Author Year Country Research Design Score Total Sample Size	Methods	Outcome
Wijesuriya et al. 2019 Australia RCT (crossover) PEDro = 8 Level 1 N = 12	**Population:** 12 male patients with chronic SCI; tetraplegia; AIS A (n = 9) or B (n = 3); mean (SD) age 52.1 (± 12.1) years; level of injury C4 (n = 3), C5 (n = 5), and C6 (n = 4); mean (SD) time since injury 22.3 (± 15.7) years; and OSA. **Treatment:** Two study visits were carried out in the participants' homes, with a 1-week washout period. At each visit, nasal spray (0.5 mL of 5% phenylephrine (PE) or placebo) was administered. **Outcome Measures:** Nasal resistance; overnight polysomnography (PSG) (apnea hypoapnea index, total sleep time, route of breathing, arousal index, 4% O_2 desaturation index, slow wave, and rapid eye movement (REM) sleep percentages, overnight respiratory and sleep events); and perceived nasal congestion (Borg-like scale of Nasal Obstruction and Congestion Quantifier five-item test).	1. Nasal resistance was reduced by 72% following administration of PE (p = 0.02; mean difference −5.20: 95% confidence interval −9.09, −1.32 $cmH_2O/L/s$). 2. No significant treatments effects were observed for apnea hypoapnea index, total sleep time, REM sleep time, arousal index, 4% O_2 desaturation index or route of breathing (in the first half of the night, or the full night) between nights where PE or placebo were administered. 3. Self-reported nasal blockage (p = 0.09; −0.88 (−2.09, 0.34) and the rate of obstructive apneas per hour (p = 0.15; −6.37 (−33.31, 20.58) were not significantly reduced following PE while overnight slow wave sleep was not significantly increased (p = 0.07; 9.88 (−4.30, 24.07)). 4. Raw PSG data demonstrated changes in sleep architecture and respiratory event severity with PE administration at an individual participant level. Nasal decongestion in all but one of the participants reduced respiratory event severity (apneas fell and

		hypopnoeas rose). The reduction in respiratory event severity with PE was not statistically significant (p = 0.28; mean difference −9.7%: 95% confidence interval −28.5, 9.1).
Maresh et al. 2020 USA RCT (crossover pilot) PEDro = 6 Level 2 N = 8	**Population:** 8 non-ventilator-dependent males with chronic SCI; mean (SD) time since injury 9.5 (± 8.5) years; mean (SD) age 47.6 (± 13.8) years; level of injury cervical (n = 5), and thoracic (n = 3); AIS A (n = 4), AIS B (n = 2), AIS C (n = 2); and sleep-disordered breathing (SDB) (AHI ≥ 5 events / h). **Intervention:** Each participant went on Trazodone (100 mg), Buspirone (30 mg), and placebo for 2 weeks each, with a washout period of ≥ 2 weeks. **Outcome Measures:** Overnight in-laboratory PSG, and induction of central sleep apnea using NIV or hypercapneia protocol. Indexes of SDB, CO_2 reserve, apneic threshold, hypocapnic chemoreflex sensitivity or controller gain, plant gain, and ventilatory parameters (V_E, V_T, breaths/min, MIP, inspiratory duration, expiratory duration, breath duration, fractional inspiratory time, $P_{ET}O_2$, $P_{ET}CO_2$, and oxyhemoglobin saturation) were assessed on a night study on day 13 of being on each medication.	1. CO_2 reserve was widened significantly on Buspirone compared with placebo (-3.6 ± 0.9 vs. -1.8 ± 1.5 mmHg, respectively, *P* < 0.001), and with Trazodone (-3.6 ± 0.9 vs. -2.5 ± 1.0 mmHg, respectively, *P* <0.009) but not on Trazadone compared with placebo (-2.5 ± 1.0 vs. -1.8 ± 1.5 mmHg, respectively, *P* = 0.061). 2. There were no significant changes in apneic threshold $P_{ET}CO_2$, and eupneic CO_2. 3. Buspirone significantly decreased controller gain compared with placebo (1.8 ± 0.4 vs. 4.0 ± 2.0 L/(mmHg· min) respectively, *P* = 0.025) but not Trazodone compared with placebo (2.5 ± 1.1 vs. 4.0 ± 2.0 L/(mmHg·min) respectively; *P* > 0.05). 4. Plant gain was not significantly different for either Buspirone (5.6 ± 1.1 mmHg·min/L, *P* > 0.05) or Trazodone (6.5 ± 2.0 mmHg·min/L, *P* > 0.05) compared with placebo (5.1 ± 1.7 mmHg·min/L). 5. There were also no significant differences between any of the interventions for apnea hypoapnea index, the

		central apnea index, obstructive apnea index, or oxygen desaturation index between groups.
Ginter et al. 2020 USA RCT (crossover) PEDro = 6 Level 2 N = 16	**Population:** 16 participants with evidence of SDB (apnea-hypopnea index ≥ 5 events/hour). Participants with SCI (n = 8): 7 males and 1 female; age 50.3 ± 12.8 years; SCI level cervical (n = 7), and thoracic (n = 1); ASIA A (n = 1), ASIA B (n = 2), ASIA C (n = 1) and ASIA D (n = 4); and mean (SD) time since injury 8.3 (± 4.7) years. Non-SCI participants (n = 8): 6 males and 2 females; age 59.5 ± 11.8 years. **Intervention:** Participants were randomized to receive oral acetazolamide (ACZ) 500 mg or placebo twice a day during a 3 days period. After completing the first drug arm, participants underwent a 1-week washout period before crossing over to the other drug arm. **Outcome Measures:** Study nights (at 3 night of intervention) included PSG and determination of the hypocapnic apneic threshold and CO_2 reserve using NIV. For participants with spontaneous central apnea, CO_2 was administered until central apnea was abolished, and CO_2 reserve was measured as the difference in $P_{ET}CO_2$ before and after. Steady-state plant gain (the response of end-tidal PCO_2 to changes in ventilation) was	1. Ventilatory parameters remained similar after placebo or ACZ except for total CO_2, which was lower after ACZ compared to placebo in both groups of participants ($p < 0.05$). 2. Treatment with ACZ for three days resulted in widening of the CO_2 reserve (-4.0 ± 1.2 vs. -3.0 ± 0.7 mmHg for non-SCI, -3.4 ± 1.9 vs. -2.2 ± 2.2 mmHg for SCI, $P < 0.0001$), and a corresponding decrease in the hypocapnic apnea threshold (28.3 ± 5.2 vs. 37.1 ± 5.6 mmHg for non-SCI, 29.9 ± 5.4 vs. 34.8 ± 6.9 mmHg for SCI, $P < 0.0001$), respectively. 3. ACZ significantly reduced plant gain when compared with placebo (4.1 ± 1.7 vs. 5.4 ± 1.8 mmHg/L min for non-SCI, 4.1 ± 2.0 vs. 5.1 ± 1.7 $mmHg \cdot L^{-1} \cdot min$ for SCI, $P < 0.01$). → Decreases susceptibility to hypocapnic central apnea. 4. ACZ significantly reduced controller gain when compared with placebo in the SCI group (2.1 ± 0.7 vs. 2.8 ± 1.3 $L \cdot min^{-1} \cdot mmHg^{-1}$) and the non-SCI group (2.2 ± 0.5 vs. 2.6 ± 0.6, $P = 0.01$). 5. Peripheral hyperoxic exposure resulted in a

	calculated from $P_{ET}CO_2$ and V_E ratio during stable sleep. Controller gain (the response of ventilatory drive to changes in end-tidal PCO_2), was defined as the ratio of change in V_E between control and hypopnea to the ΔCO_2 during stable non-REM sleep. The change in sleep parameters (apnea-hypopnea index, central apnea index, oxyhemoglobin desaturation index, respiratory effort-related arousal index, periodic leg movement arousal index, and sleep efficiency), and ventilatory and physiological parameters (V_T, V_E, respiratory rate, inspiratory durations, expiratory duration, breath duration, and oxyhemoglobin saturation and $P_{ET}CO_2$) were also collected.	significant decrease in V_E in both groups (F = 86.75, P < 0.0001) for both the placebo and acetazolamide arms. There was no significant interaction between the groups and drug arms. 6. ACZ decreased apnea-hypopnea index (28.8 ± 22.9 vs. 39.3 ± 24.1 events/h; P = 0.05), central apnea index (0.6 ± 1.5 vs. 6.3 ± 13.1 events/h; P = 0.05), and oxyhemoglobin desaturation index (7.5 ± 8.3 vs. 19.2 ± 15.2 events/h; P = 0.01) compared with placebo; in contrast, periodic leg movement arousal index was slightly increased on ACZ compared with placebo (1.1 ± 1.7 vs. 0.3 ± 0.5 events/h, respectively, F = 3.07, P = 0.05); and ACZ use was not associated with significant differences in sleep efficiency or respiratory effort-related arousal index. 7. Although further investigation in a larger sample of patients is required; ACZ may attenuate central sleep apnea and improve nocturnal O_2 saturation.
Brown et al. 2018 USA Cohort Level 2 N = 91	**Population:** 91 participants with SCI and SDB; 75 males and 16 females; mean (SD) age 48 (± 12) years; mean (SD) time since injury 17 (± 12) years; motor levels C1-C3 (4%), C4-C6 (59%), C7-C8 (12%), and T-level (26%).	1. Overall, 45% of 91 participants completed the study. 2. There was great diversity among patients with SCI in PAP utilization. 3. At 3 months (55/91) 38% of participants were high-

	74/91 participants underwent home sleep apnea test and SpO_2/tc-pCO_2 testing showing: ● 81% had evidence of OSA (50% mild, and 50% moderate or severe); of the anormal studies, there were a median of 12.4 obstructive events per hour. ● 28% had hypercapnia; in the abnormal studies, hypercapnia was present for 25% of the study time. **Intervention:** Based on SDB assessment (home sleep apnea test combined with overnight oxygen saturation (SpO_2)/transcutaneous pCO_2 (tc-pCO_2)), participants received different interventions: ● Participants diagnosed with nocturnal hypercapnia were prescribed bi-level positive airway pressure-average volume-assured pressure support (BiPAP-AVAPS; this device maintains the programmed EPAP and auto-titrates the IPAP to achieve the target average V_T). ● Participants with SDB but no hypercapnia were started on bi-level positive airway pressure-Auto (BiPAP-Auto; this device auto-titrates the EPAP to control apneic events, and the IPAP to control hypopneas). ● Participants without SDB were not prescribed a positive airway pressure	level users (87 ± 12% nights, 374 ± 115 min per night; mean ± SD), 20% were medium- level users (35 ± 16% nights, 144 ± 68 min per night), and 42% were low-level users (9 ± 9% nights, 85 ± 77 min per night). PAP therapy was effective in improving OSA in 89% and nocturnal hypercapnia in 77%. 4. Higher PAP pressures predicted higher levels of device use; at month 3: a. In participants prescribed BiPAP-Auto, average EPAP had significant predictive value for both % days used and minutes per night ($p = 0.04$) and % days used ($p = 0.04$). b. For participants prescribed BiPAP/AVAPS, average IPAP had significant predictive value for both minutes per night used ($p = 0.014$) and % days used ($p = 0.048$). c. By the other hand, SCI level or SDB severity were not predictors of device use ($p = 0.7$ and $p = 0.8$, respectively). 5. There were marked reductions in symptoms of autonomic dysreflexia ($p = 0.01$) and orthostatic hypotension ($p = 0.1$) as well as some improved indices of QOL; but larger cohorts in each user group would be necessary to describe and relationship between PAP

	(PAP) device but completed symptom logs and questionnaires. **Outcome Measures:** Adherence, daily event logs (to record episodes with symptoms of autonomic dysfunction, RI, and episodes of mucus plugging/atelectasis), SF-12v.2, Brief Pain Inventory-SF, Epworth Sleepiness Scale, and adherence (high-level use defined as ≥ 70% nights used and ≥ 240 min per night; medium-level use defined as ≥ 15% nights used and ≥ 60 min per night but less than high-level users; and low-level use defined by < 15% nights used or < 60 min per night) through PAP device data were collected at month 0, 3, 6 and 12 of the beginning of the study.	use and effects on these outcomes.
Graco et al. 2019 Australia Pre – post Level 4 N = 16	**Population:** 16 patients with traumatic cervical SCI, OSA; mean (SD) age 56.3 (± 15.5) years; 13 males and 3 females; 21.0 (± 14.9) years since injury; C1-C4, AIS A, B, C (n = 1), C5-C8, AIS A, B, C (n = 13); T1-S3, AIS A, B, C (n = 0); AIS D, at any level (n = 2); C1-C4 (n = 1); C5-T1 (n = 15); and AIS A (n = 4). **Intervention:** Auto-titrating CPAP and supported for 1 month. **Outcome Measures:** Participants completed an in-depth semi-structured interview, the Karolinska Sleepiness Scale, and a seven-item CPAP adverse events questionnaire at one, six and 12 months.	1. At one month, mean nightly CPAP use was 3.1 h, with 38% achieving at least 4 h per night. Mean nightly use dropped to 2.6 h at 6 months and 2.1 h at 12 months, with one quarter of the sample achieving at least 4 h per night in these time periods. 2. Between months one and six, two patients became adherent and four became non-adherent. No participant changed adherent status after six months. By 12 months CPAP usage was distinctly bi-model and stable, with either high usage (> 6 h

		per night) or low usage (< 3 h per night). 3. CPAP use (average nightly hours) at 6 and 12 months were strongly associated with more hours spent with the sleep scientist in the first month and greater years since injury ($p < 0.05$). 4. Mean Karolinska Sleepiness Scale score at baseline was 4.3 (± 2.1) and at 1 month review was 2.9 (± 2.1). 5. Qualitative results of interviews showed that all participants experienced burdens and adverse events from using CPAP, and the trade-off between the perceived burden and the perceived benefit appeared to impact adherence to the therapy.
Sankari et al. 2014 USA Prospective observational Level 4 N = 24	**Population:** Twenty-four participants (8 cervical SCI, 8 thoracic SCI, and 8 controls – 3 females, 5 males in each group) mean (SD) BMI: 29.2(6.6) kg/m2; most of whom were diagnosed with sleep apnea. **Treatment:** None. **Outcome Measures:** The ventilation, timing, Upper Airway resistance, and pharyngeal collapsibility, defined by critical closing pressure, were determined during non-REM sleep. Inspiratory duty cycle and V_E were observed in response to increasing severity of upper airway obstruction.	1. Compared with controls, both cervical and thoracic SCI participants demonstrated elevated passive critical closing pressure. 2. No difference in upper airway resistance was observed between groups. Participants with cervical and thoracic SCI had a similar degree of hypoventilation and dose-dependent increase in inspiratory duty cycle in response to upper airway obstruction. 3. Passive upper airway collapsibility is increased in both cervical and

		thoracic SCI compared with controls. 4. The neuromuscular compensatory responses to upper airway obstruction during sleep are preserved in chronic SCI and are independent of the level of injury.
Burns et al. 2005 USA Case series Level 4 N = 40	**Population:** 40 men after SCI (37 with tetraplegia) Mean (SD) BMI: 29.2(6.6) kg/m^2; most of whom were diagnosed with sleep apnea. **Treatment:** None. **Outcome Measures:** Survey requesting information about long-term treatment outcomes and side effects of sleep apnea treatment in persons with SCI.	1. CPAP continually used by 63% of the participants out of 32 (80%) of participants who tried it. 2. Main reasons for not using CPAP were inability to fall sleep, mask discomfort & claustrophobia. 3. Most common side effects were nasal congestion in 12 and mask discomfort in 8.
Stockhammer et al. 2002 Switzerland Pre-post Level 4 N = 50	**Population**: 50 people (40M 10F) with SCI lesion levels between C3 and C8; mean(SD) age: 48.6(14.0), range from 20- 81 years; Mean 11.4 years post injury (range from 0.5 to 37 years) . **Treatment:** CPAP. **Outcome Measures:** Sleep breathing data and oxymetric values were investigated in context with age, gender, BMI, neck circumference, type and height of lesion, time after injury, spirometric values and medication. A non-validated short questionnaire on daytime complaints was added.	1. 31 out of the 50 participants with tetraplegia had a respiratory disturbance index of 15 or more (mean 30.5) defined as SDB. 2. 16 patients accepted a trial of CPAP; of these, 11 continued to use CPAP after a few weeks. Of these 11 patients, 10 patients reported an improvement of symptoms after using long term CPAP therapy.
Biering-Sørensen et al. 1995 England Case series Level 4 N = 3	**Population**: 3 people after SCI, ages: 47, 54, 56 yrs, C6 incomplete, T2 complete; Duration of injury: 19, 6, 37 years. All 3 patients reported	1. In two patients, CPAP treatment decreased daytime sleepiness, improved sleep and oxygen saturation.

	severe daytime fatigue and sleep complaints. **Treatment:** CPAP via a nasal mask. **Outcome Measures:** Case report for each patient; measures included PSG.	2. One patient improved after losing 33 kg, reducing alcohol intake and quitting smoking.