective at preventing incidence of AD during cystolitholapaxy compared to local or general anesthesia.

5.1.1 Botulinum Toxin

Injection of botulinum toxin into the detrusor muscle is a treatment for urinary incontinence secondary to neurogenic detrusor overactivity while injection into the external urethral sphincter is a treatment for detrusor-sphincter dyssynergia and high post void residual urines.

Table 4. Botulinum Toxin and AD

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Huang et al. 2024 China Pre-post Level 4 N=25	**Population:** N=25 people with SCI at or above T6 **Treatment:** SBP, scores of the Incontinence Specific Quality of Life Instrument, maximum detrusor pressure at first detrusor overactivity, and volume at first detrusor overactivity were measured at baseline and 3 months after the treatment.	1. BTX-A injection decreased maximum sBP and change in sBP during urodynamic studies (151.44 ± 13.92 vs 133.32 ± 9.20 mmHg and 49.44 ± 12.81 vs 33.08 ± 9.11 mmHg respectively, P < 0.05.) 2. The frequency of bladder-related ADs significantly decreased from 11.04 ± 1.81–

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	Participants were injected with 200 U BTX-A. **Outcome measures:** Overall maximum sBP, frequency of AD, scores of Incontinence Specific Quality of Life Instrument, maximum detrusor pressure, and volume at first detrusor overactivity.	7.88 ± 2.15 (P < 0.001) after BTX-A injection.
Fougere et al. 2016 Canada Pre-post Level 4 N=17	**Population:** N=17, 12 males, 5 females with chronic traumatic SCI at or above T6 and concomitant autonomic dysreflexia and neurogenic detrusor overactivity Mean (SD) age: 44 (10) Mean (SD) years post injury: 21 (11) AIS-A/B/C = 9/5/3 11 cervical, 6 thoracic **Treatment:** One cycle of Botox injection (200U in 20mL 0.9% saline, injected into 20 sites of detrusor muscle), 2 weeks after baseline measurements & 1 month before post-treatment measurements CIC = clean intermittent catheterization **Outcome Measures:** Urodynamic studies (UDS), 24h ambulatory BP monitoring (ABPM), AD Health-related QoL questionnaire, I-QOL questionnaire	1. Pre vs. post-botox during UDS (mean±SD): 2. Significantly lower SBP (mmHg) at: a. First urge to preform CIC (112±17 vs. 114±14), at max volume infused (151±25 vs. 133±17), and at max SBP (153±25 vs. 134±16). 3. Significantly lower ΔSBP (mmHg) from supine baseline at: a. First urge to preform CIC (34±20 vs. 15±11), at max volume infused (40±24 vs. 18±12), and at max SBP (42±23 vs. 20±10). 4. Significantly lower ΔHR (bpm) at: a. First urge to preform CIC (-8±11 vs. -6±10), at max volume infused (-17±12 vs. -9±14), and at max SBP (-16±13 vs. -8±14). 5. Pre vs. post-botox during bladder events (mean±SD, from 24h ABPM): 6. Significantly reduced max SBP (157±21 vs. 139±21) &

Author Year; Country Score Research Design Sample Size	Methods	Outcome
		ΔSBP from seated baseline during CIC. 7. AD eliminated in 10 participants (ΔSBP <20mmHg), attenuated in 7. 8. Significantly fewer participants reporting AD symptoms post-botox (15 to 9) (p=0.034). 9. Significantly reduced frequency of AD during CIC post-treatment (67% to 25%) (p<0.001). 10. Significant improvement in all subsections and in total scores of QoL measures.
Chen & Kuo 2012 Taiwan Pre-post Level 4 N=49 (with AD=34)	**Population:** 49 patients (31 males, 18 females) with SCI and detrusor sphincter dyssynergia; Level of SCI: 27 cervical, 22 thoracic; mean age in years: 41.6, range 22-74; mean DOI in years: 8, range 1-35. **Treatment:** Patients received two sets of 200 U BoNT-A injections into the detrusor at baseline and 6 months later. **Outcome Measures:** Improvement in the severity of AD; net change in the grade of incontinence; net changes in the scores of the Urogenital Distress Inventory (UDI-6); Incontinence Impact Questionnaire; quality of life index; urodynamic parameters.	1. 15 patients did not have AD at baseline or after treatment. 2. AD was completely resolved in 3 patients, and improved in 18; treatment made no difference in 3 patients and AD was exacerbated in 10. 3. No significant differences in any urodynamic variables between patients with and without AD. 4. A significantly greater improvement in the UDI-6 was noted in patients without AD and those in whom AD improved than in those with AD (p=0.035). 5. Occurrence of AD was not significantly associated with persistent urinary

Author Year; Country Score Research Design Sample Size	Methods	Outcome
		incontinence after the BoNT-A injections. 6. No significant difference in the quality of life index between patients with and without AD at the end point.
Chen et al. 2008 Taiwan Pre-post Level 4 N=20 (with AD=4)	**Population:** 20 suprasacral SCI participants with detrusor external sphincter dyssynergia (DESD); Mean age 37.9 (15.7); 17 male; 12 cervical, 3 thoracic, 5 lumbar; AIS diagnosis: 11 AIS-A, 2 AIS-B, 4 AIS-C, 3 AIS-D. **Treatment:** A single dose of 100 IU botulinum toxin A was applied into the external urethral sphincter via cystoscopy. **Outcome Measures:** maximal detrusor pressure, maximal urethral pressure, maximal detrusor leak point pressure, integrated electromyography (IEMG) of the external urethral sphincter and, maximal pressure on static urethral pressure profilometry, recorded before and 4 weeks after the injection; post-voiding residues, measured 1, 2, 3, and 6 months post-injection.	1. 4 individuals who had AD symptoms before treatment reported decreased frequency and intensity of AD. 2. There was significant reduction in the IEMG (from 16.7(13.6) to 12.5(12.9) uV (p=0.023)), as well as static urethral pressure (from 139.4(40.5) to 104.8(30.5) cmH_2O (p=0.004)) and maximal urethral pressure (from 107.5(69.1) to 80.2(35.7) cmH_2O (p=0.049)). 3. There was no significant difference in the maximal detrusor pressure or detrusor leak point pressure. 4. Post-voiding residues were significantly reduced at 1st, 2nd, 3rd, and 6th months post-injection.
Kuo, 2008 Taiwan Pre-post Level 4 N=33 (with AD=6)	**Population:** 33 participants with detrusor sphincter dyssynergia and urinary incontinence (including 9 individuals with cervical SCI, 12 with thoracic SCI, 5 with lumbar SCI, 5 multiple sclerosis and 2 transverse	1. 3/6 patients experienced decreased symptoms of AD post-treatment. 2. Urodynamic parameters showed significant improvement in voiding detrusor pressure (45.7(22.7) vs. 30.7(15.5) cmH_2O),

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	myelitis patients); age range 23-71. **Treatment:** transurethral sphincter botox injections, injecting 100 units of botox in 4 ml normal saline into eight sites of the urethral sphincter. **Outcome Measures:** video-urodynamic studies; Urogenital Distress Inventory short form (UDI-6); Incontinence Impact Questionnaire (IIQ-7) short form.	maximum flow rate (6.8[5.7) vs. 9.2[7.7) ml/sec) and post-void residual volume (160[124) vs. 75[105) ml). 3. IIQ-7 scores were significantly improved, but not the UDI-6 scores.
Schurch et al. 2000 Switzerland Pre-post Level 4 N initial=31 N final=19	**Population:** Mean age: 36.7 yrs, mean DOI=60.2 months; 18 participants with paraplegia, 3 with tetraplegia, 17 participants with complete injuries, 4 with incomplete injuries, incontinence resistant to anticholinergic medication. **Treatment:** Botulinum-A toxin was injected (200-300 units) into the detrusor muscle. **Outcome Measures:** voiding and detrusor pressure, diary of incontinence, AD symptoms at 6, 16, and 36-wks.	1. At 6-week follow-up, 17/19 patients were completely continent. 2. 3 patients with tetraplegia with severe AD with bladder emptying found this disappeared after treatment.
Dykstra et al. 1988 USA Pre-post Level 4 N=11 (with AD=7)	**Population:** Detrusor-sphincter dyssynergia **Treatment:** low dose botulinum A toxin at the neuromuscular junction. **Outcome Measures:** urethral pressure, symptoms of AD.	1. Urethral pressure profile decreased 27 cm H_20 (n=7). 2. Self-assessed improvement of AD symptoms in 5 of 7 AD patients. 3. Toxin effects lasted an average of 50 days.

Discussion

Five pre-post studies (Dykstra et al. 1988; Schurch et al. 2000; Chen et al. 2008; Kuo 2008; Chen & Kuo 2012) found injection of Botulinum toxin into the detrusor muscle or bladder sphincter to be an effective method for treating urinary incontinence or retention secondary to neurogenic detrusor overactivity and bladder sphincter dyssynergia. In these conditions, Botulinum toxin injections either allowed increased urinary bladder capacity (i.e., reduced overactivity of the bladder) or facilitated improved evacuation of urine (reduced bladder sphincter dyssynergia). The duration of effect was reported to last up to 9 months (Schurch et al. 2000). All studies were level 4 and showed positive effects. In fact, following treatment with Botulinum toxin, 3 individuals reported fewer episodes of AD (Kuo, 2008), 4 individuals reported decreased frequency and intensity of AD (Chen et al. 2008), 3 individuals reported AD was completely resolved (Chen & Kuo 2012), 18 individuals experienced improvement in AD symptoms (Chen & Kuo 2012), and 3 individuals who experienced severe AD during bladder emptying reported disappearance of these symptoms altogether (Schurch et al. 2000). Similarly, Huang et al (2024) found Botulinum toxin injections to decrease the frequency of bladder-related ADs as well as decreased maximum sBP and reduced the change in sBP. While the evidence suggests that Botulinum toxin may be a viable treatment for neurogenic detrusor overactivity, the evidence supporting the application of Botulinum toxin specifically for the prevention of AD is inconclusive.

Conclusion

There is level 4 evidence (from 1 pre-post study) (Huang et al. 2024) that Botulinum toxin injections decreased the frequency of bladder-related ADs during urodynamic studies.

There is level 4 evidence (from 5 pre-post studies) (Dykstra et al. 1988; Schurch et al. 2000; Chen et al. 2008; Kuo, 2008; Chen & Kuo 2012) that Botulinum toxin injections into the detrusor muscle or external urethral sphincter seem to be a safe and valuable therapeutic option in SCI patients who perform clean intermittent self-catheterization and have incontinence resistant to anticholinergic medications.

Key Points

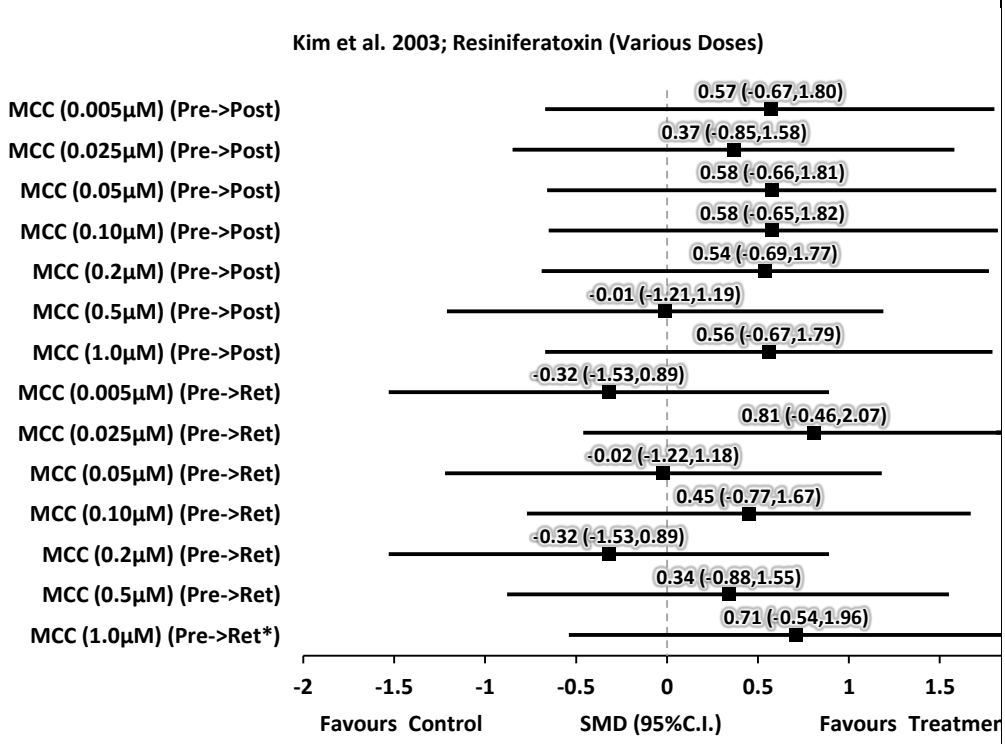
Botulinum toxin injections into the detrusor muscle or external urethral sphincter seem to be a safe and valuable therapeutic option for people with SCI who perform clean intermittent self-catheterization and have incontinence resistant to anticholinergic medications. Its use in the prevention of AD is less well-defined.

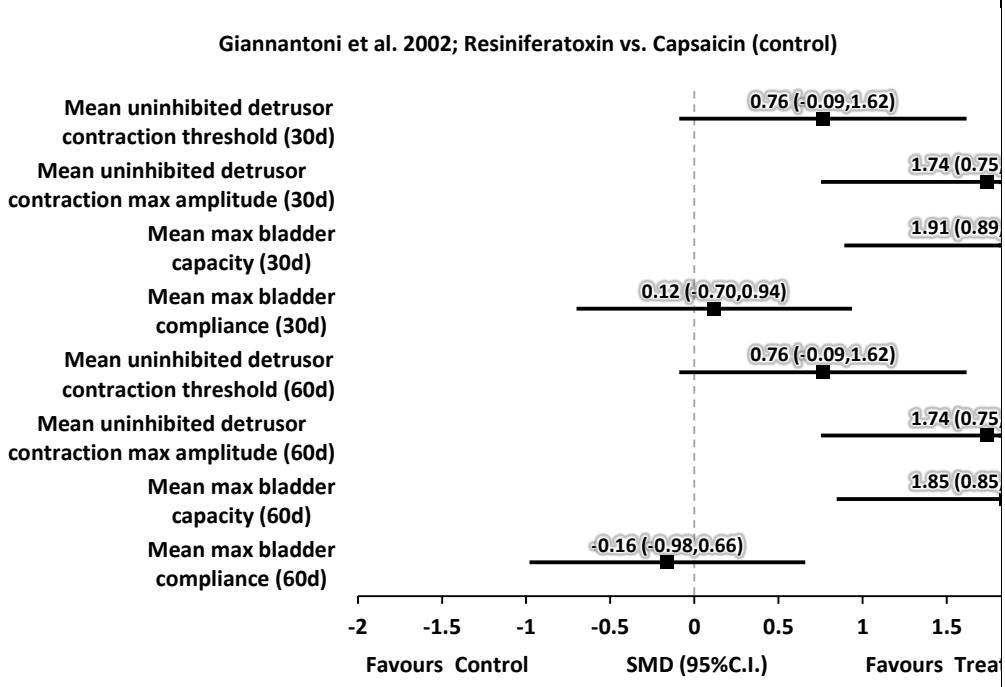
5.1.2 Intravesical Capsaicin

Capsaicin is an extract from red pepper and exerts a selective action on certain sensory nerves, most notably those involved in reflex contractions of the bladder after spinal cord injury.

Table 5. Capsaicin

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Kim et al. 2003 USA PEDro=9 RCT Level 1 N=36	**Population:** 22 males, 14 females, neurologically impaired patients (20 SCI, 7 Multiple Sclerosis, and 9 others) with urodynamically verified detrusor hyperreflexia. **Treatment:** Randomized double blind, placebo-controlled trial. Intravesical instillation of Resiniferatoxin (RTX) 0.005, 0.025, 0.05, 0.10, 0.2, 0.5, or 1.0 microM of RTX (n=4 each group) or placebo (n=8). **Outcome Measures:** incontinence episodes, bladder capacity.	1. No statistical significance due to small sample sizes. 2. Intravesical RTX administration was well tolerated. This patient group was refractory to all previous oral pharmacologic therapy, yet some patients responded with improvement in bladder capacity and continence function shortly after RTX administration. 3. In some cases, mean cystometric capacity increased up to 500% over baseline. 4. Incontinence episodes decreased by over 50% for the 2 highest doses. 5. No data available on long term effect of RXT on AD.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- to post-intervention data and pre-intervention to retention/follow-up data	

Author Year; Country Score Research Design Sample Size	Methods	Outcome
		
[Giannantoni et al. 2002](#) Italy PEDro=6 RCT Level 1 N=23	**Population:** Refractory detrusor hyperreflexia. **Treatment:** Randomized two treatments a) single dose of 2 mM. capsaicin in 30 ml ethanol plus 70 ml 0.9% sodium chloride OR b) 100 mM. resiniferatoxin in 100 ml 0.9% sodium chloride. **Outcome Measures:** Urodynamics, frequency of daily catheterizations, incontinence episodes and side effects.	1. Capsaicin group showed no significant urodynamic or clinical improvements at 30 and 60 days. 2. Resiniferatoxin group demonstrated significant urodynamic improvement at 30 and 60 days. 3. Most patients receiving capsaicin, but none receiving resiniferatoxin developed AD, limb spasms, suprapubic discomfort and hematuria.

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- to post-intervention data  **Effet size calculated for 1) pre-intervention to 30 days (30d) post-intervention and 2) pre-interventio to 60 days (60d) post-intervention**	
Igawa et al. 2003 Japan Pre-post Level 4 N=7	**Population:** 5 participants with cervical injuries and 2 participants with thoracic injuries. **Treatment:** bladder instillation with capsaicin solution under general anesthesia. **Outcome Measures:** blood pressure, heart rate, serum catecholamines, blood ethanol concentration.	1. Capsaicin attenuated elevated BP secondary to bladder distention (empty or full) post-treatment. 2. In all individuals, episodes of AD become negligible and well tolerated > 3 months.

Discussion

One RCT (Giannantoni et al. 2002) and one pre-post study (Igawa et al. 2003) evaluated the effect of capsaicin. Capsaicin exerts a selective action on sensory nerves involved in reflex contractions of the bladder after SCI. Igawa et al. (2003) demonstrated that intravesical capsaicin decreased episodes of AD in people with SCI during catheterization, thereby suggesting its therapeutic potential for both AD and detrusor hyperreflexia in individuals with SCI. Moreover, Giannantoni et al. (2002) used an analogue of capsaicin (resiniferatoxin RXT) that is more than 1,000 times more potent in desensitizing C-fiber bladder afferents, and found reduced episodes of AD. Additionally, Giannantoni et al. (2002) found that intravesical administration of resiniferatoxin within 60 days of treatment did not cause the inflammatory side effects often seen with capsaicin, suggesting superior urodynamic results and clinical benefits. However, long-term effects of capsaicin or resiniferatoxin on AD have not been evaluated.

Conclusion

There is level 1 evidence (from 2 RCTs) (Kim et al. 2003; Giannantoni et al. 2002) that intravesical resiniferatoxin is effective for reducing episodes of AD in patients with SCI.

There is level 1 evidence (from 1 RCT) (Giannantoni et al. 2002) that intravesical resiniferatoxin is more effective than intravesical capsaicin.

There is level 4 evidence (from 1 pre-post study) (Igawa et el. 2003) that intravesical capsaicin is effective for reducing episodes of AD in SCI.

Key Points

Capsaicin and its analogue, resiniferatoxin, are effective in reducing the episodes of AD in people with SCI.

5.1.3 Anticholinergics and Antimuscarinics

Anticholinergics are a class of medications that inhibit the binding of the neurotransmitter, acetylcholine, to its receptors. Acetylcholine is released by the parasympathetic nerve fibers innervating the urinary bladder and contributes to detrusor contraction and activation of the bladder afferents. These afferent stimuli activate spinal sympathetic circuits that trigger AD. In theory, anticholinergic agents could therefore decrease afferent activation, and consequently AD.

Antimuscarinics are a group of anticholinergic agents that block muscarinic receptors from the action of acetylcholine. Muscarinic receptors play a role in parasympathetic functions including involuntary functions such as contracting smooth muscle, dilating blood vessels, and increasing heart rate. Thus, antimuscarinics work by inhibiting the functions of the parasympathetic nervous system, and subsequently decreasing AD.

Table 6. Anticholinergics and Antimuscarinics

Author Year; Country Score Research Design Sample Size	Methods	Outcome
Walter et al. 2023 Canada Pre-post Level 4 N=12	**Population:** N=12, 8M, 4F Median age: 42 years **Treatment:** AD was confirmed in all participants, and frequency and severity of AD in daily life was recorded using 24-hour BP monitoring. Participants completed questionnaires on urinary incontinence-related QoL, health-related QoL, bowel function, and cognitive function prior to the 12-week treatment of fesoterodine. Participants took 4mg of fesoterodine daily and had the option to increase their dose to 8mg. 10-12 weeks after the start of treatment, all measures were repeated. **Outcome measures:** BP, frequency and severity of AD, urinary incontinence-related QoL, bowel function, and cognitive function	1. Fesoterodine reduced the increase in sBP compared to baseline: 40 mmHg vs 27 mmHg (p=0.08). 2. The severity (59 mmHg vs 36 mmHg, p=0.05, r=-0.58), and frequency (14 vs 3, p=0.004) of AD during daily life were significantly reduced with fesoterodine.
Giannantoni et al. 1998 Italy Observational Level 5 N=48	**Population:** SCI patients. **Treatment:** Anticholinergic drugs. **Outcome Measures:** Neurological and urological examination and urodynamic evaluation with concurrent recording of blood pressure, heart rate, symptoms of AD.	1. Presence of detrusor uninhibited contractions and bladder distension both contribute to AD crisis. 2. Treatment with anticholinergic drugs is not sufficient to prevent AD starting from the bladder, unless it induces detrusor areflexia.

Discussion

Only one study has examined the use of anticholinergics (Giannantoni et al. 1998). These authors did not observe a correlation between anticholinergic drugs and reduced incidence of AD, unless treatment resulted in detrusor areflexia.

A study by Walter et al. (2023) examined the use of antimuscarinics, specifically fesoterodine, on the management of AD. They found fesoterodine to reduce the severity and frequency of AD, as well as reduce the increase in sBP compared to baseline. However, more research should be conducted to determine the effectiveness of fesoterodine.

Conclusion

There is level 4 evidence (from 1 pre-post study) (Walter et al. 2023) that fesoterodine reduces the severity and frequency of AD.

There is level 5 evidence (from 1 observational study) (Giannantoni et al. 1998) that anticholinergics are not associated with reduced incidence of AD episodes.

Key Points

Anticholinergics do not appear to be sufficient for the management of AD in SCI.

One small study showed that antimuscarinics (fesoterodine) reduced the severity and frequency of AD.

5.1.4 Sacral Denervation

When detrusor hyperreflexia post-SCI does not respond to conservative treatment and patients are not eligible for ventral sacral root stimulation for electrically induced micturition, sacral bladder denervation may be considered as a stand-alone procedure to treat urinary incontinence and AD.

Table 7. Sacral Denervation

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Kutzenberger, 2007 Germany	**Population:** 440 SCI patients (190 tetra, 274 para) ranging from 0.5 to 46 years since injury.	1. Autonomic dysreflexia disappeared in all cases with the exception of two. In these individuals, blood pressure was

Case series Level 4 Initial N=464 Final N=440	**Treatment:** Sacral deafferentation and implantation of a sacral anterior root stimulator. **Outcome Measures:** Presence of AD.	maintained at less dangerous levels.
Hohenfellner et al. 2001 Germany Pre-post Level 4 N=9 (with AD=5)	**Population:** detrusor hyperreflexia. **Treatment:** sacral bladder denervation. **Outcome Measures:** bladder capacity, blood pressure, symptomatic AD.	1. Episodes of detrusor hyperreflexia and AD were eliminated in all cases. 2. In the 5 patients with AD, both SBP and DBP were reduced 196(16.9) to 124(9.3) mmHg and 114(5.1) to 76(5.1) mmHg, respectively.
Schurch et al. 1998 Switzerland Case series Level 4 N=10	**Population:** 10 SCI patients with AD. **Treatment:** sacral deafferentation. **Outcome measures:** continuous non-invasive recordings of BP and HR during urodynamic recordings, pre- and post-operative data**.**	1. There was a marked elevation in systolic and diastolic BP with bradycardia during the urodynamic examination in all eight patients, despite complete intra-operative deafferentation of the bladder in five. 2. AD persisted in patients with SCI even post complete sacral deafferentation, consistently occurring during the stimulation-induced voiding phase.

Discussion

Three level 4 studies (Schurch et al. 1998; Hohenfellner et al. 2001; Kutzenberger, 2007) examining sacral denervation have reported conflicting results in response to sacral denervation. Hohenfellner et al. (2001) reported that sacral bladder denervation was a valuable treatment option for eliminating detrusor hyperreflexia and AD in all 9 of their participants. However, in Schurch et al.'s (1998) 10 participants, it was shown that complete bladder deafferentation does not abolish AD during urodynamic investigations. In Kutzenberger's (2007) review, sacral deafferentation eliminated AD in 438 of 440 participants.

Conclusion

There is level 4 evidence (from one pre-post study and one case series study) (Hohenfellner et al. 2001; Kutzenberger, 2007) that sacral deafferentation may be effective in preventing AD.

Key Points

Sacral deafferentation may reduce AD during urodynamic investigations.

5.1.5 Bladder and Urethral Sphincter Surgery

The association between episodes of AD and the presence of detrusor sphincter dyssynergia, high intravesical pressure, and urethral pressure has led to the development of surgical procedures to alleviate voiding dysfunctions and consequently AD in people with SCI.

Table 8. Bladder and Urethral Sphincter Surgery

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
van der Merwe et al. 2012 South Africa Case series Level 4 N=28	**Population:** 28 male patients with neuropathic bladder dysfunction after SCI who had dual flange Memokath stents inserted in the period March 2008 to October 2011; Age in yrs: mean 37.4, range 23-64; Level of injury: 23 cervical, 5 thoracic. **Treatment:** Stents were placed rather than performing an external sphincterotomy in selected patients. With the patient under deep general anesthesia, a thermosensitive expandable metallic stent was positioned over the internal and external urethral sphincters; patients were followed-up at 1 month and again between 3 and 6 months.	1. 33 stents were placed in 28 patients. 2. 6 patients reported severe autonomic dysreflexia related to poor bladder emptying as their reason for stent placement. 3. Severe AD decreased significantly from 17 cases before stent placement to 7 after stent placement. 4. New severe AD was a complication of stent placement in one case, after which the stent was removed.

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	Outcome Measures: stent failure rate, incidence of AD post-stent placement, complications.	
Ke & Kuo 2010 Taiwan Case series Level 4 N=22	**Population:** 19 males; 13 participants with cervical SCI, 9 with thoracic SCI. 17 individuals reported AD. Mean age at diagnosis of BND = 46.7 years. Lower urinary tract symptoms experienced for mean of 3.8 years. **Treatment:** transurethral incision of the bladder neck (TUI-BN) **Outcome Measures**: urodynamic parameters; satisfactory outcome (increase of AUA/IPSS quality-of-life index score by ≥2); autonomic dysreflexia occurrence; spontaneous voiding; detrusor pressure; post void residual; Qmax; bladder outlet resistance.	1. Spontaneous voiding resumed in 19 patients, persistent urinary retention in 3 patients. 2. Urodynamic parameters: For patients with a Pdet > 15cmH2O at baseline, after surgery: Pdet and PVR decreased, Qmax increased significantly from 3.7(5.7) to 8.3(5.4)mL/sec; 3. For patients with a Pdet ≤15cmH2O at baseline, after surgery: Pdet and Qmax increased, PVR decreased significantly from 369(160) to 117(136)mL. 4. Degree of AD during micturition was less severe or disappeared in 15 patients (88.2%) after surgery. 5. 18 (82%) patients reported satisfactory improvement in QoL index after TUI-BN, and voiding by volitional drills or lower abdominal tapping maneuvers became easier.
Perkash, 2007 USA Case series Level 4 N=46	**Population:** 46 males; 31 participants with tetraplegia and 15 with paraplegia; Type of injury: 43 AIS A and B, 3 AIS C. **Treatment:** Transurethral sphincterotomy (TURS). **Outcome Measures:** Autonomic dysreflexia during cystometrogram (measures the contractile	1. During cystometrogram, mean maximal systolic pressure was 160(23) pre and 108(17) mmHg post. Mean diastolic pressure was 88(15) pre and 62(11) mmHg post. 2. Mean decrease in systolic BP and diastolic BP after TURS was 55(26) and 30(17) mmHG, respectively. 3. Amelioration in symptoms of AD. 4. Mean post-void residual urine

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	force of the bladder when voiding), blood pressure.	decreased significantly from 233(152) to 137(0.35) mL after TURS. 5. 4 patients still exhibited AD within 1 year of laser TURS.
Seoane-Rodriguez et al. 2007 Spain Case series Level 4 N=47	**Population:** 47 males; 32 participants with cervical, 11 with thoracic, and 4 with lumbar injuries; mean post-injury time to stenting was 103.8 months. Mean follow-up time from implantation 67 months. Type of injury: 36 AIS A; 4 AIS B and 7 AIS C. **Treatment:** intraurethral stent. **Outcome Measures:** Urodynamic parameters; presence or absence of symptomatic UTI; autonomic dysreflexia; appearance of complications of the upper urinary tract (UUT); bladder management before and after surgery; prosthesis complications.	1. Decrease in symptomatic UTI by 25%. 2. Decrease in post void residual urine volume by an average of 224.3 cm^3. 3. Episodes of dysreflexia decreased from 35.1% to 16.2%. 4. Complications in the UUT decreased from 46.8 to 23.4%. 5. Urodynamic study showed an average reduction of 44.4 cm^3 H2O in the maximum detrusor pressure. 6. Most frequent stent complication was displacement, followed by stenosis, lithiasis (pathological formation of mineral concentrations in the body), and intraprosthetic calcification. 8.5% required stent removal.
Sidi et al. 1990 USA Pre-post Level 4 N=12	**Population:** 9 participants with complete SCI, 3 with incomplete injuries; Level of Injury: C5-T11; 2-27 years post-injury. **Treatment:** augmentation enterocystoplasty. **Outcome Measures:** functional bladder capacity, levels of blood urea	1. By 4 months post-op, 11/12 patients were totally continent on clean intermittent self-catheterization every 4-6 hours. 2. Of the 3 patients who had an artificial urinary sphincter, 2 became continent after sphincter activation and 1 had achieved continence without sphincter activation. No patients experienced symptoms of AD

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	nitrogen, creatinine, electrolytes.	during intermittent catheterization post-operatively.
Barton et al. 1986 USA Case series Level 4 N=16	**Population:** 5 participants with thoracic, and 8 with cervical injuries, 47-285 months post-injury. **Treatment:** modified transurethral external sphincterotomy with follow-up to 26 weeks. **Outcome Measures:** bladder and urethral pressures and volumes, blood pressures.	1. Intravesical and urethral pressures decreased compared to before sphincterotomy. 2. Blood pressure responses decreased during urodynamic stimulation. 3. Other cardiovascular responses related to AD during bladder filling markedly attenuated.

Discussion

Four surgical studies (Barton et al. 1986; Sidi et al. 1990; Perkash, 2007; Ke & Kuo 2010) included indicators of AD (e.g., blood pressure changes). An older study by Barton et al. (1986) demonstrated reduced AD with an external sphincterotomy. Additionally, a long-term follow-up of patients treated with transurethral sphincterotomies showed the procedure provided subjective relief of AD and was correlated with a significant decrease in blood pressure (Perkash, 2007). Further, post-void residual urine decreased significantly after surgery (Perkash, 2007). Similar results were found by Ke and Kuo in 2010. Patients reported decreased severity in the degree of AD during micturition, as well as a significant decrease in post-void residual urine and improvement in quality of life (QoL) index after bladder surgical augmentations.

Sphincterotomies are now rarely performed due to their association with significant risks, including hemorrhage, erectile dysfunction and the need for repeat procedures (Ahmed et al. 2006). Alternatives including intraurethral stents and Botulinum toxin injections have been investigated and shown some success (Ahmed et al. 2006; Seoane-Rodriguez et al. 2007; Pannek et al. 2011; van der Merwe et al. 2012). Additionally, augmentation enterocystoplasty has demonstrated long-term success based on urodynamic evaluation and has been found to reduce symptoms of AD (Sidi et al. 1990). Furthermore, enterocystoplasty with a Mitrofanoff procedure has become a more frequent choice of bladder augmentation in individuals with SCI due to more favorable long-term outcomes. Moreover, Memokath stent placement in the external sphincter region has demonstrated a significant reduction in post-void residual urine as well as in UTI symptoms (Pannek et al. 2011; van der Merwe et al. 2012). Dual flange Memokath stent placement over the internal and external urethral sphincters in 28 patients with neuropathic

bladder dysfunction was shown by van der Merwe et al. (2012) to reduce severe AD from 17 cases to 7 cases.

Conclusion

There is level 4 evidence (from four pre-post/case series studies) (Barton et al. 1986; Sidi et al. 1990; Perkash, 2007; Ke & Kuo 2010) that urinary bladder surgical augmentations may result in a decrease of intravesical and urethral pressure and therefore diminish or resolve episodes of AD.

There is level 4 evidence (from 2 case series) (van der Merwe et al. 2012; Seoane-Rodriguez et al. 2007) that an intraurethral stent decreases incidence of AD and may be an effective means for the long-term management of detrusor-sphincter dysynergia for individuals with SCI, including those who have previously undergone sphincterotomy.

Key Points

Urinary bladder surgical augmentations may diminish or resolve episodes of AD.

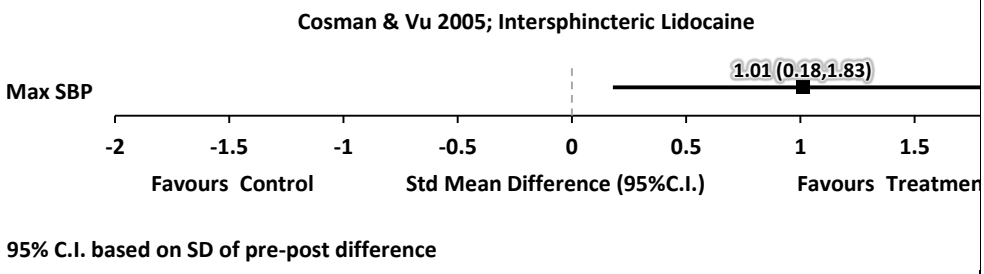
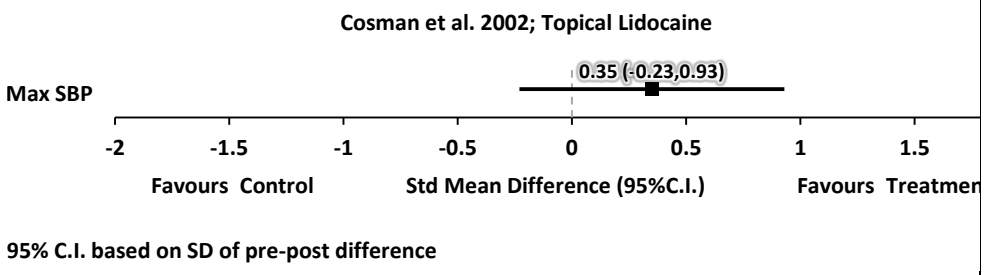
5.2 Prevention of AD during Anorectal Procedures

The second most common cause of AD is pain or irritation within the colorectal area. Constipation, hemorrhoids, and anal fissures are all frequently observed in people with SCI and contribute to episodes of AD (Teasell et al. 2000; McGuire & Kumar 1986; Hawkins et al. 1994; Teichman et al. 1998). Digital stimulation, a common component of bowel routines in individuals with SCI, can also trigger AD (Furusawa et al. 2007), especially in the presence of hemorrhoids and/or anal fissures. Additionally, rectosigmoid distension and anal manipulation are common iatrogenic triggers of AD (Cosman & Vu 2005).

Table 9. Prevention of AD during Anorectal Procedures

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Solinsky & Linsenmeyer 2018 USA Prospective controlled trial Level 2 N=50	**Population:** N=50, treatment group N=27, control group N=23 SCI at or above T6 **Treatment:** Treatment group had 10ml of 2% lidocaine hydrochloride gel instilled through a	1. Treatment group: four individuals out of 27 (14.8%) experienced AD with the catheter change. 2. Control group: the rate of AD was 47.8%. 3. There is a significant decrease in AD incidence following

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	catheter. BP was recorded every 30-60 seconds for 4-6 minutes. The catheter was changed per normal sterile protocol and immediate BP was taken within the first 30 seconds. Control group had baseline BP taken at routine catheter change. Catheter was removed and 10ml of 2% lidocaine was injected prior to immediate placement of new catheter. Anaesthetic effects of intravesical lidocaine were assumed not to act in this group based on results from previous studies. BP was taken after catheter change. **Outcome measures:** BP	pretreatment with lidocaine (p=0.011). 4. The mean increase in SBP following catheter change from baseline for the treatment group was 9.5 mmHg. This was significantly less than the increase experienced by individuals in the control group (26.9 mmHg, P = .014). 5. After receiving intravesical lidocaine, 14 individuals in the treatment group experienced decreased SBP when comparing baseline to SBP at the time of catheter change (mean SBP prior to catheter change of 110 mmHg for treatment group).
Cosman & Vu 2005 USA PEDro=11 RCT Level 1 N=25	**Population:** All participants with complete SCI; age 46-49 years; 15-25 years post-injury; level of injury: C4-T1 **Treatment:** intersphincteric anal block with either: a) 300 mg 1% lidocaine or b) normal saline (placebo) before sigmoidoscopy or anoscopic hemorrhoid ligation procedure. **Outcome Measures:** blood pressure.	1. The mean maximal systolic blood pressure increase for the lidocaine group (22(14) mmHg) was lower than the placebo group (47(31) mmHg) suggesting that AD risk was reduced with lidocaine.

<table>
<tr><th>Author Year;
Country
Score
Research Design
Sample Size</th><th>Methods</th><th>Outcome</th></tr>
<tr><td></td><td colspan="2">Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data
 
</td></tr>
<tr><td rowspan="2"><a>Cosman et al. 2002
USA
PEDro=9
RCT
Level 1
N=45</td><td>Population: 45 patients (44 male, 1 female) with chronic, complete SCI, injury level of T6 or above, undergoing anoscopy and/or flexible sigmoidoscopies.
Treatment: a) 2% topical lidocaine jelly (n=18) or; b) nonmedicated lubricant (control, n=32) just prior to the procedure.
Outcome Measures: blood pressure.</td><td>1. Topical lidocaine had no significant effect on mean maximal systolic blood pressure (increased 35(25) mmHg in the lidocaine group vs. 45(30) mmHg in the control group).
2. Greater SBP increase with anoscopic procedure compared to sigmoidoscopic procedures (49(29) vs. 25(20) mmHg, respectively).</td></tr>
<tr><td colspan="2">Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data
 
</td></tr>
<tr><td><a>Furusawa et al. 2009
Japan</td><td>Population: 25 individuals with cervical SCI (22 men, 3 women); Level of injury: C4-</td><td>1. 10 participants in the control group reported symptoms of AD,</td></tr>
</table>

<table>
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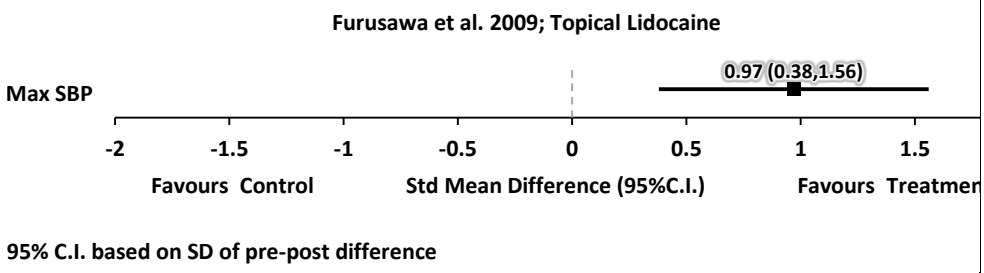
Country
Score
Research Design
Sample Size</th><th>Methods</th><th>Outcome</th></tr>
<tr><td rowspan="2">PEDro=8
RCT
Level 1
N=25</td><td>C7; mean(SD) time post-injury: 23.4(36.4), range 3-172 months.
Treatment: 10mL of 2% Lidocaine treatment group (placebo jelly for control group); both groups then underwent digital bowel stimulation to initiate and augment stool flow.
Outcome Measures: blood pressure; heart rate; symptoms of autonomic dysreflexia.</td><td>compared to 4 patients in the treatment group.
2. Systolic blood pressure was significantly lower in treatment group, compared to the control.
3. No significant difference in diastolic blood pressure or heart rate.</td></tr>
<tr><td colspan="2">Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data
 
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Discussion

Two RCTs (Cosman & Vu 2005; Cosman et al. 2002) compared the effect of topical local anesthesia to the anorectal area to a nonmedicated control gel for the prevention of AD during anorectal procedures. Cosman et al. (2002) found that AD was not abolished with the use of topical lidocaine; however, the same investigators later demonstrated that intersphincteric anal block with lidocaine was effective in limiting anorectal procedure-associated AD (Cosman & Vu 2005). Further, Cosman et al. (2002) found that anoscopy, which involves stretching the anal sphincters, was a more potent stimulus for AD than flexible sigmoidoscopy, which involves gaseous distention of the rectosigmoid. In an RCT by Furusawa et al. (2009), investigators found that topical lidocaine applied to the rectum prior to digital bowel stimulation significantly reduced systolic blood pressure and reports of AD over the duration of the bowel program when compared to the control group. Similarly, Solinsky and Linsenmeyer (2018) found that intravesical lidocaine decreased the incidence and severity of AD following catheter change.

Conclusion

There is level 1 evidence (from 1 RCT) (Cosman & Vu 2005) that lidocaine anal block significantly limits the AD response in susceptible patients undergoing anorectal procedures.

There is level 1 evidence (from 1 RCT) (Cosman et al. 2002) that topical lidocaine does not limit or prevent AD in susceptible patients during anorectal procedures.

There is level 1 evidence (from 1 RCT) (Furusawa et al. 2009) that topical lidocaine may help to prevent AD during gentle bowel stimulation.

There is level 2 evidence (from 1 prospective controlled trial) (Solinsky & Linsenmeyer 2018) that the incidence and severity of AD during catheter change were reduced after treatment with intravesical lidocaine.

Key Points

Lidocaine anal block can limit the AD response in susceptible patients undergoing anorectal procedures.

Topical lidocaine may prevent AD during digital bowel stimulation but does not prevent AD during anorectal procedures.

5.3 Prevention of AD during Pregnancy and Labour

In North America, women represent a third of the SCI population (Ackery et al. 2004). Approximately 3,000 American women of childbearing age are affected by SCI (Cross et al. 1992). The ability of women to have children is not usually affected by SCI once their menstrual cycle resumes (Jackson & Wadley 1999), and there are increasing numbers of women with SCI who have healthy babies (Cross et al. 1992). However, during labour and delivery, women with SCI are at high risk of developing uncontrolled AD (Sipski, 1991; Sipski & Arenas 2006). Thus, recognition and prevention of this life-threatening emergency is critical for managing labour in women with SCI (McGregor & Meeuwsen 1985). The majority of women with SCI above T10 experience uterine contractions as only abdominal discomfort, an increase in spasticity, and AD (Hughes et al. 1991).

Table 10. Prevention of AD during Pregnancy and Labour

Author Year; Country Score Research Design Sample Size	Methods	Outcome
Sharpe et al. 2015 USA Case Series Level 4 N=8	**Population:** Eight patients with SCI undergoing nine deliveries Median time from injury to time of delivery = 13 years (range 2–19 years) ASIA A=6, ASIA B=1, ASIA D=1 Pre-pregnancy AD: n=4 **Treatment:** 5 with epidural anesthesia, 2 with spinal anesthesia, 2 with general anesthesia **Outcome Measures:** Outcomes of pregnancies, presence of AD	1. Only patients with previous AD episodes presented AD symptoms during peripartum period. 2. Of the 4 patients with pre-pregnancy AD, 3 had AD symptoms peripartum. 3. One experienced AD during epidural placement, one during the second stage of labor, and all 3 experienced AD in the postpartum period. 4. No blood pressure measurements were recorded during these episodes, suggesting staff may not be aware of risk of AD in SCI patients
Skowronski & Hartman 2008 Australia Case series Level 4 N=5	**Population:** 5 females with tetraplegia who gave birth a total of 7 times (two individuals gave birth twice). **Treatment:** N/A **Outcome Measures:** Complication, management, and outcomes of pregnancy; hospital records.	1. AD occurred in 6 of 7 pregnancies. 2. AD was managed pre-emptively by insertion of an epidural either before or in the early stages of labour, with generally good results 3. Dangerously high peaks were managed by the administration of either sublingual nifedipine or intramuscular clonidine. 4. Other major complications include urinary tract infection (present in all pregnancies) and muscle spasms (4 of 7 pregnancies).
Cross et al. 1992 USA Case series Level 4 N=22	**Population:** 22 women with SCI, 11 with cervical and 11 with thoracic injuries; 10 with incomplete and 12 with complete injuries. **Treatment:** epidural	1. AD was experienced in 9/16 > T6. 2. One patient had two grand mal seizures during labour, which may have been triggered by her severe AD and the subsequent intravenous administration of

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	anesthesia. **Outcome Measures:** presence of autonomic hyperreflexia, type of anesthesia, type of delivery, complications.	diazepam. 3. Six patients had epidural anesthesia, which was effective for the control of AD.
Cross et al. 1991 USA Observational Level 5 N=16	**Population:** 7 participants with cervical and 9 with thoracic injuries. **Treatment:** questionnaire (in person or telephone) and hospital records review. **Outcome Measures**: outcomes of pregnancies.	1. Of the 16 women, 25 pregnancies occurred, resulting in 22 babies and 3 abortions. 2. 2/15 vaginal deliveries and 5/7 Caesarean section had AD during delivery with 4 participants receiving epidural anesthesia for the control of AD. 3. 1 patient required epidural catheter 5 days postpartum to control AD.
Hughes et al. 1991 UK Observational Level 5 N=15	**Population:** 17 pregnancies in 15 women with SCI, level of injury: T4-L3. **Treatment:** management and outcome of pregnancies in women with SCI. **Outcome Measures**: antenatal care and problems, labour diagnosis and outcome.	1. Labour tended to be diagnosed by dysreflexic symptoms or membrane rupture with confirmation by palpation of contractions and vaginal examination. 2. Initial management of AD included elevation of head of the bed, nifedipine and nitrates. 3. The most effective measure for controlling AD was to identify and interrupt the triggering afferent input to the spinal cord.
Ravindran et al. 1981 USA Case report Level 4 N=1	**Population:** 19 yr-old female with C5 complete tetraplegia admitted to the obstetrical intensive care unit for intra-amniotic prostaglandin F2-alpha injection for uterine	1. 100 mg/min of sodium nitroprusside decreased SBP from 170 mmHg to 120 mmHg caused by vaginal speculum introduction. 2. Prostaglandin induced uterine contraction further elevated BP to 200/70 mmHg; headache and sweating.

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	evacuation of a dead fetus of 20 wks gestation. **Treatment:** Sodium nitroprusside (100 mg/min to 700 mg/min). **Outcome measures:** BP and AD symptoms.	3. Administration of 700 mg/min of sodium nitroprusside decreased SBP and alleviated AD. 4. Following cessation of uterine contraction, the patient developed hypotension (70/30 mmHg) requiring vasopressor therapy. 5. Sodium nitropruside was stopped and epidural analgesia was initiated for further management of AD.

Discussion

Numerous observational studies, case reports, and expert opinions recommend adequate anesthesia for women with SCI during labour and delivery, despite the apparent lack of sensation. However, there are only six studies (Cross et al. 1992; Hughes et al. 1991; Cross et al. 1991; Ravindran et al. 1981; Skowronski & Hartman 2008; Sharpe et al. 2015) with observational evidence recording the management specific to AD during labour. The American College of Obstetrics and Gynecology (2002) emphasized the importance of obstetricians being aware of the specific problems related to SCI.

Conclusion

There is level 4 evidence (from one case-series) (Cross et al. 1992) that women with SCI may safely give birth vaginally. With vaginal delivery or when Caesarean or instrumental delivery is indicated, adequate anaesthesia (spinal or epidural if possible) is needed to reduce the episodes of AD associated with birth.

There is level 4 and 5 evidence (from 3 case series and 2 observational studies) (Cross et al. 1992; Hughes et al. 1991; Cross et al. 1991; Skowronski & Hartman 2008; Sharpe et al. 2015) that epidural anaesthesia is preferred and effective for most patients with AD during labour and delivery.

Key Points

Adequate anesthesia (spinal or epidural if possible) is needed with vaginal delivery, Caesarean delivery, and instrumental delivery.

Epidural anesthesia is preferred and effective for most women with AD during labour and delivery.

5.4 Prevention of AD during General Surgery

Despite the partial or total loss of sensation below the level of injury, surgical procedures or manipulations can potentially initiate episodes of AD in people with SCI. Therefore, anesthesiologists and surgeons performing surgery on this population must be aware of the interactions and effects of the anaesthetic and how to prevent or manage AD during these procedures.

Table 11. Prevention of AD during Surgery

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Eltorai et al. 1997 USA Observational Level 5 N=591	**Population**: Level of injury: C1-T10, mean length of injury: 22.3 yrs. **Treatment:** retrospective review of anesthetic methods during surgery. **Outcome Measures:** blood pressure.	1. AD occurred most commonly during the start of anesthesia (induction) with the greatest frequency when no anesthesia was provided. 2. During induction, systolic blood pressure increased in 68.7% of procedures during combined local anesthesia and intravenous (IV) sedation, in 65.4% of IV sedation alone, in 62.1% of local anesthesia alone, in 51.5% of spinal or epidural anesthesia, in 51.5% of general anesthesia, and in 88.8% of no anesthesia.
Lambert et al. 1982 USA Observational	**Population:** Participants had injuries that were above T6, and complete; mean of 6.5 years post-injury.	1. Intraoperative hypertension occurred more significantly with topical or no anesthesia (15/19) compared to general anesthesia (3/13) or spinal anesthesia (3/46).

Author Year; Country Score Research Design Sample Size	Methods	Outcome
Level 5 N=50	**Treatment:** Retrospective review of 78 procedures. Three groups: 1) topical or no anesthesia sedation (n=19), 2) general anesthesia (n=13), and; 3) spinal anesthesia (n=46). **Outcome Measures:** blood pressure.	2. Intraoperatively systolic BP increased significantly by 37 mmHg in patients receiving topical or no anesthesia. No significant difference in BP changes between general and spinal anesthesia groups.

Discussion

Two observational studies (Lambert et al. 1982; Eltorai et al. 1997) presented evidence that AD is a common complication during general surgery in individuals with SCI. Up to 90% of people with SCI undergoing surgery with topical anesthesia or no anesthesia developed AD during the procedure. Both studies concluded that patients at risk for AD could be protected by either general or spinal anesthesia.

Conclusion

There is level 5 evidence (from 2 observational studies) (Lambert et al. 1982; Eltorai et al. 1997) that indicates that people at risk for autonomic dysreflexia are protected from developing intraoperative hypertension by either general or spinal anaesthesia.

Key Points

Anesthesiologists and surgeons working with people with SCI must know how to recognize AD, how to prevent its occurrence, and how to manage it.

Anesthesia should be used during surgical procedures in individuals with SCI despite an apparent lack of sensation.

5.5 Prevention of AD during FES Exercise

Functional electrical stimulation (FES) is a widely-used modality in the rehabilitation of individuals with SCI (Sampson et al. 2000; Wood et al. 2001). Similar to any non-noxious or noxious stimuli below the level of injury, FES itself may also lead to significant afferent stimulation and trigger the development of AD (Ashley et al. 1993; Matthews et al. 1997).

Table 12. Prevention of AD during FES Exercise

Author Year Country Score Research Design Sample Size	Methods	Outcome
Matthews et al. 1997 Canada PEDro=7 RCT Level 1 N=7	**Population:** Injury level: C4-C7; all injuries were complete; age range: 23-44 years; 3-21 years post-injury. **Treatment:** Randomized to: a) topical anesthetic or: b) placebo creams applied to the quadriceps muscles during graded FES exercise. **Outcome Measures:** heart rate, blood pressure, serum catecholamines.	1. No differences in HR, BP or catecholamine responses or FES force were seen between the two conditions.

Discussion

One RCT assessed the effect of topical anaesthetic and placebo creams applied to the skin area over the quadriceps muscle 1 hour prior to FES on two different days (Matthews et al. 1997). As cardiovascular and AD responses during FES were unaffected by topical anaesthetic cream application at the stimulation site, the authors suggested that mechanisms other than skin nociception contributed to FES-induced AD.

Conclusion

There is level 1 evidence (from one RCT) (Matthews et al. 1997) supporting no effect of topical anesthetic for the prevention of AD during FES.

Key Points

Topical anesthetic is not effective for the prevention of AD during FES.

5.6 Prevention of AD with Stoma

Neurogenic bowel dysfunction is increasingly recognized as a major barrier to increasing quality of life in people with SCI. Bowel management difficulties include constipation, abdominal pain, fecal incontinence, prolonged transit time, and AD. The treatment of neurogenic bowel dysfunction with stoma usually takes place when other interventions such as transanal irrigation, pharmacological agents, etc. have failed.

Table 13. Prevention of AD with Stoma

Author Year; Country Score Research Design Sample Size	Methods	Outcome
Coggrave et al. 2012 UK Cross-sectional Level 4 N=92	**Population:** 92 individuals with SCI and stoma (64M, 28F); mean (SD) age in yrs: 56(9), range 24-86; mean (SD) age at injury (yrs): 30(13), range 6-64; 26 cervical (15 complete, 10 incomplete, 1 unknown), 61 thoracic (49 complete, 10 incomplete, 2 unknown), 1 missing data on level of injury; 91% colostomy, 9% ileostomy. **Treatment:** Retrospective analysis of a self-report postal survey of individuals with SCI who had a stoma. **Outcome Measures:** Tennessee Self-Concept Scale; Satisfaction with Life Scale; Hospital Anxiety and Depression Scale; rating scales for satisfaction, ability to live with bowel dysfunction and how much bowel care restricts life.	1. 19 respondents reported autonomic dysreflexia as their reason for stoma surgery. 2. Autonomic dysreflexia associated with bowel management was reported by significantly fewer respondents following stoma surgery (37% before, 18% after stoma formation).

Discussion

One cross-sectional study (Coggrave et al. 2012) completed a retrospective analysis on participants who had stomas. Following stoma surgery, significantly fewer respondents reported AD associated with bowel management (37% before, 18% after).

Conclusion

There is level 4 evidence (from one cross-sectional study) (Coggrave et al. 2012) that AD associated with bowel management decreases following stoma surgery.

5.7 Prevention of AD in Acute Care

The primary mechanisms of SCI are irreversible; therefore, prevention of AD in acute care are mainly focused on the attenuation of the effects of secondary injuries which are delayed, prolonged, and reversible.

Table 14. Prevention of AD in Acute Care

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Chen et al. 2012 China Case control Level 3 N=295	**Population:** 295 adults who underwent surgical decompression for acute traumatic SCI; mean (SD) age in yrs: 42.11(13.75); sex (ratio): 1.63:1 (male: female); preoperative AIS: A (n=135), B (n=29), C (n=36), D (n=95); preoperative ASIA motor index total score: 42.64(27.02); preoperative motor score of injured level: 4.02(0.46); preoperative sensory score of injured level: 3.02(0.45). **Treatment:** Cases were extracted and assigned into 3 groups on the basis of the timing of surgery by a physician: Urgent group (n=99, within 8 h after injury), Early group (n=86, from 8h to 48 h after injury), Delayed group (n=110, after 48 h); neurological outcomes and medical complications were compared before the operation, after the operation, at 6 months, and at 1 year. **Outcome Measures:** ASIA motor index total score; ASIA	1. Rates for AD differed by surgical decompression group. • Urgent group: • Post-operative 2.2%; 6 months 5.7% • Early group: • Post-operative 1.7%; 6 months 5.3% • Delayed group: • Post-operative 1.9%; 6 months 10.2%

	Impairment Scale (AIS); Motor and sensory scores of injured level; medical complications.	

Discussion

One retrospective study (Chen et al. 2012) assessed people with SCI with surgical decompression at different times (urgent, early and delayed). All groups had higher incidence of AD post-operatively and at 6 months, though the delayed group had the biggest increase. However, as the study was not randomized, we cannot determine why this occurred.

Conclusion

There is level 3 evidence (from one case control) (Chen et al. 2012) that earlier surgical decompression after acute SCI results in decreased AD incidence as compared to delayed surgical compression.

6 Management of Acute AD Episodes

There is growing evidence that education, knowledge, and management of this life-threatening condition is crucial for both medical personnel and people with SCI (McGillivray et al. 2009).

There is a well-established protocol for the management of AD developed by the Consortium for Spinal Cord Medicine (Consortium for Spinal Cord Medicine, 2020). When AD develops, the initial management of an episode involves placing the patient in an upright position to take advantage of an orthostatic reduction in blood pressure, and the loosening of any tight clothing (Consortium for Spinal Cord Medicine, 2020). Throughout the episode, blood pressure should be checked every 3-5 minutes. It is then necessary to search for and eliminate the precipitating stimulus where one can be identified, most commonly (in 85% of cases) related to either bladder distension or bowel impaction (Mathias & Frankel 2002; Teasell et al. 2000). If bladder catheterization or bowel disimpaction is not needed, a physical examination looking for pressure spots, ulcers, or ingrown nails should be performed (Krassioukov et al. 2020). The use of antihypertensive drugs, such as nitroglycerin paste, should be considered as a last resort, but may be necessary if the systolic blood pressure remains at 150 mmHg or greater following the steps outlined above (Consortium for Spinal Cord Medicine, 2020; Krassioukov et al. 2020). The goal of such an intervention is to alleviate symptoms and avoid the complications associated with uncontrolled hypertension (Eltorai et al. 1992; Pine et al. 1991; Vallès et al. 2005; Yarkony et al. 1986).

Despite appropriate preventative strategies, AD remains common among individuals with SCI. As previously noted, episodes of AD can be asymptomatic even when accompanied by a significant increase in arterial blood pressure, especially in individuals with cervical or high thoracic injuries (Linsenmeyer et al. 1996; Ekland et al. 2008). The Guidelines of the Consortium for Spinal Cord Medicine for management of AD recommends employing non-pharmacological measures initially; if they fail and systolic blood pressure continues to be at or above 150 mmHg

in adults, 120 mmHg in children under 5 years old, 130 mmHg in children 6-12 years old, and 140 mmHg in adolescents, then pharmacological agents should be initiated (Krassioukov et al. 2021; Consortium for Spinal Cord Medicine, 2006).

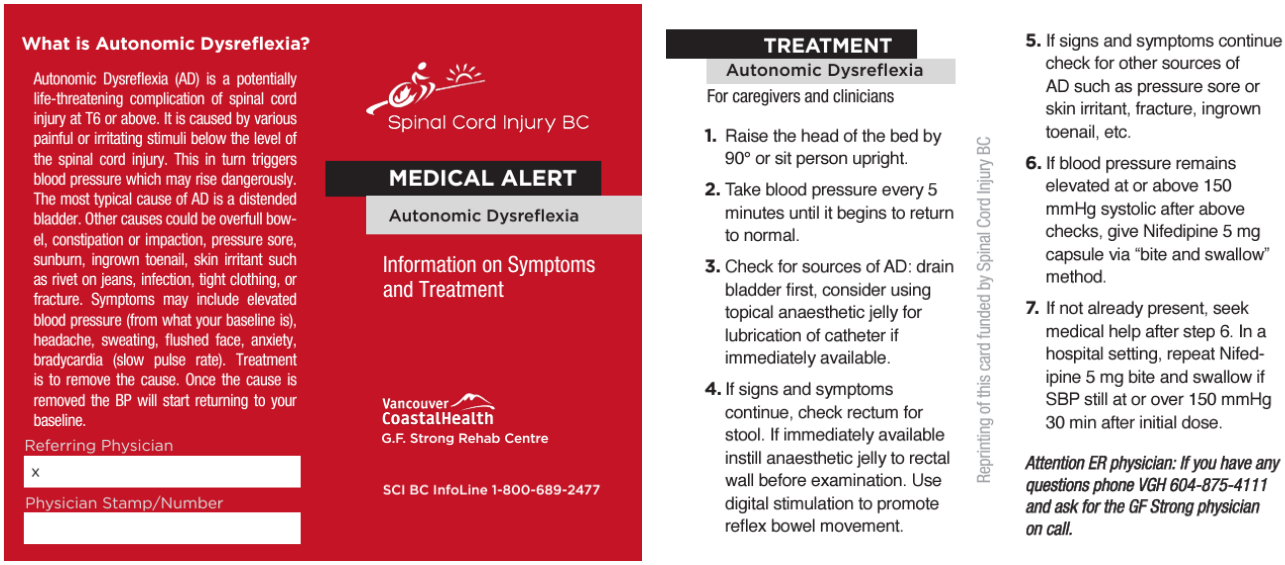


Figure 3. Autonomic Dysreflexia Symptom and Treatment care from SCI-BC (*https://sci-bc.ca/*)

6.1 Non-Pharmacological Management of AD

The initial management of an episode of AD involves placing the individual in an upright position to take advantage of an orthostatic reduction in blood pressure (Krassioukov et al. 2021; Consortium for Spinal Cord Medicine, 2020). While there are no studies that evaluate the effect of a sit-up position on blood pressure during episodes of AD, significant decreases in resting blood pressure have been shown during a tilt or sit-up test from supine position in individuals with SCI (Claydon & Krassioukov 2006; Krassioukov & Harkema 2006; Sidorov et al. 2007). It is proposed that an upright posture will induce pooling of blood into the abdominal and lower extremity vessels as peripheral vasoconstriction is compromised or lost following SCI; thus reducing arterial blood pressure. The next step is to loosen any tight clothing and constrictive devices (Consortium for Spinal Cord Medicine, 2001). This procedure will also allow more blood to pool into the vessel beds below the level of injury, as well as removal of a possible trigger of peripheral sensory stimulation. Blood pressure should be checked at a minimum of 5 minute intervals until the individual is stable (Consortium for Spinal Cord Medicine, 2001), at which time it is necessary to search for and eliminate the precipitating stimulus, which in 85% of cases can be found to relate to either bladder distention or bowel impaction (Teasell et al. 2000; Mathias & Bannister 2002). The use of antihypertensive drugs should be considered as a last resort and used if the systolic blood pressure remains at 150 mmHg or greater following the steps outlined above (Consortium for Spinal Cord Medicine, 2001). The goal of such an intervention is to alleviate symptoms and avoid the complications associated with uncontrolled hypertension (Yarkony et al. 1986; Pine et al. 1991; Eltorai et al. 1992; Vallès et al. 2005).

6.1.1 Epidural Stimulation

Epidural stimulation has emerged in the literature on spinal cord injury and may present a new method for managing symptoms of SCI. Epidural stimulation is a form of FES that uses electrical currents on the lower spinal cord to stimulate the nerves and elicit muscle contractions. An electrode is placed in the epidural space behind the spine and electrical currents are sent directly to the bypassing brain-to-spinal cord pathways to help reactivate remaining intact neural networks that may facilitate the movements to stand and walk, for example.

Table 15. Epidural Stimulation

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Herrity et al. 2021 USA Prospective controlled trial Level 2 N=65	**Population:** N=85, 71% male, 29% female Cross-sectional cohort: 65, mean age: 37 years Usual care cohort: 10, mean age: 10 years Interventional cohort: 10, mean age 29 years All motor complete SCI **Treatment:** All participants received two urodynamic assessments at least 5 months apart (usual care). Those in the intervention group had a 16-electrode array surgically implanted at the T11-L1 vertebrae level and underwent a total of 160 sessions of activity-based recovery training (ABRT-scES); 6 of them receiving alternating stand and step recovery-based training with scES. **Outcome Measures:** Blood pressure	1. In the interventional group, sBP responses to bladder distension did not differ following ABRT-scES (Pre-training, 131 ± 15 mmHg; Post-training, 140 ± 13 mmHg), nor were there significant changes at follow-up (149 ± 26 mmHg) compared to baseline or post-training. 2. The change in systolic blood pressure from pre-fill values (catheters in place) to values captured at the point of maximum cystometric capacity during the study indicates that ABRT-scES did not attenuate bladder-distention associated increases in systolic blood pressure (Pre-training change, 22 ± 20 mmHg; Post-training change, 25 ± 11 mmHg) ($p<0.05$). 3. Participants receiving ABRT-scES had significantly lower sBP responses to bladder distention post-training (140 ± 13 mmHg, $p<0.05$) compared

Author Year; Country Score Research Design Sample Size	Methods	Outcome
		to those in usual care (157 ± 18 mmHg. 4. The greatest blood pressure responses (>150 mmHg) were present in those using suprapubic catheters and having bladder capacity less than 300 ml [n = 17, (26%) of all participants]. 5. Blood pressure responses at maximum capacity were similar between those performing intermittent catheterization vs. those with suprapubic catheters (148 ± 25 mmHg vs. 159 ± 18 mmHg, respectively).
Pino et al. 2022 USA Prospective cohort study Level 2 N=14	**Population:** N=14, 11 males, 3 females Mean age: 38 years All participants were AIS grade A or B **Treatment:** 16-contact epidural paddle lead was implanted at the level of T12, then participants underwent tilt tests while strapped to an automated tilt table. After 10 mins of recording baseline BP and ECG in supine position, participants were passively moved to a 70-degree head-up tilt (HUT). Participants remained in this position until orthostasis symptoms were demonstrated, at follow up, scES was applied until BP normalised or until symptoms of orthostatic intolerance were ameliorated. If sBP remained	1. Did not observe an increased frequency or severity of AD with scES. 2. Maximum continuous SBP readings (mean (SD)) during supine (132 (11) mmHg), HUT (mean (SD) 127 (16) mmHg), and HUT with scES conditions (mean (SD) 128 (14) mmHg) were comparable. 3. The mean (SD) change in SBP between the end and start of each scES program at maximum intensity was 1 (8) mmHg. 4. Percentage time with SBP > 150 mmHg for ≥ 30 s was not significantly different between supine, HUT, and HUT with scES conditions. 5. Two out of ten participants experienced elevations in

Author Year; Country Score Research Design Sample Size	Methods	Outcome
	>150 mmHg for ≥30 s, this was deemed representative of an episode of AD. **Outcome Measures:** Blood pressure, heart function, ECG	sBP > 150 mmHg for ≥30 s during the application of scES.
Samejima et al. 2023 USA Case series Level 4 N=3	**Population:** N=3, 2 males with traumatic cervical SCI, 1 female with traumatic thoracic SCI AIS A: 1 AIS B: 2 Age: 23-41 years **Treatment:** Baseline BP and HR were measured and an ABPM device was applied to record sBP, dBP, and HR in each participant, along with cardiovascular parameters ever 15 minutes during the daytime and every 60 minutes during the nighttime. Digital anorectal stimulation (DARS) was delivered to each participant and hemodynamic data, BP, and HR were recorded to monitor cardiovascular safety and AD severity. DARS was performed twice without eSCS and twice with eSCS initiated 60 seconds prior to DARS and sustained for 60 seconds after DARS was completed. **Outcome Measures:** BP, HR (incidence of AD)	1. The effect of eSCS on resting cardiovascular parameters showed that there were minimal changes in resting SBP, DBP and HR between the stimulation conditions in all participants. DARS without eSCS induced an elevation in SBP of greater than 20 mmHg (Participant 1: 31 ± 14 mmHg, Participant 2: 22 ± 1 mmHg, Participant 3: 26 ± 2 mmHg) and a simultaneous reduction in HR, indicative of AD. 2. Active eSCS during DARS prevented AD, as evidenced by a marginal elevation in SBP of less than the 20 mmHg threshold for AD diagnosis (Participant 1: 16 ± 0.2 mmHg, Participant 2: 13 ± 3 mmHg, Participant 3: 8 ± 5 mmHg) and a minimal reduction in HR

Discussion

Two prospective studies examined the effect of scES on blood pressure in individuals with SCI and neither found sufficient evidence to suggest that scES could attenuate or remove episodes of AD (Herrity et al. 2021; Pino et al. 2022). Herrity et al. (2021) did not observe differences in sBP in response to bladder distention following ABRT-scES; however, participants receiving ABRT-scES had lower sBP responses to bladder distention post-training compared to those in usual care. On the other hand, Pino et al. (2022) found no differences in sBP between supine to head-up-tilt (HUT) and HUT with scES. Furthermore, there was no increase in frequency or severity of AD with the application of scES, although 2 of the 10 participants experienced elevations in sBP enough to represent AD (> 150 mmHg for ≥30) (Pino et al. 2022).

On the other hand, a case series by Samejima et al. (2023) found the application of eSCS to prevent AD during digital anorectal stimulation (DARS), with each participant experiencing only a marginal elevation in sBP that does not meet the threshold for AD diagnosis.

Evidence is too preliminary at this time to support or deny the use of scES for AD management in people with SCI. However, Herrity et al. (2021) suggest that the training effect found in their study supports the role of intersystem stimulation; that integrating an scES protocol for both bladder and cardiovascular function could improve responses to bladder distention.

Conclusion

There is level 2 evidence (from one prospective controlled trial) (Herrity et al. 2021) that elevated blood pressure elicited during bladder distention was not attenuated with ABRT-scES, but post-training, the ABRT-scES group had significantly lower sBP responses than the usual care group during bladder distention.

There is level 2 evidence (from one prospective cohort study) (Pino et al. 2022) that scES does not increase the frequency of severity of AD, although 2 of 10 participants experienced elevations of sBP enough to represent an episode of AD (> 150 mmHg for ≥30 s).

There is level 4 evidence (from one case series) (Samejima et al. 2023) that the application of eSCS prevents AD during digital anorectal stimulation.

6.2 Pharmacological Management of AD

Episodes of AD in people with SCI can vary in severity, but in some cases can be asymptomatic and be managed by the individual once they are familiar with their own triggers and symptoms (Linsenmeyer et al. 1996). However, in some individuals it is difficult to find the trigger and so immediate medical attention is required (Elliott & Krassioukov 2006).

Antihypertensive drugs with a rapid onset and short duration of action should be used in the management of acute episodes if non-pharmacological measures fail and arterial blood pressure remains at 150 mmHg or greater (Blackmer, 2003; Consortium for Spinal Cord Medicine, 2001). However, while numerous pharmacological agents (e.g., nifedipine, nitrates, captopril, terzaosin, prazosin, phenoxybenamine, Prostaglandin E2, sildanefil) have been proposed for management of AD (Consortium for Spinal Cord Medicine, 2001; Blackmer, 2003; Naftchi & Richardson

1997), the Consortium for Spinal Cord Medicine (2001) does not identify any particular medication as the standard. A survey by Solinsky (2023) found that of 60 physicians who treated patients with SCI, 82% used nitroglycerin ointment as a first-line medication when conservative treatments failed. Moreover, 67% of physicians had explicit second-line medications to manage AD, commonly hydralazine (48%), nifedipine (28%), prazosin (5%), and clonidine (5%) (Solinsky, 2023). Additionally, the majority of the recommendations are based on the clinical management of hypertensive crises in populations without SCI, as well as case reports and anecdotal evidence. Characteristics and outcomes of studies assessing pharmacological interventions for the management of AD are presented in the following sections.

The literature supporting pharmacological management of AD using fast-acting antihypertensive drugs is specific to SCI. Although the use of fast-acting anti-hypertensives is strongly discouraged in populations without SCI, there is a clinical need for immediate action in individuals with SCI due to the mechanisms of hypertensive crisis and the risk of intracranial bleed, myocardial infarction, or death (Ho & Krassioukov 2010; Yoo et al. 2010). Episodes of AD are typically short-lasting events; thus, they could be well controlled with the use of fast-acting antihypertensive medications. Therefore, the use of these medications for the management of hypertension is less likely to result in the deleterious effects observed in populations without SCI, provided that it is given at a low dose and only as needed.

Key Points

In people with SCI, episodes of AD are typically well-controlled with the use of fast-acting antihypertensive medications, and are less likely to result in the deleterious effects observed in populations without SCI due to the short-lasting nature of AD events.

6.2.1 Nifedipine (Adalat, Procardia)

Nifedipine, a calcium ion influx inhibitor (Ca-channel blocker), selectively inhibits calcium ion influx across the cell membrane of cardiac muscle and vascular smooth muscle while maintaining serum calcium concentrations. In humans, Nifedipine decreases peripheral vascular resistance and creates a modest fall in systolic and diastolic pressure (5-10mm Hg systolic although sometimes larger). Nifedipine is generally given using the "bite and swallow" method, in a dose of 10 mg.

Table 15. Nifedipine (Adalat, Procardia)

Author Year; Country Score Research Design Sample Size	Methods	Outcome
Thyberg et al. 1994 Sweden Pre-post Level 4 N=10	**Population:** 10 individuals with cervical or high thoracic SCI. **Treatment:** 10 mg nifedipine sublingually during cystometry. **Outcome Measures:** blood pressure and heart rate.	1. Participants demonstrated decreased maximum SBP and DBP after the administration of nifedipine. 2. Maximum SBP decreased from 147 mmHg to 118 mmHg. 3. The decrease in BP was due to a decrease in baseline pressure and BP response during cystometry.
Kabalin et al. 1993 USA Case series Level 4 N=20	**Population:** 10 individuals with tetraplegia, 10 with paraplegia. **Treatment:** 10-30 mg nifedipine sublingually during Extracorporal shock wave lithotripsy (ESWL) for kidney stone treatment. **Outcome Measures:** electrocardiogram, blood pressure, pulse rate, peripheral oxygen saturation.	1. All but one participant with SCI demonstrated AD during ESWL with maximal increase in systolic BP of 74 mmHg. 2. Nifedipine was administered sublingually and controlled BP elevation. 3. For severe, acute increases in BP, ESWL stimulation was momentarily discontinued until pharmacological control of the BP was achieved, after which treatment was continued.
Steinberger et al. 1990 USA Prospective controlled trial Level 2 N=10	**Population:** All participants with injury levels above T5; mean 9 years post-injury (range 3-21 years). **Treatment:** 10-30 mg nifedipine sublingually 15 min prior to electroejaculation or no nifedipine. **Outcome Measures:** blood pressure, voltage and current delivered during electroejaculation.	1. In 9/10 participants, blood pressures were markedly lower after nifedipine pretreatment. 2. Compared with no treatment, SBP during electroejaculation was lower with nifedipine pretreatment (168 mmHg vs. 196 mmHg). 3. In 9/10 participants, tolerance to electrical stimulation was ≥ post nifedipine pretreatment.

Author Year; Country Score Research Design Sample Size	Methods	Outcome
Dykstra et al. 1987 USA Pre-post Level 4 N=7	**Population:** Individuals with complete, cervical injuries. **Treatment:** 10 mg nifedipine during cystosopy procedure. **Outcome measures:** blood pressure, presence of AD.	1. Nifedipine alleviated AD when given sublingually during cystoscopy and prevented autonomic hyperreflexia when given orally 30 minutes before cystoscopy. 2. No adverse drug effects were observed.
Lindan et al. 1985 USA Prospective controlled trial Level 2 N=12	**Population:** 12 individuals with tetraplegia. **Treatment**: phenoxybenzamine (10mg bid) versus nifedipine (20mg bid) administration at least 4 days prior cystometry. 11 patients were also tested for the efficacy of 10 mg nifedipine (sublingually or by mouth) for controlling AD symptoms. **Outcome Measures:** blood pressure.	1. Neither drug prevented AD secondary to bladder filling, and a significant number of patients developed hypotension. 2. Sublingual dose of nifedipine (10 mg) was effective in managing acute attacks of AD.

Discussion

Five studies (Steinberger et al. 1990; Lindan et al. 1985; Thyberg et al. 1994; Kabalin et al. 1993; Dykstra et al. 1987) have evaluated the effects of Nifedipine. Four of these five studies saw a reduction or alleviation of AD with nifedipine (Steinberger et al. 1990; Thyberg et al. 1994; Kabalin et al. 1993; Dykstra et al. 1987. Steinberger and co-investigators (1990) reported that sublingual nifedipine decreased peak systolic, diastolic, and mean blood pressure in individuals with SCI undergoing electroejaculation. Braddom and Rocco (1991) surveyed 86 physicians with an average of 16.8 years of experience in managing AD in individuals with SCI. They found that while pharmacologic treatment of AD varied greatly from physician to physician, antihypertensive medications were the most frequently used medications, with Nifedipine being a drug of choice in minor AD cases for 48% of physicians and in severe symptomatic cases for 58% of physicians. Although nifedipine has been the most commonly used agent for management of AD in individuals with SCI (Thyberg et al. 1994; Dykstra et al. 1987; Esmail et al. 2002; Braddom & Rocco 1991), its use has declined recently (Frost, 2002; Anton & Townson 2004). There have been no reported adverse events from the use of nifedipine in the treatment of

AD (Blackmer, 2003), although all studies had a very small sample size. However, a review of nifedipine for the management of hypertensive emergencies not specific to SCI found serious adverse effects such as stroke, acute myocardial infarction, death and numerous instances of severe hypotension (Grossman et al. 1996). Due to several reports of serious adverse reactions occurring after administration of immediate-release nifedipine, the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (1997) has discouraged use of this drug.

Conclusion

There is level 2 evidence (from 2 prospective controlled trials) (Steinberger et al. 1990; Lindan et al. 1985) that Nifedipine may be useful to prevent dangerous blood pressure reactions, e.g. during cystoscopy and other diagnostic or therapeutic procedures in SCI injured patients with AD.

There is level 5 evidence (from clinical consensus) (Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure, 1997), that serious adverse effects from Nifedipine may occur and these have been reported in other populations.

Key Points

Nifedipine may be useful to prevent or control AD in individuals with SCI; however, serious adverse effects may occur, similar to those reported in other populations.

6.2.2 Nitrates (Nitroglycerine, Depo-Nit, Nitrostat, Nitrol, Nitro-Bid)

Nitrates are used for the management of acute episodes of AD as they relax vascular smooth muscle, thus producing vasodilation on peripheral arteries and veins. Dilation of post-capillary vessels, including large veins, promotes peripheral pooling of blood and reduces venous return to the heart, thereby reducing left ventricular end-diastolic pressure (pre-load) and arterial blood pressure. Further, arteriolar relaxation reduces systemic vascular resistance, which leads to reduced arterial pressure (after-load). If an individual with SCI and acute AD has used sildenafil within the previous 24 hours the use of an alternative short acting, rapid-onset antihypertensive agent is recommended. Nitrates are the second most commonly used agent after nifedipine for management of AD in individuals with SCI (Consortium for Spinal Cord Medicine, 2001; Braddom & Rocco 1991). However, with the exception of one case report with intravenous use of nitroprusside (Ravindran et al. 1981) and expert opinions (Consortium for Spinal Cord Medicine, 2001), no studies exist to support their use in SCI.

Conclusion

There is level 5 evidence (from clinical consensus) that supports the use of nitrates in acute management of AD (Consortium for Spinal Cord Medicine, 2001; Braddom & Rocco 1991), but

there are no clinical studies testing the use of nitrates in the acute management of AD in people with SCI.

Key Points

Nitrates are commonly used in the control of AD in SCI; however, no studies have been done to show their effectiveness or safety in SCI.

6.2.3 Captopril

Captopril is a specific competitive inhibitor of angiotensin I-converting enzyme (ACE). During an episode of AD, 25mg of captopril is recommended for sublingual administration.

Table 16. Captopril

Author Year Country Score Research Design Sample Size	Methods	Outcome
Esmail et al. 2002 Canada Pre-post Level 4 N=7	**Population:** 26 consecutive patients older than 15 years with SCI above T6. **Treatment:** administration of a) captopril 25mg sublingually if systolic blood pressure (SBP) was at or above 150mmHg, b) 5mg of immediate-release nifedipine if SBP remained elevated 30 minutes after captopril administration. **Outcome Measures:** SBP	1. A total of 33 autonomic dysreflexia episodes were documented in 7 patients. 2. The 18 episodes documented in 5 patients were treated with drug therapy. 3. Captopril alone was effective in reducing SBP in 4 of 5 the patients (80%). The mean SBPs at baseline and 30 minutes after captopril were 178(18) mmHg and 133(28)mmHg, respectively. 4. The addition of nifedipine successfully reduced blood pressure from 170/108 to 110/80 after 30 minutes in the one patient who did not respond to the administration of captopril.

Discussion

In a pre-post study by Esmail et al. (2002), captopril was safe and effective in 4 out of 5 episodes for AD management. This prospective open labelled study and numerous experts' opinion suggest the use of the captopril as a primary medication in management of AD (Consortium for Spinal Cord Medicine 2001; Frost, 2002; Anton & Townson 2004).

Conclusion

There is level 4 evidence (from one pre-post study) (Esmail et al. 2002) for the use of captopril in the acute management of AD in SCI.

Key Points

Preliminary evidence suggests that captopril is effective for the management of AD in SCI.

6.2.4 Terazosin

Terazosin is a long-acting, alpha-1 adrenoceptor selective blocking agent. Selective alpha 1 blockade has been suggested as a good pharmacological choice in the management of AD because of its dual effect at the bladder level: inhibition of urinary sphincter and relaxation of the smooth muscles of blood vessels.

Table 17. Terazosin

Author Year Country Score Research Design Sample Size	**Methods**	**Outcome**
Vaidyanathan et al. 1998 UK Pre-post Level 4 N=24	**Population:** 18 adults with tetraplegia (17 male, 1 female), 3 children with ventilator-dependent tetraplegia and 3 adult males with paraplegia. All had AD in the absence of an acute factor. **Treatment:** Administration of Terazosin with starting dose of 1 mg (adults) or 0.5 mg (children). Step-wise increments of these doses	1. The AD symptoms subsided completely with the Terazosin therapy in all the patients. 2. Adult patients required a dose between 1-10 mg and children required between 1-2 mg. 3. The side effects of postural hypotension and drowsiness were transient and mild. One tetraplegic patient developed persistent dizziness and therapy was discontinued.

Author Year Country Score Research Design Sample Size	Methods	Outcome
	were given at 3-4 day intervals. **Outcome Measures:** drug-induced hypotension, adverse effects, AD symptoms.	
Chancellor et al. 1994 USA Pre-post Level 4 N=21	**Population:** 21 participants with complete SCI; injury level C3-T5. **Treatment:** Terazosin administration. **Outcome Measures**: blood pressure and autonomic dysreflexia frequency and severity scores	1. Decrease in the AD severity score from baseline at one week, 1 month and 3 months. 2. Degree of muscle spasm and degree of headache did not improve. 3. Decrease in the frequency of AD at 1-week follow-up and was maintained at 1 and 3 months. 4. 4. SBP did not statistically change after 3 months of Terazosin.
Swierzewski et al. 1994 USA Pre-post Level 4 N=12	**Population**: 6 participants with paraplegia, 6 with quadriplegia. **Treatment:** nightly Terazosin administration for 4 weeks (5 mg starting dose). **Outcome Measures:** physical examination, cystoscopy, AD symptoms.	1. Detrusor compliance improved in all patients during the treatment phase. 2. Change in bladder pressure and safe bladder volume were statistically and clinically significant. 3. Terazosine abolished AD in 3 patients and decreased the incidence and the severity of symptoms in 1 patient.

Discussion

Regular doses of Terazosin over weeks or months appeared to be effective in preventing AD without erectile function impairment in three pre-post studies (Vaidyanathan et al. 1998; Swierzewski et al. 1994; Chancellor et al. 1994). Patients reported moderate to excellent improvement (Chancellor et al. 1994) or even complete termination of the dysreflexic symptoms (Vaidyanathan et al. 1998) during a 3-month period of Terazosin administration.

Conclusion

There is level 4 evidence (from 3 pre-post studies) (Vaidyanathan et al. 1998; Swierzewski et al. 1994; Chancellor et al. 1994) that regular use of Terazosin may have positive effects on both incontinence and AD.

Key Points

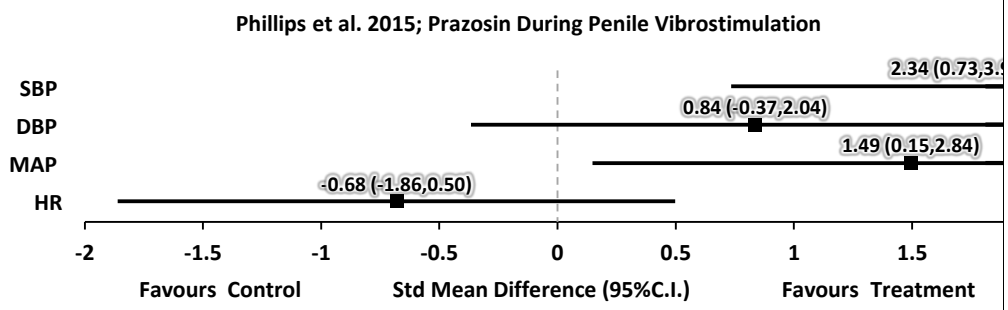
There is some evidence for the use of Terazosin as an agent for control of AD in people with SCI, particularly in bladder management and AD.

6.2.5 Prazosin (Minipress)

Prazosin, a postsynaptic alpha-1 adrenoceptor blocker, lowers blood pressure by relaxing blood vessels. Prazosin has a minimal effect on cardiac function due to its alpha-1 receptor selectivity. The recommended starting dose in adults is 0.5 or 1 milligram (mg) taken two or three times a day.

Table 18. Prazosin (Minipress)

Author Year Country Score Research Design Sample Size	Methods	Outcome
Phillips et al. 2015 Canada PEDro = 9 RCT Level 1 N= 6	**Population**: N=6 males with complete, chronic SCI above T6 Mean (SD) age: 36.7 (4.8) years Mean (SD) time since injury: 139 (47.3) months ASIA A=3; ASIA B=1; ASIA D=2 Cause of SCI: MVA=3; Athletics=2; Fall=1 **Treatment**: Participants had 2 penile vibrostimulation (PVS) trials; one with prazosin, other with a placebo (sugar capsule) **Outcome Measures:** Cardiovascular parameters (HR and continuous beat-to-beat BP)	1. All participants experienced AD during PVS regardless of treatment: BP increased in all patients but HR did not change 2. On average, systolic BP was 44 mm Hg lower when prazosin was administered. 3. SBP increased an average of 140 +/- 19 mm Hg with placebo, and increased only 96 +/- 14 mm Hg with prazosin 4. Of the six participants, five had a mitigation of SBP increases when treated with prazosin compared to placebo (the remaining participant had no change in BP response)

		5. Prazosin had no effect on resting BP
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data 	
Krum et al. 1992 Australia PEDro=9 RCT Level 1 N=15	**Population:** Level of injury: T6 or above, at least 2 episodes of AD in last 7 days. **Treatment:** double-blind, randomized to Prazosin 3 mg bid. (n=8) or placebo (n=7) for 2 weeks. **Outcome Measures**: frequency and severity of AD, blood pressure.	1. Prazosin was well tolerated and did not significantly lower resting BP. Compared to baseline, the Prazosin group had fewer severe episodes of AD (reduced rise in BP, shorter symptom duration and less need for acute antihypertensive medication). 2. The severity of headache during individual AD episodes was also diminished with Prazosin therapy.

Discussion

In a small (Krum et al. 1992), but high quality RCT, Prazosin twice daily was well tolerated and did not affect baseline blood pressure; AD episodes were also less severe and shorter in duration over a 2-week period. Phillips et al. (2015) found similar results during penile vibrostimulation trials, where Prazosin lowered systolic blood pressure when administered without affecting resting blood pressure.

Conclusion

There is level 1 evidence (from two RCTs) (Phillips et al. 2015; Krum et al. 1992), that Prazosin is superior to placebo in the prophylactic management of AD.

Key Points

Prazosin can prophylactically reduce the severity and duration of AD episodes for people with SCI.

6.2.6 Phenoxybenzamine (Dibenzyline)

Phenoxybenzamine, a long-acting, adrenergic, alpha-receptor blocking agent, can increase blood flow to skin, mucosae, and abdominal viscera, as well as lower supine and standing blood pressures. The initial dose is 10 mg of Dibenzyline (phenoxybenzamine hydrochloride) bid with increases once daily, usually up to 20-40 mg 2-3 times/days.

Table 19. Phenoxybenzamine (Dibenzyline)

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Lindan et al. 1985 USA Pre-post Level 4 N=12	**Population:** 12 participants with tetraplegia **Treatment:** phenoxybenzamine (10 mg bid) and nifedipine (20 mg bid) for 4 days prior cystometry **Outcome Measures:** blood pressure during cystometry.	1. Neither drug effectively prevented AD secondary to bladder filling and a significant number of patients developed troublesome hypotension. 2. Sublingual dose of nifedipine (10 mg) was effective in managing acute attacks of AD.
McGuire et al. 1976 USA Case series Level 4 N=9	**Population:** 9 individuals with SCI and severe AD. **Treatment:** 6 patients treated daily with phenoxybenzamine (alpha-sympatholytic agent) in doses ranging from 10 to 20 mg. **Outcome Measures:** blood, bladder and urethral pressures.	1. Hypertension, headache and anxiety of AD could no longer be provoked with bladder filling but sweating continued. 2. Mean resting urethral pressure (based on 30 cc bladder volume) decreased after treatment with phenoxybenzamine from 40.6 to 34.0. 3. Mean maximum urethral pressure change with filling decreased after the treatment from +20cmH2O to -30cmH2O.

Discussion

McGuire et al. (1976) reported that hypertension, headache, and anxiety of AD could no longer be provoked with bladder filling (but sweating continued to occur) in the six participants who took phenoxybenzamine (dose range from 10 to 20mg) daily. However, this result is opposite to Lindan et al.'s (1985) findings where blood pressure rose with bladder distension in ten participants and remained at baseline in only two participants after taking phenoxbenzamine for 4 or more days.

Conclusion

There is level 4 evidence (from one pre-post study and one case series study) for use of Phenoxybenzamine in the management of AD; however, the results are conflicting with no effects seen in one study (Lindan et al. 1985) and positive effects in another (Lindan et al. 1985; McGuire et al. 1976).

Key Points

It is not known whether Phenoxybenzamine is effective for the management of AD in SCI.

6.2.7 Prostaglandin E2

Prostaglandin E2 is a group of hormone-like substances that contribute to a wide range of bodily functions including the contraction and relaxation of smooth muscle, the dilation and constriction of blood vessels, and the control of blood pressure.

Table 20. Prostaglandin E2

Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Frankel & Mathias 1980 UK Prospective controlled trial Level 2 N=5	**Population:** 5 patients with complete SCI; age range: 25-37 years; level of injury: C5-T4, 5-108 months post-injury. **Treatment:** trans-rectal electrical ejaculation with and without intravenous administration of Prostaglandin E2.	1. Resting BP decreased and resting HR increased with Prostaglandin E2. 2. BP decreased during electrical stimulation, which enabled tolerance of more intense stimulation and successful ejaculation in 2 patients.

	Outcome Measures: heart rate, blood pressure, electrocardiogram.	

Discussion

Frankel and Mathias (1980) studied five individuals; 3 participants underwent administration with and without Prostaglandin E2 and showed that the level of BP recorded during electrical ejaculation decreased with the drug.

Conclusion

There is level 2 evidence (from one prospective controlled study) (Frankel & Mathias 1980) which used participants as their own controls and showed that the level of BP recorded during electrical ejaculation was substantially reduced with Prostaglandin E2.

Key Points

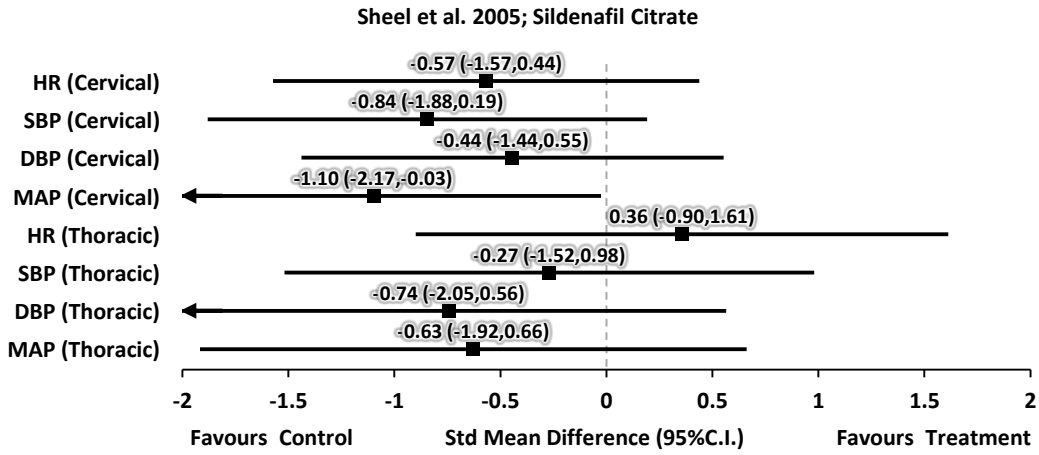
One study found that Prostaglandin E2 is effective for reducing BP responses during electroejaculation.

6.2.8 Sildenafil (Viagra)

Sildenafil inhibits phosphodiesterase type 5 (PDE5), relaxes smooth muscle, and increases levels of cGMP and blood flow to the corpus cavernosum. Sildenafil at recommended doses has no effect in the absence of sexual stimulation. The recommended dose is 50 mg taken as needed approximately 1 hour before sexual activity, but it may be taken anywhere from 0.5 hour to 4 hours before sexual activity. Sildenafil is known to enhance the hypotensive effects of nitrates. Thus, nitrates in any form are contraindicated with sildenafil use.

Table 21. Sildenafil (Viagra)

Author Year; Country Score Research Design Sample Size	**Methods**	**Outcome**
Sheel et al. 2005 Canada PEDro=5	**Population:** 13 males, 8 participants with cervical and 5 with thoracic injuries. **Treatment:** oral dose of sildenafil citrate (25-100 mg) or	1. Sildenafil decreased base BP in participants with cervical SCI. 2. Men with cervical SCI had more pronounced AD during penile

<table>
<tr><td rowspan="2">RCT
Level 2
N=13</td><td>no medication during penile vibratory stimulation.
Outcomes Measures: ECG, blood pressure.</td><td>vibrostimulation than men with thoracic SCI.
3. Administration of sildenafil had no effect on HR or BP during AD triggered by penile vibratory stimulation in men with SCI.</td></tr>
<tr><td colspan="2">Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data
 
</td></tr>
</table>

Discussion

The effect of sildenafil on AD was reported in one small RCT (Sheel et al. 2005). Although sildenafil decreased resting BP, no effect on the magnitude of AD resulting from penile vibrostimulation in men with SCI was observed.

Conclusion

There is level 2 evidence (from one RCT) (Sheel et al. 2005) that sildenafil citrate had no effect on changes in BP during episodes of AD initiated by vibrostimulation in men with SCI.

Key Points

One study found that Sildenafil has no effect on AD responses in men with SCI during ejaculation.

6.2.9 Other Pharmacological Agents Tested for Management of AD

Other pharmacological agents have been used to manage AD in individuals with SCI and their use has been reported in the literature (e.g., expert opinion, case report). However, they currently do not have sufficient evident to warrant recommendation. These include the use of

Phenazopyridine for AD associated with cystitis (Paola et al. 2003), Diazoxide (Hyperstat) for acute AD episodes (Erickson, 1980), intrathecal baclofen for AD associated with spasticity (Kofler et al. 2009; Del Fabro et al. 2018) and magnesium sulfate for AD associated with labour (Maehama et al. 2000) or life-threatening AD in intensive care (Jones & Jones 2002). In addition, there have been reports on the use of beta blockers (Pasquina et al. 1998), Mecamylamine (Inversine) (Braddom & Rocco 1991), and Hydralzine (Apresoline) (Erickson, 1980) for the general management of AD symptoms in individuals with SCI.

Table 22. Other Pharmacological Agents Tested for Management of AD

Drug Name	Evidence	Author
Hydralazine (Apresoline)	Expert opinion	Erickson, 1980
Beta blockers	Case report	Pasquina et al. 1998
Mecamylamine (Inversine)	Case report	Braddom & Rocco 1991
Magnesium sulphate	Case report	Jones & Jones 2002; Maehama et al. 2000
Diazoxide (Hyperstat)	Expert opinion	Erickson, 1980
Phenazopyridine	Case report	Paola et al. 2003
Intrathecal Baclofen	Case report, Retrospective chart review	Kofler et al. 2009; Del Fabro et al. 2018

7 Other Autonomic Dysfunctions

There are a variety of other autonomic dysfunctions that can occur after SCI. During the first weeks post-injury (period of neurogenic shock), alterations in autonomic function require close medical management and may be life-threatening (Guly et al. 2008; Krassioukov et al. 2007; Tuli et al. 2007). Low resting arterial blood pressure, severe bradycardia, and even asystole can be seen in individuals with cervical injuries (Biering-Sørensen et al. 2017). However, even those who are not in severe distress need to be carefully monitored for autonomic instability during the initial post-injury period and beyond. We have briefly summarized some of the most common general autonomic dysfunction issues post-SCI (for a more complete discussion of Bladder, Bowel and Sexual Health issues post-SCI, please refer to the specific chapters in the Evidence section of SCIRE).

7.1 Thermodysregulation

Thermodysregulation is a well-recognized, clinical phenomenon after SCI (Colachis & Otis 1995; Schmidt & Chan 1992). It typically occurs during the acute phase of SCI though it can potentially last a lifetime. Although thermoregulation is at least partly regulated by autonomic function, the precise mechanisms of thermodysregulation after SCI are not yet fully understood. The degree of dysregulation appears to be related to injury level and perhaps to degree of completeness of SCI, similar to the pattern of AD (Guttman, 1976). Body temperature is under direct autonomic control via hypothalamic regulation; peripheral cold and warm receptors send messages to the hypothalamus via the spinal cord (Downey et al, 1973). Overall, temperature is easy to measure and classify, even in the early stages post-injury, and therefore tracking thermodysregulation may be a useful means of early assessment of autonomic function.

Even under conditions when the environment is temperature controlled (i.e., not too hot or too cold), people with SCI can have difficulty regulating their body temperature. Individuals with tetraplegia and those with lesions at T6 or above usually exhibit more marked differences in thermoregulation than individuals with paraplegia, most likely due to a lack of hypothalamic connections to the spinal sympathetic circuits and the reduced surface area that can respond (Krassioukov et al. 2007).

Data suggests that individuals with tetraplegia after SCI have episodes of subnormal body temperature in normal ambient environments, and that cold temperatures have a greater negative impact on personal comfort and ability in people with tetraplegia compared to those without SCI (Khan et al. 2007; Hanrakis et al. 2016). There is a clinically recognized, though not widely studied, phenomenon known as “quad fever” where people with tetraplegia or high paraplegia present with a fever exceeding 40 °C (101.5 °F) without a significant rise in core body temperature or an infectious source (Krassioukov et al. 2007).

7.1.1 Thermoregulation during Exercise

Exercise-induced hyperthermia has been more widely studied in recent years. Generally, people with tetraplegia experience a greater rise in body temperature with exercise than people with paraplegia, even when exercising at similar output/exertion levels, likely due to an increased difficulty in dispersing endogenously produced heat (Price & Campbell 2003). Price and Campbell (2003) also found that neither persons with paraplegia nor those with tetraplegia showed any alteration in thigh skin temperature despite changes in core body temperature post-exercise.

It is also common for people with tetraplegia to take longer to cooldown after exercise; Boot et al. (2006) found that when exercising in the cold, mean body temperature decreases in people with high-level SCI and lower-level SCI were both greater than participants without SCI.

Differentiating between those with and without temperature dysregulation may be helpful in discerning those with autonomic incompleteness (whether or not there is motor and sensory completeness). Both skin and core body temperature above and below the level of injury can be helpful in assessing autonomic function (Krassioukov et al. 2007). Regardless, precautions should be taken for people with SCI when exercising in the cold or heat; techniques as simple as

asking about the person's experience with exercise and their temperature fluctuations, or cool-water foot baths before or during exercise, can be successful in restoring normal body temperature (Boot et al. 2006; Hagobian et al. 2004).

7.1.2 Sweating

Profuse sweating is a common complaint among people with SCI and research has documented that many experience periodic increased sweating associated with AD, orthostatic hypotension, or posttraumatic syringomyelia (Khurana, 1987, Jane et al. 1982, Kramer & Levine 1997). Although the most common pattern in SCI is excessive sweating above the lesion level, sweating below the lesion level can also occur. These likely represent different autonomic mechanisms, the pathways of which have not yet been clarified.

7.2 Bradycardia

The central autonomic input (both sympathetic and parasympathetic) is crucial for cardiovascular control; therefore, spinal cord injuries can interfere with its function (Henrich, 1982; Lehmann et al. 1987). Bradycardia, defined as a heart rate of less than 60 bpm, is a common cardiovascular complication that is often lesion-dependent and unique to each SCI. Generally, higher-level injuries result in greater degrees of cardiovascular impairment; investigators have also reported a higher incidence of bradycardia in persons with tetraplegia than in persons with paraplegia (Mirkowski et al. 2018; Dixit, 1995; Biering-Sørensen et al. 2017). The relationship between injury completeness and the resulting cardiovascular dysregulation is less well-understood, no clear association has yet been established even though researchers have reported ECG abnormalities in the SCI population compared with the non-SCI population (West et al. 2013; Prakash et al. 2002).

It should be emphasized that bradycardia and other dysrhythmias, particularly atrial fibrillation, could also occur during episodes of AD in individuals with high-level SCI and may require immediate pharmacological intervention (Pine et al. 1991; Forrest, 1991). Current pharmacological management of bradycardia in individuals with SCI involves the use of different agents including phosphodiesterase inhibitors (e.g., aminophylline, theophylline) and chronotropic agents (e.g., atropine, epinephrine, and norepinephrine) (Mirkowski et al. 2018). Further, for those who do not respond to pharmacologic treatment, cardiac pacemakers for bradycardia may be implanted (Evans et al. 2014; Franga et al. 2006; Ruiz-Arango et al. 2006; Sadaka et al. 2010; Wood et al. 2014).

8 "Boosting" – Autonomic Dysreflexia in Sport

Definition and Background:

In disability sport, there is a performance enhancement method known as "Boosting," which is when someone intentionally causes a bout of Autonomic Dysreflexia (AD) to improve athletic performance (Gee et al. 2018; Nightingale et al. 2022; Gee et al. 2015; Mills & Krassioukov 2011; Blauwet et al. 2013).

Most people with SCI, often those with injuries at T6 or above, cannot regulate blood pressure and heart rate in the same way as others (Fossey et al. 2022; West et al. 2013). Athletes that excel in sports often have superior cardiac output and/or oxygen uptake. During competition, a wheelchair athlete's heart rate may not increase according to the body's demands, resulting in low blood pressure, fatigue, and often a loss of endurance and poor performance.

What Happens:

Some athletes have learned that they can subvert these cardiovascular dysfunctions and increase their blood pressure and other cardiac outputs (in the short-term) by causing pain or discomfort in an area below their injury. Athletes with SCI may do this by:

- Clamping of the urinary catheter to produce bladder distension
- Excessive tightening of the leg straps
- Twisting and/or sitting on the scrotum
- Breaking their big toe before the competition
- Abdominal binders or pressure stockings on legs

Consequences:

Athletes with SCI who self-inflict physical suffering in order to improve athletic performance take tremendous health risks (i.e., hypertension, cerebral hemorrhage, stroke and sudden death).

Two case studies on boosting have shown enhanced athletic performance (Nightingale et al. 2022; Gee et al. 2018). A male wheelchair rugby athlete who had unintentionally boosted via bladder overdistension showed considerably higher average HR during 20m sprints compared to when 'unboosted' (Gee et al. 2018). Similarly, a male with SCI performing cardiopulmonary exercise testing (CPET) unintentionally boosted, resulting in relative tachycardia with an increase of 8.1-17.5% in peak HR (Nightingale et al. 2022). In both cases, performance was marginally enhanced; the rugby athlete sprinted faster than when 'unboosted' (6.7s vs 6.87s) (Gee et al. 2018), and the male performing CPET showed elevated power output (Δ19W), oxygen intake (Δ3.61 ml· kg·$^{-1}$min^{-1}) and ventilation (Δ11.4 L ·min^{-1}) compared to when 'unboosted' (Nightingale et al. 2022).

In a study of 99 athletes with SCI, 54.5% had previously heard of AD while 39.4% were unaware; 16.7% (all males) had used AD to enhance performance, despite participants reporting that AD is somewhat dangerous (48.9%), dangerous (21.3%), or very dangerous (25.5%) to health (Bhambhani et al. 2010). These findings indicate the need for educational programs directed towards enhancing knowledge on AD in rehabilitation professionals, coaches, and trainers working with individuals with SCI (Bhambhani et al. 2010).

The International Paralympic Committee considers AD doping and has banned its use. Any deliberate attempt to induce AD, if detected, will lead to disqualification from the sporting event and subsequent investigation by the IPC Legal and Ethics Committee.

9 Complications

Table 23. Complications

Author Year; Country Score Research Design Sample Size	Methods	Outcome
Wan & Krassioukov 2014 Canada Systematic (Clinical) Review Level 1 N=26	**Methods:** Keyword search on PubMed as well as manual searches of retrieved articles. Outcomes were categorised into three main classes: central nervous system (CNS), cardiovascular (CV), and pulmonary. **Databases:** PubMed	1. 26 manuscripts describing 32 cases of life-threatening complications or death associated with episodes of AD were identified. 2. 7 cases resulted in death, 6 of which were due to CNS-related complications, and the remaining death was due to pulmonary edema. 3. 23 cases of CNS-related complications following episodes of AD, most commonly hemorrhage, which occurred in 11 of the cases. Cerebral ischemia/ infarction occurred in four, seizures or convulsions were described in 9, and one case experienced both seizure and hemorrhage. 4. 7 cases of CV complications (none resulting in death) including one case of cardiac arrest, 5 cases involving arrhythmia, and one case resulting in silent myocardial ischemia. 5. 2 cases of pulmonary complications, specifically pulmonary edema, were identified.

Author Year; Country Score Research Design Sample Size	Methods	Outcome
Dolinak & Balraj 2007 USA Case report Level 5 N=1	**Population:** One 62-year-old male with tetraplegia **Treatment:** Nitroglycerin paste **Outcome measures:** BP	1. Patient was hospitalised for extended care due to chronic complications, and experienced AD characterized by labile hypertension with intermittent episodes of severe hypertension (BP escalating into the 200-230 mmHg/ 100-120mmHg range). These episodes were accompanied by abrupt and intense headaches, followed by abnormal mental status, and was treated with nitroglycerine paste. 2. CT scan of the head revealed a hemorrhage in the right caudate nucleus that had ruptured into the ventricles, resulting in severe subarachnoid hemorrhage. 3. The decision was made to withdraw care and he passed soon after.

Discussion

Two studies reported the complications that may result from bouts of AD in individuals with SCI (Wan & Krassioukov 2014; Dolinak & Balraj 2007). In a systematic review of clinical studies, Wan and Krassioukov (2014) found CNS-related, CV, and pulmonary complications following episodes of AD. CNS-related complications were most commonly hemorrhage, but cerebral ischemia/ infarction and seizures or convulsions were also present (Wan & Krassioukov 2014). CV complications included cardiac arrest, arrhythmia, and silent myocardial ischemia; while pulmonary complications identified were pulmonary edemas (Wan & Krassioukov 2014). A case study by Dolinak and Balraj (2007) found that episodes of AD in a 62-year-old male were accompanied by abrupt and intense headaches, abnormal mental status, and resulted in a severe subarachnoid hemorrhage and death, despite treatment with nitroglycerin paste.

Conclusion

There is level 1 evidence (from one systematic review) (Wan & Krassioukov 2014) that cases of AD may result in CNS-related, CV, and pulmonary complications, including those resulting in death.

There is level 5 evidence (from one case report) (Dolinak & Balraj 2007) that AD episodes were accompanied by headaches, followed by abnormal mental status, resulting in a severe subarachnoid hemorrhage and death.

References

Ackery A, Tator C, Krassioukov. A global perspective on spinal cord injury epidemiology. J Neurotrauma 2004; 21:1355-1370.

Ahmed HU, Shergill IS, Arya M, Shah PJ. Management of detrusor-external sphincter dyssynergia. Nat Clin Pract Urol 2006; 3: 368-380.

Alexander M, Biering-Sorensen, F, Bodner, D, Brackett, N, Cardenas, D, Charlifue, S, Creasey, G, Dietz, V, Ditunno, J, Donovan, W, Elliott, S, Estores, I, Graves, D, Green, B, Gousse, A, Jackson, A, Kennelly, M, Karlsson, A, Krassioukov, A, Krogh, K, Linsenmeyer, T, Marino, R, Mathias, C, Perkash, I, Sheel, A, Schilero, G, Schurch, B, Sonksen, J, Stiens, S, Wecht, J, Wuermser, L, Wyndaele, J. International standards to document remaining autonomic function after spinal cord injury. Spinal Cord 2009; 47(1), 36–43.

American College of Obstetrics and Gynecology. ACOG committee opinion. Obstetric management of patients with spinal cord injuries. Number 275, September 2002. Committee on Obstetric Practice. American College of Obstetrics and Gynecology. Int J Gynaecol Obstet 2002; 79: 189-191.

Anton HA, Townson A. Drug therapy for autonomic dysreflexia. CMAJ 2004; 170: 1210.

Arnold JM, Feng QP, Delaney GA, Teasell RW. Autonomic dysreflexia in tetraplegic patients: evidence for alpha-adrenoceptor hyper-responsiveness. Clin Auton Res 1995; 5: 267-270.

Ashley EA, Laskin JJ, Olenik LM, Burnham R, Steadward RD, Cumming DC, Wheeler GD. Evidence of autonomic dysreflexia during functional electrical stimulation in individuals with spinal cord injuries. Paraplegia 1993; 31: 593-605.

Barton CH, Khonsari F, Vaziri ND, Byrne C, Gordon S, Friis R. The effect of modified transurethral sphincterotomy on autonomic dysreflexia. J Urol 1986; 135: 83-85.

Bhambhani Y, Mactavish J, Warren S, Thompson WR, Webborn A, Bressan E, De Mello MT, Tweedy S, Malone L, Frojd K, Van De Vliet P, Vanlandewijck Y. Boosting in athletes with high-level spinal cord injury: knowledge, incidence and attitudes of athletes in paralympic sport. Disabil Rehabil. 2010; 32(26): 2172-90.

Biering-Sørensen F, Biering-Sørensen T, Liu N, Malmqvist L, Wecht JM, Krassioukov A. Alterations in cardiac autonomic control in spinal cord injury. Auton Neurosci. 2017 Feb 15. pii: S1566-0702(17)30044-9. doi: 10.1016/j.autneu.2017.02.004. [Epub ahead of print]

Blackmer J. Rehabilitation medicine: 1. Autonomic dysreflexia. CMAJ 2003; 169: 931-935.

Bladder management for adults with spinal cord injury: A clinical practice guideline for health-care providers. Consortium for Spinal Cord Medicine. Paralyzed Veterans of America; 2006.

Blauwet CA, Benjamin-laing H, Stomphorst J, Van de vliet P, Pit-grosheide P, Willick SE. Testing for boosting at the Paralympic games: policies, results and future directions. Br J Sports Med. 2013;47(13):832-7.

Boot CR, Binkhorst RA, Hopman MT. Body temperature responses in spinal cord injured individuals during exercise in the cold and heat. Int J Sports Med 2006 Aug;27(8):599-604.

Braddom RL, Rocco JF. Autonomic dysreflexia. A survey of current treatment. Am J Phys Med Rehabil 1991; 70: 234-241.

Calderón-Juárez M, Miller T, Samejima S, Shackleton C, Malik RN, Sachdeva R, Dorey TW, Krassioukov AV. Heart Rate Variability-Based Prediction of Autonomic Dysreflexia After Spinal Cord Injury. J Neurotrauma. 2024 May;41(9-10):1172-1180. doi: 10.1089/neu.2023.0583. Epub 2024 Jan 31. PMID: 38214089.

Chancellor MB, Erhard MJ, Hirsch IH, Stass WE. Prospective evaluation of terazosin for the treatment of autonomic dysreflexia. J Urol 1994; 151: 111-113.

Chancellor MB, Rivas DA, Erhard MJ, Hirsch IH, Bagley DH. Flexible cystoscopy during urodynamic evaluation of spinal cord-injured patients. J Endourol 1993; 7: 531-535.

Chen Q, Li F, Fang Z, Zhang Z, Zhang Y, Wu W, Yao G. Timing of surgical decompression for acute traumatic cervical spinal cord injury: a multicenter study. Neurosurg Q 2012; 22: 61-68.

Chen SF, Kuo HC. Improvement in autonomic dysreflexia after detrusor onabotulinumtoxinA injections in patients with chronic spinal cord injuries. Tzu Chi Medical Journal 2012; 24: 201-204.

Chen SL, Bih LI, Huang YH, Tsai SJ, Lin TB, Kao YL. Effect of single botulinum toxin A injection to the external urethral sphincter for treating detrusor external sphincter dyssynergia in spinal cord injury. J Rehabil Med 2008; 40: 744-748.

Cívicos Sánchez N, Acera M, Murueta-Goyena A, Sagastibeltza N, Martínez R, Cuadrado M, Orueta A, Tijero B, Fernández T, Del Pino R, Gabilondo I, Jauregui Abrisqueta ML, Gómez Esteban JC. Quantitative analysis of dysautonomia in patients with autonomic dysreflexia. J Neurol. 2021 Aug;268(8):2985-2994. doi: 10.1007/s00415-021-10478-w. Epub 2021 Feb 25. PMID: 33634338.

Claydon VE, Krassioukov AV. Orthostatic hypotension and autonomic pathways after spinal cord injury. J Neurotrauma 2006; 23: 1713-1725.

Coggrave MJ, Ingram RM, Gardner BP, Norton CS. The impact of stoma for bowel management after spinal cord injury. Spinal Cord 2012; 50: 848-852.

Colachis SC 3rd, Otis SM. Occurrence of fever associated with thermoregulatory dysfunction after acute traumatic spinal cord injury. Am J Phys Med Rehabil. 1995;74(2): 114–19.

Consortium for Spinal Cord Medicine. Acute management of autonomic dysreflexia: Individuals with spinal cord injury presenting to health-care facilities. Paralyzed Veterans of America; 2001.

Consortium for Spinal Cord Medicine. Evaluation and management of autonomic dysreflexia and other autonomic dysfunctions: Preventing the highs and lows. In Clinical practice guidelines. Paralyzed Veterans of America; 2020.

Cosman BC, Vu TT, Plowman BK. Topical lidocaine does not limit autonomic dysreflexia during anorectal procedures in spinal cord injury: a prospective, double-blind study. Int J Colorectal Dis 2002; 17: 104-108.

Cosman BC, Vu TT. Lidocaine anal block limits autonomic dysreflexia during anorectal procedures in spinal cord injury: a randomized, double-blind, placebo-controlled trial. Dis Colon Rectum 2005; 48: 1556-1561.

Courtois F, Rodrigue X, Cote I, Boulet M, Vezina J-G, Charvier K, Dahan V. Sexual function and autonomic dysreflexia in men with spinal cord injuries: How should we treat?. Spinal Cord 2012; 50: 869-877.

Cross LL, Meythaler JM, Tuel SM, Cross AL. Pregnancy following spinal cord injury. West J Med 1991; 154: 607-611.

Cross LL, Meythaler JM, Tuel SM, Cross LA. Pregnancy, labor and delivery post spinal cord injury. Paraplegia 1992; 30: 890-902.

Currie KD, Hubli M, MacDonald MJ, Krassioukov AV. Associations between arterial stiffness and blood pressure fluctuations after spinal cord injury. Spinal Cord. 2019 Dec;57(12):1057-1063. doi: 10.1038/s41393-019-0316-y. Epub 2019 Jun 19. PMID: 31217517.

Curt A, Nitsche B, Rodic B, Schurch B, Dietz V. Assessment of autonomic dysreflexia in patients with spinal cord injury. J Neurol Neurosurg Psychiatry 1997; 62: 473-477.

Del Fabro AS, Mejia M, Nemunaitis G. An investigation of the relationship between autonomic dysreflexia and intrathecal baclofen in patients with spinal cord injury. J Spinal Cord Med. 2018 Jan;41(1):102-105. doi: 10.1080/10790268.2017.1314878. Epub 2017 Apr 13. PMID: 28406070; PMCID: PMC5810793.

DeVivo MJ, Krause JS, Lammertse DP. Recent trends in mortality and causes of death among persons with spinal cord injury. Arch Phys Med Rehabil 1999; 80: 1411-1419.

Dixit S. Bradycardia associated with high cervical spinal cord injury. Surg Neurol. 1995;43(5):514.

Dolinak D, Balraj E. Autonomic dysreflexia and sudden death in people with traumatic spinal cord injury. Am J Forensic Med Pathol. 2007 Jun;28(2):95-8. doi: 10.1097/PAF.0b013e3180600f99. PMID: 17525555.

Downey JA, Huckaba CE, Myers SJ, Darling RC. Thermoregulation in the spinal man. J Appl Physiol. 1973; 34(6):790–94.

Dykstra DD, Sidi AA, Anderson LC. The effect of nifedipine on cystoscopy-induced autonomic hyperrelfexia in patients with high spinal cord injuries. J Urol 1987; 138: 1155-1157.

Dykstra DD, Sidi AA, Scott AB, Pagel JM, Goldish GD. Effects of botulinum A toxin on detrusor-sphincter dyssynergia in spinal cord injury patients. J Urol 1988; 139: 919-922.

Ekland M, Krassioukov A, McBride KE, Elliott SL. Incidence of autonomic dysreflexia and silent autonomic dysreflexia in men with SCI undergoing sperm retrieval: Implications for clinical practice. J Spinal Cord Med 2008; 30: 43-50.

Elliott S, Krassioukov A. Malignant autonomic dysreflexia in spinal cord injured men. Spinal Cord 2006; 6: 386-392.

Eltorai I, Kim R, Vulpe M, Kasravi H, Ho W. Fatal cerebral hemorrhage due to autonomic dysreflexia in a tetraplegic patient: case report and review. Paraplegia 1992; 30: 355-360.

Eltorai IM, Wong DH, Lacerna M, Comarr, AE, Montroy R. Surgical aspects of autonomic dysreflexia. J Spinal Cord Med 1997; 20: 361-364.

Erickson RP. Autonomic hyperreflexia: pathophysiology and medical management. Arch Phys Med Rehabil 1980; 61: 431-440.

Esmail Z, Shalansky KF, Sunderji R, Anton H, Chambers K, Fish W. Evaluation of captopril for the management of hypertension in autonomic dysreflexia: a pilot study. Arch Phys Med Rehabil 2002; 83: 604-608.

Evans CH, Duby JJ, Berry AJ, Schermer CR, Cocanour CS. Enteral albuterol decreases the need for chronotropic agents in patients with cervical spinal cord injury-induced bradycardia. J Trauma Acute Care Surg, 2014;76(2):297-302.

Forrest GP. Atrial fibrillation associated with autonomic dysreflexia in patients with tetraplegia. Arch Phys Med Rehabil. 1991;72(8):592–594.

Fossey MPM, Balthazaar SJT, Squair JW, Williams AM, Poormasjedi-Meibod MS, Nightingale TE, Erskine E, Hayes B, Ahmadian M, Jackson GS, Hunter DV, Currie KD, Tsang TSM, Walter M, Little JP, Ramer MS, Krassioukov AV, West CR. Spinal cord injury impairs cardiac function due to impaired bulbospinal sympathetic control. Nat Commun. 2022 Mar 16;13(1):1382. doi: 10.1038/s41467-022-29066-1. PMID: 35296681; PMCID: PMC8927412.

Fougere RJ, Currie KD, Nigro MK, Stothers L, Rapoport D, Krassioukov AV. Reduction in Bladder-Related Autonomic Dysreflexia after OnabotulinumtoxinA Treatment in Spinal Cord Injury. J Neurotrauma. 2016;33(18):1651-7.

Franga DL, Hawkins ML, Medeiros RS, Adewumi D. Recurrent asystole resulting from high cervical spinal cord injuries. Am Surgeon, 2006;72(6):525-9.

Frankel HL, Mathias CJ. Severe hypertension in patients with high spinal cord lesions undergoing electroejaculation - management with prostaglandin E2. Paraplegia 1980; 18: 293-299.

Frost F. Antihypertensive therapy, nifedipine, and autonomic dysreflexia. Arch Phys Med Rehabil 2002; 83: 1325-1326.

Furlan JC, Fehlings MG, Shannon P, Norenberg MD, Krassioukov AV. Descending vasomotor pathways in humans: Correlation between axonal preservation and cardiovascular dysfunction after spinal cord injury. J Neurotrauma 2003; 20: 1351-1363.

Furusawa K, Sugiyama H, Ikeda A, Tokuhiro A, Koyoshi H, Takahashi M, Tajima F. Autonomic dysreflexia during a bowel program in patients with cervical spinal cord injury. Acta Medica Okayama 2007; 61: 221-227.

Furusawa K, Sugiyama H, Tokuhiro A, Takahashi M, Nakamura T, Tajima F. Topical anesthesia blunts the pressor response induced by bowel manipulation in subjects with cervical spinal cord injury. Spinal Cord 2009;47:144-148.

Furusawa K, Tokuhiro A, Sugiyama H, Ikeda A, Tajima F, Genda E, Uchida R, Tominaga T, Tanaka H, Magara A, Sumida M. Incidence of symptomatic autonomic dysreflexia varies according to the

bowel and bladder management techniques in patients with spinal cord injury. Spinal Cord. 2011 Jan;49(1):49-54. doi: 10.1038/sc.2010.94. Epub 2010 Aug 10. PMID: 20697419.

Gee C.M., Lacroix M.A. & West C.R. (2018). Effect of Unintentional Boosting on Exercise Performance in a Tetraplegic Athlete. Medicine and science in sports and exercise, 50(12), 2398-2400. https://doi.org/10.1249/MSS.0000000000001738

Gee CM, West CR, Krassioukov AV. Boosting in Elite Athletes with Spinal Cord Injury: A Critical Review of Physiology and Testing Procedures. Sports Med. 2015;45(8):1133-42.

Giannantoni A, Di Stasi SM, Scivoletto G, Mollo A, Silecchia A, Fuoco U, Vespasiani G. Autonomic dysreflexia during urodynamics. Spinal Cord 1998;36:756-860.

Giannantoni A, Di Stasi SM, Stephen RL, Navarra P, Scivoletto G, Mearini E, Porena M. Intravesical capsaicin versus resiniferatoxin in patients with detrusor hyperreflexia: a prospective randomized study. J Urol 2002; 167: 1710-1714.

Gray K, Sheehan W, McCracken L, Krogh K, Sachdeva R, Krassioukov AV. Are local analgesics effective in reducing autonomic dysreflexia in individuals with spinal cord injury? A systematic review. Spinal Cord. 2023 Jan;61(1):1-7. doi: 10.1038/s41393-022-00840-8. Epub 2022 Aug 12. PMID: 35962043.

Grossman E, Messerli FH, Grodzicki T, Kowey P. Should a moratorium be placed on sublingual nifedipine capsules given for hypertensive emergencies and pseudoemergencies? JAMA 1996; 276: 1328-1331.

Guly HR, Bouamra O, Lecky FE. The incidence of neurogenic shock in patients with isolated spinal cord injury in the emergency department. Resuscitation. 2008;76(1):57-62.

Guttman L. Spinal cord injuries: Comprehensive management and research. 2nd ed. Philadelphia (PA): Blackwell Science Ltd; 1976.

Hagobian TA, Jacobs KA, Kiratli BJ, Friedlander AL. Foot cooling reduces exercise-induced hyperthermia in men with spinal cord injury. Med Sci Sports Exerc. 2004;36(3): 411–17.

Hanrakis JP, Rosado-Rivera D, Singh K, Swonger K, Azarelo F, Lombard AT, Spungen AM, Kirshblum SC, Bauman WA. Self-reported effects of cold temperature exposure in persons with tetraplegia. Journal of Spinal Cord Medicine 2016, Issue TBD: Published online: 08 Mar 2016.

Hawkins RL Jr, Bailey HR, Donnovan WH. Autonomic dysreflexia resulting from prolapsed hemorrhoids. Report of a case. Dis Colon Rectum 1994; 37: 492-493.

Henrich WL. Autonomic insufficiency. Arch Intern Med 1982;142: 339-44.

Herrity AN, Aslan SC, Ugiliweneza B, Mohamed AZ, Hubscher CH, Harkema SJ. Improvements in Bladder Function Following Activity-Based Recovery Training With Epidural Stimulation After Chronic Spinal Cord Injury. Front Syst Neurosci. 2021 Jan 5;14:614691. doi: 10.3389/fnsys.2020.614691. PMID: 33469421; PMCID: PMC7813989.

Ho CP, Krassioukov AV. Autonomic dysreflexia and myocardial ischemia. Spinal Cord 2010; 48: 714-715.

Hohenfellner M, Pannek J, Botel U, Bahms S, Pfitzenmaier J, Fichtner J, et al. Sacral bladder denervation for treatment of detrusor hyperreflexia and autonomic dysreflexia. Urol 2001; 58: 28-32.

Huang M, Zheng H, Huang T, Yang X, Liu Q, Li Q, Tang P, Xie K, Chen H. Intravesical injection of botulinum toxin type a may be an effective treatment option for autonomic dysreflexia in patients with high-level spinal cord injury. J Spinal Cord Med. 2024 Jan;47(1):74-78. doi: 10.1080/10790268.2022.2135230. Epub 2022 Oct 21. PMID: 36269317; PMCID: PMC10795643.

Hughes SJ, Short DJ, Usherwood MM, Tebbutt H. Management of the pregnant woman with spinal cord injuries. Br J Obstet Gynaecol 1991; 98: 513-518.

Huh S, Ko HY. Determinants of prolonged baseline blood pressure restoration following autonomic dysreflexia for individuals with spinal cord injuries. J Spinal Cord Med. 2024 Apr 3:1-8. doi: 10.1080/10790268.2024.2335693. Epub ahead of print. PMID: 38568108.

Igawa Y, Satoh T, Mizusawa H, Seki S, Kato H, Ishizuka O, Nishizawa O. The role of capsaicin-sensitive afferents in autonomic dysreflexia in patients with spinal cord injury. BJU Int 2003; 91: 637-641.

Jackson AB, Wadley V. A multicenter study of women's self-reported reproductive health after spinal cord injury. Arch Phys Med Rehabil 1999; 80: 1420-1428.

Jane MJ, Freehafer AA, Hazel C, Lindan R, Joiner E. Autonomic dysreflexia. A cause of morbidity and mortality in orthopedic patients with spinal cord injury. Clin Orth Relat Res. 1982;(169):151–154.

Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. Arch Intern Med 1997; 157: 2413–2445.

Jones NA, Jones SD. Management of life-threatening autonomic hyper-reflexia using magnesium sulphate in a patient with a high spinal cord injury in the intensive care unit. Br J Anaesth 2002; 88: 434-438.

Kabalin JN, Lennon S, Gill HS, Wolfe V, Perkash I. Incidence and management of autonomic dysreflexia and other intraoperative problems encountered in spinal cord injury patients undergoing extracorporeal shock wave lithotripsy without anesthesia on a second generation lithotriptor. J Urol 1993; 149: 1064-1067.

Karlsson AK. Autonomic dysreflexia. Spinal Cord 1999; 37: 383-391.

Ke QS, Kuo HC. Transurethral incision of the bladder neck to treat bladder neck dysfunction and voiding dysfunction in patients with high-level spinal cord injuries. Neuro Uro 2010; 29: 748-752.

Khan S, Plummer M, Martinez-Arizala A, Banovac K. Hypothermia in patients with chronic spinal cord injury. J Spinal Cord Med. 2007; 30(1): 27–30.

Khurana RK. Orthostatic hypotension-induced autonomic dysreflexia. Neurology. 1987;37(7):1221–24.

Kim JH, Rivas DA, Shenot PJ, Green B, Kennelly M, Erickson, JR, O'Leary M, Yoshimura N, Chancellor MB. Intravesical resiniferatoxin for refractory detrusor hyperreflexia: a multicenter, blinded, randomized, placebo-controlled trial. J Spinal Cord Med 2003; 26: 358-363.

Kofler M, Poustka K, Leopold S. Intrathecal baclofen for autonomic instability due to spinal cord injury. Autonomic Neuroscience: Basic and Clinical 2009; 146: 106-110.

Kramer KM, Levine AM. Posttraumatic syringomyelia: A review of 21 cases. Clin Orthop Relat Res. 1997;(334):190–99.

Krassioukov, A, Biering-Sorensen, F, Donovan, W, Kennelly, M, Kirshblum, S, Krogh, K, Alexander, M, Vogel, L, Wecht, J. (2012). International standards to document remaining autonomic function after spinal cord injury (ISAFSCI), First Edition 2012. Top Spinal Cord Inj Rehabil 18, 283–296.

Krassioukov AV, Bunge RP, Ruckett WR, Bygrave MA. The changes in human spinal cord sympathetic preganglionic neurons after spinal cord injury. Spinal Cord 1999; 37: 6-13.

Krassioukov A, Claydon VE. The clinical problems in cardiovascular control following spinal cord injury: an overview. Prog Brain Res 2006; 152: 223-229.

Krassioukov AV, Furlan JC, Fehlings MG. Autonomic dysreflexia in acute spinal cord injury: an under-recognized clinical entity. J Neurotrauma 2003; 20: 707-16.

Krassioukov AV, Harkema SJ. Effect of harness application and postural changes on cardiovascular parameters of individuals with spinal cord injury. Spinal Cord 2006; 44: 780-6.

Krassioukov AV, Johns DG, Schramm LP. Sensitivity of sympathetically correlated spinal interneurons, renal sympathetic nerve activity, and arterial pressure to somatic and visceral stimuli after chronic spinal injury. J Neurotrauma 2002; 19: 1521-1529.

Krassioukov AV, Karlsson AK, Wecht JM, Wuermser LA, Mathias CJ, Marino RJ. Assessment of autonomic dysfunction following spinal cord injury: Rationale for additions to International Standards for Neurological Assessment. Journal of Rehabilitation Research and Development, 44 (1), 2007; 103-112.

Krassioukov A, Linsenmeyer TA, Beck LA, Elliott S, Gorman P, Kirshblum S, Vogel L, Wecht J, Clay S. Evaluation and Management of Autonomic Dysreflexia and Other Autonomic Dysfunctions: Preventing the Highs and Lows: Management of Blood Pressure, Sweating, and Temperature Dysfunction. Top Spinal Cord Inj Rehabil. 2021 Spring;27(2):225-290. doi: 10.46292/sci2702-225. PMID: 34108837; PMCID: PMC8152175.

Krassioukov A, Stillman M, Beck LA. A Primary Care Provider's Guide to Autonomic Dysfunction Following Spinal Cord Injury. Top Spinal Cord Inj Rehabil. 2020 Spring;26(2):123-127. doi: 10.46292/sci2602-123. PMID: 32760191; PMCID: PMC7384539.

Krassioukov A, Warburton DE, Teasell R, Eng JJ. A systematic review of the management of autonomic dysreflexia after spinal cord injury. Arch Phys Med Rehabil 2009; 90: 682-695.

Krassioukov A. Which pathways must be spared in the injured human spinal cord to retain cardiovascular control? Prog Brain Res 2006; 152: 39-47.

Krum H, Louis WJ, Brown DJ, Howes LG. A study of the alpha-1 adrenoceptor blocker prazosin in the prophylactic management of autonomic dysreflexia in high spinal cord injury patients. Clin Auton Res 1992; 2: 83-88.

Kuo HC. Satisfaction with urethral injection of botulinum toxin A for detrusor sphincter dyssynergia in patients with spinal cord lesion. Neurourol Urodyn 2008; 27: 793-796.

Kutzenberger J. Surgical therapy of neurogenic detrusor overactivity (hyperreflexia) in paraplegic patients by sacral deafferentation and implant driven micturition by sacral anterior root stimulation: methods, indications, results, complications, and future prospects. Acta Neurochir Suppl 2007; 97: 333-339.

Lambert DH, Deane RS, Mazuzan JE. Anesthesia and the control of blood pressure in patients with spinal cord injury. Anesth Analg 1982; 61: 344-348.

Lehmann KG, Lane JG, Piepmeier JM, Batsford WP. Cardiovascular abnormalities accompanying acute spinal cord injury in humans: Incidence, time course and severity. *J Am Coli Cardiol 1987;10:46-52*.

Lindan R, Leffler EJ, Kedia KR. A comparison of the efficacy of an alpha - I - adrenergic blocker in the slow calcium channel blocker in the control of autonomic dysreflexia. Paraplegia 1985; 23: 34-38.

Linsenmeyer TA, Campagnolo DI, Chou IH. Silent autonomic dysreflexia during voiding in men with spinal cord injuries. J Urol 1996; 155: 519-22.

Liu N, Zhou M, Biering-Sørensen F, Krassioukov AV. Iatrogenic urological triggers of autonomic dysreflexia: a systematic review. Spinal cord. 2015 Jul 1;53(7):500-9.

Maehama T, Izena H, Kanazawa K. Management of autonomic hyperreflexia with magnesium sulfate during labor in a woman with spinal cord injury. Am J Obstet Gynecol 2000; 183: 492-493.

Mathias CJ, Bannister R. Autonomic disturbances in spinal cord lesions. In: Bannister R, Mathias CJ. (ed). Autonomic Failure: A Textbook of Clinical Disorders of the Autonomic Nervous System. Oxford University Press, NYC NY, 2002, p 839-881.

Mathias CJ, Frankel HL. Cardiovascular control in spinal man. Ann Rev Physiol 1988; 50: 577-592.

Mathias CJ, Frankel HL(2002). Autonomic disturbances in spinal cord lesions. In: Bannister R, Mathias CJ. (Ed). Autonomic Failure: A Text book of Clinical Disorders of the Autonomic Nervous System. Oxford University Press, NYC NY p839-881.

Matthews JM, Wheeler GD, Burnham RS, Malone LA, Steadward RD. The effects of surface anaesthesia on the autonomic dysreflexia response during functional electrical stimulation. Spinal Cord 1997; 35: 647-651.

McGillivray CF, Hitzig SL, Craven BC, Tonack MI, Krassioukov AV. Evaluating knowledge of autonomic dysreflexia among individuals with spinal cord injury and their families. J Spinal Cord Med. 2009;32:54-62.

McGregor JA, Meeuwsen, J. Autonomic hyperreflexia: a mortal danger for spinal cord-damaged women in labor. Am J Obstet Gynecol 1985;151:330-333.

McGuire J, Wagner FM, Weiss RM. Treatment of autonomic dysreflexia with phenoxybenzamine. J Urol 1976; 115: 53-55.

McGuire TJ, Kumar VN. Autonomic dysreflexia in the spinal cord-injured. What the physician should know about this medical emergency. Postgrad Med 1986; 80: 81-84, 89.

Mills PB, Krassioukov A. Autonomic function as a missing piece of the classification of paralympic athletes with spinal cord injury. Spinal Cord. 2011;49(7):768-76.

Mirkowski M, Faltynek P, Benton B, McIntyre A, Krassioukov A, Teasell RW. (2018). Cardiovascular Complications during the Acute Phase of Spinal Cord Injury. In Eng JJ, Teasell RW, Miller WC, Wolfe DL, Townson AF, Hsieh JTC, Noonan VK, Mortenson WB, Loh E, Querée M, McIntyre A, editors. Spinal Cord Injury Research Evidence. Version 7.0: p 1-24).

Naftchi NE, Richardson JS. Autonomic dysreflexia: pharmacological management of hypertensive crises in spinal cord injured patients. J Spinal Cord Med 1997; 20: 355-360.

Nightingale TE, Eginyan G, Balthazaar SJT, Williams AMM, Lam T, Krassioukov AV. Accidental boosting in an individual with tetraplegia - considerations for the interpretation of cardiopulmonary exercise testing. J Spinal Cord Med. 2022 Nov;45(6):969-974. doi: 10.1080/10790268.2020.1871253. Epub 2021 Jan 29. PMID: 33513073; PMCID: PMC9661994.

Osborn JW, Taylor RF, Schramm LP. Chronic cervical spinal cord injury and autonomic hyperreflexia in rats. Am J Physiol 1990; 258: R169-R174.

Pannek J, Gocking K, Bersch U. Clinical Usefulness of the Memokath Stent as a Second-Line Procedure After Sphincterotomy Failure. J Endour 2011; 25: 335-339.

Paola FA, Sales D, Garcia-Zozaya I. Phenazopyridine in the management of autonomic dysreflexia associated with urinary tract infection. J Spinal Cord Med 2003; 26: 409-411.

Pasquina PF, Hkowouston RM, Belandres PV. Beta blockade in the treatment of autonomic dysreflexia: a case report and review. Arch Phys Med Rehabil 1998; 79: 582-584.

Perkash I. Transurethral sphincterotomy provides significant relief in autonomic dysreflexia in spinal cord injured male patients: Long-term followup results. J Urol 2007; 177: 1026-1029.

Phillips AA, Elliott SL, Zheng MM, Krassioukov AV. Selective alpha adrenergic antagonist reduces severity of transient hypertension during sexual stimulation after spinal cord injury. Journal of neurotrauma. 2015 Mar 15;32(6):392-6.

Pine ZM, Miller SD, Alonsa JA. Atrial fibrillation associated with autonomic dysreflexia. Am J Phys Med Rehabil 1991; 70: 271-273.

Pino IP, Nightingale TE, Hoover C, Zhao Z, Cahalan M, Dorey TW, Walter M, Soriano JE, Netoff TI, Parr A, Samadani U, Phillips AA, Krassioukov AV, Darrow DP. The safety of epidural spinal cord stimulation to restore function after spinal cord injury: post-surgical complications and incidence of cardiovascular events. Spinal Cord. 2022 Oct;60(10):903-910. doi: 10.1038/s41393-022-00822-w. Epub 2022 Jun 14. PMID: 35701485.

Prakash M, Raxwal V, Froelicher VF, Kalisetti D, Vieira A, O'Mara G, Marcus R, Myers J, Kiratli J, Perkash I. Electrocardiographic findings in patients with chronic spinal cord injury. Am J Phys Med Rehabil. 2002;81(8):601–8.

Price MJ, Campbell IG. Effects of spinal cord lesion level upon thermoregulation during exercise in the heat. Med Sci Sports Exerc. 2003;35(7):1100–1107.

Ravindran RS, Cummins DF, Smith IE. Experience with the use of nitroprusside and subsequent epidural analgesia in a pregnant quadriplegic patient. Anesth Analg 1981; 60: 61-63.

Ruiz-Arango AF, Robinson VJB, Sharma GK. Characteristics of patients with cervical spinal injury requiring permanent pacemaker implantation. Cardiol Rev, 2006;14(4):e8-11.

Sadaka F, Naydenov SK, Ponzillo JJ. Theophylline for bradycardia secondary to cervical spinal cord injury. Neurocrit Care, 2010;13(3):389-92.

Samejima S, Shackleton C, Malik RN, Cao K, Bohorquez A, Nightingale TE, Sachdeva R, Krassioukov AV. Spinal Cord Stimulation Prevents Autonomic Dysreflexia in Individuals with Spinal Cord Injury: A Case Series. J Clin Med. 2023 Apr 16;12(8):2897. doi: 10.3390/jcm12082897. PMID: 37109234; PMCID: PMC10146034.

Sampson EE, Burnham RS, Andrews BJ. Functional electrical stimulation effect on orthostatic hypotension after spinal cord injury. Arch Phys Med Rehabil 2000; 81: 139-143.

Schmidt KD, Chan CW. Thermoregulation and fever in normal persons and in those with spinal cord injuries. Mayo Clin Proc. 1992;67(5):469–75.

Schurch B, Knapp PA, Jeanmonod D, Rodic B, Rossier AB. Does sacral posterior rhizotomy suppress autonomic hyper-reflexia in patients with spinal cord injury? Br J Urol 1998; 81: 73-82.

Schurch B, Stohrer M, Kramer G, Schmid DM, Gaul G, Hauri D. Botulinum-A toxin for treating detrusor hyperreflexia in spinal cord injured patients: a new alternative to anticholinergic drugs? Preliminary results. J Urol 2000; 164: 692-697.

Seoane-Rodriguez S, Sanchez R-Losada J, Montoto-Marques A, Salvador-de la Barrera S, Ferreiro-Velasco ME, Alvarez-Castelo L, Balsa-Mosquera B, Rodriguez-Sotillo A. Long-term follow-up study of intraurethral stents in spinal cord injured patients with detrusor-sphincter dyssynergia. Spinal Cord 2007; 45: 621-626.

Sharpe EE, Arendt KW, Jacob AK, Pasternak JJ. Anesthetic management of parturients with pre-existing paraplegia or tetraplegia: a case series. International journal of obstetric anesthesia. 2015 Feb 28;24(1):77-84.

Sheel AW, Krassioukov AV, Inglis JT, Elliott SL. Autonomic dysreflexia during sperm retrieval in spinal cord injury: influence of lesion level and sildenafil citrate. J Appl Physiol 2005; 99: 53-58.

Sidi AA, Becher EF, Reddy PK, Dykstra DD. Augmentation enterocystoplasty for the management of voiding dysfunction in spinal cord injury patients. J Urol 1990; 143: 83-85.

Sidorov EV, Townson AF, Dvorak MF, Kwon BK, Steeves J, Krassioukov A. Orthostatic hypotension in the first month following acute spinal cord injury. Spinal Cord 2007. [Epub ahead of print].

Silver JR. Early autonomic dysreflexia. Spinal Cord 2000; 38: 229-233.

Sipski ML, Arenas A. Female sexual function after spinal cord injury. Prog Brain Res 2006; 152: 441-447.

Sipski ML. The impact of spinal cord injury on female sexuality, menstruation and pregnancy: a review of the literature. J Am Paraplegia Soc 1991; 14: 122-126.

Skowronski E, Hartman K. Obstetric management following traumatic tetraplegia: case series and literature review. Aust N Z J Obstet Gynaecol 2008; 48: 485-491.

Snow JC, Sideropoulos HP, Kripke BJ, Freed MM, Shah NK, Schlesinger RM. Autonomic hyperreflexia during cystoscopy in patients with high spinal cord injuries. Paraplegia 1978; 15: 327-332.

Solinsky R. Autonomic dysreflexia: Current pharmacologic management. PM R. 2023 Dec;15(12):1519-1523. doi: 10.1002/pmrj.13051. Epub 2023 Sep 13. PMID: 37545115; PMCID: PMC10841367.

Solinsky R, Linsenmeyer TA. Intravesical lidocaine decreases autonomic dysreflexia when administered prior to catheter change. J Spinal Cord Med. 2018 Sep 10;42(5):1-5. doi: 10.1080/10790268.2018.1518764. Epub ahead of print. PMID: 30199342; PMCID: PMC6758603.

Steinberger RE, Ohl DA, Bennett CJ, McCabe M, Wang SC. Nifedipine pretreatment for autonomic dysreflexia during electroejaculation. Urol 1990; 36: 228-231.

Swierzewski SJ, Gormley EA, Belville WD, Sweetser PM, Wan J, McGuire EJ. The effect of terazosin on bladder function in the spinal cord injured patient. J Urol 1994; 151: 951-954.

Teasell RW, Arnold JM, Krassioukov A, Delaney GA. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system following spinal cord injuries. Arch Phys Med Rehabil 2000;81:506-516.

Teichman JM, Barber DB, Rogenes VJ, Harris JM. Malone antegrade continence enemas for autonomic dysreflexia secondary to neurogenic bowel. J Spinal Cord Med 1998; 21: 245-247.

Thyberg M, Ertzgaard P, Gylling M, Granerus G. Effect of nifedipine on cystometry-induced elevation of blood pressure in patients with a reflex urinary bladder after a high level spinal cord injury. Paraplegia 1994; 32: 308-313.

Tuli S, Tuli J, Coleman WP, Geisler FH, Krassioukov A. Hemodynamic parameters and timing of surgical decompression in acute cervical spinal cord injury. J Spinal Cord Med. 2007;30(5):482-90.

Vaidyanathan S, Singh G, Soni BM, Hughes PL, Mansour P, Oo T, Bingley J, Sett P. Do spinal cord injury patients always get the best treatment for neuropathic bladder after discharge from regional spinal injuries centre? Spinal Cord 2004; 42: 438-442.

Vaidyanathan S, Soni BM, Dundas S, Krishnan KR. Urethral cytology in spinal cord injury patients performing intermittent catheterization. Paraplegia 1994;32:493-500.

Vaidyanathan S, Soni BM, Sett P, Watt JW, Oo T, Bingley J. Pathophysiology of autonomic dysreflexia: long-term treatment with terazosin in adult and paediatric spinal cord injury patients manifesting recurrent dysreflexic episodes. Spinal Cord 1998; 36: 761-770.

Vallès M, Benito J, Portell E, Vidal J. Cerebral hemorrhage due to autonomic dysreflexia in a spinal cord injury patient. Spinal Cord 2005;43:738-740.

van der Merwe A, Baalbergen E, Shrosbree R, Smit S, Heyns C. Outcome of dual flange metallic urethral stents in the treatment of neuropathic bladder dysfunction after spinal cord injury. J Endourol 2012; 26: 1210-1215.

Waites KB, Canupp KC, DeVivo MJ. Epidemiology and risk factors for urinary tract infection following spinal cord injury. Arch Phys Med Rehabil 1993a; 74: 691-695.

Waites KB, Canupp KC, DeVivo MJ. Eradication of urinary tract infection following spinal cord injury. Paraplegia 1993b; 31: 645-652.

Walter M, Knüpfer SC, Cragg JJ, Leitner L, Schneider MP, Mehnert U, Krassioukov AV, Schubert M, Curt A, Kessler TM. Prediction of autonomic dysreflexia during urodynamics: a prospective cohort study. BMC Med. 2018 Apr 13;16(1):53. doi: 10.1186/s12916-018-1040-8. PMID: 29650001; PMCID: PMC5898013.

Walter M, Kran SL, Ramirez AL, Rapoport D, Nigro MK, Stothers L, Kavanagh A, Krassioukov AV. Intradetrusor OnabotulinumtoxinA Injections Ameliorate Autonomic Dysreflexia while Improving Lower Urinary Tract Function and Urinary Incontinence-Related Quality of Life in Individuals with Cervical and Upper Thoracic Spinal Cord Injury. J Neurotrauma. 2020 Sep 15;37(18):2023-2027. doi: 10.1089/neu.2020.7115. Epub 2020 Jul 23. PMID: 32631152; PMCID: PMC7470218.

Walter M, Ramirez AL, Lee AHX, Nightingale TE, Rapoport D, Kavanagh A, Krassioukov AV. Fesoterodine Ameliorates Autonomic Dysreflexia While Improving Lower Urinary Tract Function and Urinary Incontinence-Related Quality of Life in Individuals With Spinal Cord Injury: A Prospective Phase IIa Study. J Neurotrauma. 2023 May;40(9-10):1020-1025. doi: 10.1089/neu.2022.0333. Epub 2022 Oct 25. PMID: 36178342.

Wan D, Krassioukov AV. Life-threatening outcomes associated with autonomic dysreflexia: a clinical review. J Spinal Cord Med. 2014 Jan;37(1):2-10. doi: 10.1179/2045772313Y.0000000098. Epub 2013 Nov 26. PMID: 24090418; PMCID: PMC4066548.

Wecht JM, Krassioukov AV, Alexander M, Handrakis JP, McKenna SL, Kennelly M, Trbovich M, Biering-Sorensen F, Burns S, Elliott SL, Graves D, Hamer J, Krogh K, Linsenmeyer TA, Liu N, Hagen EM, Phillips AA, Previnaire JG, Rodriguez GM, Slocum C, Wilson JR. International Standards to document Autonomic Function following SCI (ISAFSCI): Second Edition. Top Spinal Cord Inj Rehabil. 2021 Spring;27(2):23-49. doi: 10.46292/sci2702-23. PMID: 34108833; PMCID: PMC8152176.

West CR, Bellantoni A, Krassioukov AV. Cardiovascular function in individuals with incomplete spinal cord injury: a systematic review. Top Spinal Cord Inj Rehabil, 2013;19(4):267-78.

Wood DE, Dunkerley AL, Tromans AM. Results from bone mineral density scans in twenty-two complete lesion paraplegics. Spinal Cord 2001; 39: 145-148.

Wood GC, Boucher AB, Johnson JL, Wisniewski JN, Magnotti LJ, Croce MA, et al. Effectiveness of pseudoephedrine as adjunctive therapy for neurogenic shock after acute spinal cord injury: a case series. Pharmacotherapy, 2014;34(1):89-93.

Xiong Y, Yang S, Liao W, Song C, Chen L. Autonomic dysreflexia during cystolitholapaxy in patients with spinal cord injury. Minerva urologica e nefrologica= The Italian journal of urology and nephrology. 2015 Jun;67(2):85-90.

Yarkony GM, Katz RT, Wu Y. Seizures secondary to autonomic dysreflexia. Arch Phys Med Rehabil 1986; 67: 834-835.

Yoo KY, Jeong CW, Kim WM, Lee HK, Kim SJ, Jeong ST, Lee JK, Lee J. Fatal cerebral hemorrhage associated with autonomic hyperreflexia during surgery in the prone position in a quadriplegic patient: a case report. Minerva Anestesiol 2010; 76: 554-8.

Abbreviations

ACE	angiotensin I-converting enzyme
AD	autonomic dysreflexia
AIS	ASIA Impairment Scale
AUA	American Urological Association
BND	bladder neck disorder
BoNT-A	botulinum toxin A
BP	blood pressure
DBP	diastolic blood pressure
DESD	detrusor external sphincter dyssynergia
DVT	deep vein thrombus
ECG	electrocardiogram
eSCS	epidural spinal cord stimulation
FES	functional electrical stimulation
HR	heart rate
IEMG	integrated electromyography
IIQ-7	Incontinence Impact Questionnaire
IU	international unit (measurement unit of drugs)
IV	intravenous
MAP	mean arterial pressure
MCC	mean cystometric capacity
M/F	male/female
NBD	neurogenic bowel disorder
Para	paraplegic
PDE5	phosphodiesterase type 5
QoL	quality of life
RCT	randomized controlled trial
RTX	resiniferatoxin
SBP	systolic blood pressure
scES	spinal cord epidural stimulation
SCI	spinal cord injury
Tetra	tetraplegic
TURS	transurethral sphincterotomy
UDI-6	Urogenital Distress Inventory
UUT	upper urinary tract
UTI	urinary tract infection