Author Year; Country Score Research Design Total Sample Size	Methods	Outcome
Rosman et al. 2008 USA RCT Level 1 (PEDro = 8) N=7	**Objective:** To evaluate the effect of neostigmine/glycopyrrolate injections in patients with SCI and defecatory difficulties. **Population:** 7 SCI participants with defecatory problems (mean (SD) age: 46.9 (3.4) yrs, range 30 – 56 yrs); 4 cervical, 3 thoracic. **Treatment:** injections of neostigmine (2 mg) and glycopyrrolate (0.4 mg) for 1 week, wash-out period for 1 week, and placebo for 1 week, in random order **Outcome Measures:** Total bowel evacuation time; time to first flatus; time to beginning of stool flow; time to end of stool flow.	1. Compared with placebo, neostigmine/glycopyrrolate significantly reduced the total bowel evacuation time (mean (SD)) from 98.1 (7.2) min to 74.8 (5.8) min ($p<0.05$). 2. Neostigmine/glycopyrrolate significantly reduced the mean (SD) time to first flatus from 56.9 (5.4) min to 21.8 (4.5) min ($p=0.001$). 3. Neostigmine/glycopyrrolate significantly reduced the mean (SD) time to beginning of stool flow from 69.8 (2.8) to 42.3 (6.4) min ($p=0.01$), and time to end of stool flow from 80.3 (4.0) to 53.3 (8.3) min ($p<0.05$).
Krogh et al. 2002 Denmark RCT Level 1 (PEDro = 7) N=22	**Objective:** To evaluate the tolerability and pilot efficacy of prucalopride in the treatment of CC due to SCL. **Population:** mean (SD) age: 34.7 (2.5) yrs (placebo), 36.5 (3.9) yrs (1mg group), 44.3 (3.1) yrs (2mg group). No information on level of injury was reported. **Treatment:** Participants randomized with double blind design to treatment with prucalopride 1mg or placebo, taken once daily for 4 wks. A 2nd group of participants was randomized to prucalopride	1. Compared with baseline, constipation severity decreased with prucalopride. The VAS score for treatment efficacy showed a clear dose response (medians 4, 52, and 73 for placebo, 1 and 2 mg, respectively). 2. Self-report diary showed an improvement in average weekly frequency of all bowel movements over 4 wks within the 2 mg group (median 0.6). 3. 3 participants (2 mg group) reported moderate/severe abdominal pain and 2 discontinued treatment.

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	2mg or placebo for 4wks **Outcome Measures:** constipation; urinary habit; constipation severity and symptoms; colonic transit times	Adverse events (AEs) were reported by 6/7 in the placebo group, and by 7/8 and 6/8 in the 1 and 2mg groups. The most common AEs were gastrointestinal (flatulence, abdominal pain and diarrhea).
Korsten et al. 2005 USA RCT Level 1 (PEDro=6) N=13	**Objective:** To test the hypothesis that neostigmine, a medication that increases cholinergic tone by blocking the metabolism of acetylcholine, might promote bowel evacuation in people with SCI, in addition to whether neostigmine side effects such as bradycardia and bronchoconstriction could be prevented by coadministration of neostigmine with glycopyrrolate, an anticholinergic agent that has limited activity on the muscarinic receptors of the colon. **Population:** Level of injury: C4-T12 (5 tetraplegics, 8 paraplegics; 12/13 motor complete, 5/13 sensory incomplete); Age: mean (range) 46 (25-69)yrs; Duration of injury: mean (range) 14 (1-31) yrs **Treatment:** On different days, participants received, in a randomized, double-blinded design, one of three intravenous infusions (normal	1. Neostigmine and the combination of neostigmine and glycopyrrolate both caused a similar expulsion of the stool, which was greater than with normal saline (median score 3 vs. 4 vs. 0, respectively) 2. Mean time to expulsion was 11.5 min (range 5-20 min) after neostigmine and 13.5 min (range 4-23 min) after the combination. 3. There was no correlation between the level of SCI and likelihood of bowel evacuation with any of the infusions

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	saline, 2 mg neostigmine, or 2 mg neostigmine and 0.4 mg glycopyrrolate) **Outcome Measures:** time to bowel evacuation using barium paste	
Segal et al. 1987 USA Prospective controlled trial Level 2 N=28	**Objective:** To study the time-course of gastric emptying in people with SCI. **Population:** 11 participants with tetraplegia, 9 participants with paraplegia (all complete SCI), 8 able-bodied controls; Age range: 20-55yrs **Treatment:** participants ingested a liquid meal, then within 2 weeks, ingested 2nd liquid meal while metoclopramide (10mg) was administered intravenously; gastric emptying (GE) was evaluated after each liquid meal **Outcome Measures:** half time of gastric emptying, gastric emptying patterns in the early and later phases	1. The mean GE half time for a liquid meal decreased in the participants with tetraplegia from 104.8 min to 18.8 min after treatment with metoclopramide. 2. The pretreatment mean GE of 111.5 min decreased to 29.1 min among the participants with paraplegia.
Korsten et al. 2018 USA Prospective controlled trial Level 2 N=25	**Objective:** To investigate the effectiveness and safety of neostigmine/glycopyrrolate transdermal administration by iontophoresis in comparison to intravenous administration to elicit bowel movement in people with SCI **Population:**	1. No significant difference in bowel evacuation time between the three doses of drug (p=0.37) 2. Of the original 25 people, the 40% response (combination of high-dose and low-dose findings) to the transdermal administration was significantly lower in comparison to the intravenous Neo/Gly response

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	Age: 50 ± 15 y 15 paraplegia 10 tetraplegia Level: 11 cervical, 13 thoracic, 1 lumbar Severity: 12 A, 3 B, 7 C, 3 D Time since injury: 9.0 ± 9.0 y **Treatment:** Neostigmine and glycopyrrolate by Iontophoresis versus by intravenous administration. **Outcome Measures:** Efficacy of transdermal Neo/Gly by iontophoresis to promote bowel movement, and safety/tolerability of this method, quantified through side effect monitoring	rate (72%) (p=0.083) 3. Of the 21 people who responded to the intravenous administration, there was a 48% response to the transdermal-iontophoresis administration 4. Individuals who received intravenous administration reported greater number of side effects compared to transdermal administration: eye/facial twitching (p<0.001); light-headedness (p=0.029), headache (p=0.039); dry mouth (p=0.006) 5. At the five minute interval the individuals who received intravenous administration showed greater change in mean arterial pressure in comparison to the transdermal groups (p=0.008), and significant changes in systolic blood pressure (p=0.021, which was also significant at the 15-minute interval (p=0.047).
Bauman et al. 2021 USA Pre-post Level 4 N=6	**Objective:** to investigate if a dual drug approach (neostigmine and glycopyrrolate) by transcutaneous route to standard of care (SOC) for the bowel management confers any clinical or patient-reported benefits over that of SOC alone **Population:** Mean age: 57 ± 10 years (range: 39–66 years)	1. Average length of bowel care session was shortened with SOC neostigmine and glycopyrrolate to 41 ± 20 min from average of 107 ± 68 min at the end of the SOC control (p<0.001). 2. Difference in length of time of bowel care between control and drug-treatment arms ranged from 42 to 88 min (CI:95%) 3. No significant change in body weight after one-week of SOC or

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	Time since injury: 18 ± 17 years (range: 3–47 years) Level: 3 complete motor lesion with partial sensory sparing; 3 motor-incomplete lesions with partial sensory; 5 above T6 **Treatment:** Neotstigmine and glycopyrrolate by transcutaneous route vs. standard care for bowel management. **Outcome Measures:** bowel evacuation time	change in abdominal radiographic images of stool burden. 4. Average loss by 2.8 +- 1.0 kg of body weight observed after 2-week SOC with dual drug-treatment (86 +- 25 kg vs. 83 +- 26 kg, P<0.0001) with initial 1.2 +- 1.2 kg loss at the end of the first week. 5. Weight loss was due to reduction in retained stool, as confirmed by abdominal radiographs.