ORIGINAL ARTICLE

Relationship between gut-specific autonomic testing and bowel dysfunction in spinal cord injury patients

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Study design: Investigation of bowel function in 55 patients and 26 healthy volunteers using radiological, anorectal physiological and laser Doppler blood flow monitoring.

Objectives: Bowel dysfunction is common after spinal cord injury (SCI). We aimed to determine whether hindgut testing of autonomic innervation provides insight into presence of symptoms, altered motor function (transit) and level of injury.

Setting: St Mark's Hospital, UK and The Spinal Injuries Unit, Royal National Orthopaedic Hospital, UK.

Methods: A total of 55 patients with chronic complete SCI and 26 healthy volunteers were studied. Twenty-four patients had lesions above T5 and 31 had lesions below T5. Thirty-five patients complained of constipation: 75% (18/24) of patients with lesions above T5 and 55% (17/31) of those with lesions below T5. Gut transit, rectal electrosensitivity and rectal blood flow were measured.

Results: Slow gut transit occurred in 65% of patients and in all the 35 patients complaining of constipation. Delay was pancolonic. All patients had an elevated sensory threshold. The threshold was significantly higher in those with subjective constipation ($P < 0.01$), slow transit ($P < 0.04$) and high SCI ($P = 0.046$). Mucosal blood flow was lower in SCI patients with constipation ($P < 0.04$) and slow transit ($P < 0.03$). It was higher than normal in high-SCI volunteers ($P = 0.056$), reflecting loss of sympathetic inhibition.

Conclusions: In SCI, subjective constipation correlates closely with slow gut transit. Delay is pancolonic, regardless of the site of lesion. Sensory testing provides evidence for completeness of lesion, offering further evidence for pain transmission through sympathetic pathways. Studies in SCI patients provide further evidence of mucosal blood flow as a marker of altered autonomic innervation.

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Introduction

Incidence of spinal cord injury (SCI) is 10–83 cases per million.¹ Prevalence is between 700 and 900 cases per million, with an estimated 50 000 chronic SCI patients in the United Kingdom.^{2,3} These patients have a large burden of gastrointestinal illness, with 25–41%^{4–6} reporting moderate to severe symptoms. SCI patients rank neurogenic bowel dysfunction and associated symptoms as one of their major life-limiting problems^{4–7} typically associated with constipation, incontinence and pain. To overcome these problems, patients have to implement a strict bowel management

regimen that can be both time-consuming⁸ and requiring large amounts of healthcare resource.

Two main factors determining the development of symptoms are the completeness and level of injury.^{9–13} SCI patients lose a variable proportion of their extrinsic autonomic innervation to their gut, depending on the level of injury, whereas the intrinsic enteric nervous system remains intact.³ The gut intrinsic nervous system may lose integrity with time because of the loss of extrinsic supply. Whether hindgut denervation leads to a loss of facilitation or inhibition of intrinsic neural activity has not been established. It is unclear what contributions the enteric and extrinsic autonomic innervations have in the control of gut motility and sensitivity in SCI patients. Sympathetic outflow to the gut arises above the level of T5. Lesions above this level isolate the gut from supraspinal extrinsic sympathetic control.

This study is based on the hypothesis that testing of the hindgut may provide direct evidence for the degree of

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completeness of spinal cord injury and the degree of disturbance of gut function. It aimed to determine whether specific tests that reflect autonomic gut innervation correlate with the presence of symptoms, motility changes and injury level.

Physiological testing comprised measurement of rectal mucosal blood flow and rectal mucosal sensitivity to electrical current. Laser Doppler flowmetry is a reproducible and validated^{14,15} measure of hindgut extrinsic autonomic innervation. Transmucosal electrostimulation induces intensity-related perception in the lower and upper^{16,17} gut allowing quantitative assessment for hindgut extrinsic neurological impairment. A primary aim was to identify whether laser Doppler measurement of rectal mucosal blood flow corresponded with the level of injury, particularly in relation to level of sympathetic outflow. It also intended to assess the relative contributions of sympathetic and parasympathetic innervation in spinal cord injured patients with gut symptoms.

Materials and methods

Volunteers

A total of 55 patients (45 male, mean age 36, range 19–68) with complete spinal cord injury (mean time since injury 34 months, range 13–134) were studied, representative of all patients treated in this supra-regional centre. Twenty-four patients (18 male, mean age 34) had lesions above T5, and 31 (27 male, mean age 37) had lesions below T5. T5 was used as a cutoff point for this study, as spinal sympathetic outflow to the colon originates above this level and any lesion at or above T5 would be expected to isolate the gut from the majority of the spinal sympathetic influence. Patients with lesions between T6–L1 would be expected to have some degree of sympathetic impairment, and volunteers with lesions at the level of L2–S1 would be expected to have intact sympathetic innervation but loss of supraspinal control of parasympathetic outflow. Pelvic parasympathetic reflexes would be expected to remain intact.

Full ethical approval and informed consent to participate were obtained. Thirty-five (27 male, mean age 36, range 20–68) of the patients were symptomatically constipated, defined by spontaneous bowel frequencies of less than three times per week, unsatisfied defaecation or the need to strain. These 35 patients represented 75% (18/24) of those with lesions above T5 studied and 55% (17/31) of those with lesions below T5. None of these patients had undergone any abdominal or perineal surgery and patients denied having bowel symptoms before their injury. Organic and metabolic causes of constipation had been excluded by an earlier endoscopy or barium enema where appropriate, and by blood testing. All had a normal diameter colon. For these 35 patients, the mean bowel frequency of medications was 1.4 bowel actions per week (range 0.5–4), and the mean time spent per episode of toileting was 59 min (range 15–120). Twenty-three patients used oral laxatives to achieve defaecation, seven used enemas and ten relied on digital reflex stimulation; a total of 34 patients used some method to aid defaecation. The mean onset of constipation symptoms

after the spinal injury in these 35 patients was 18 months (range 3–34).

Twenty (18 male, mean age 36, range 19–58) patients denied constipation. Their spontaneous bowel frequency was 3.3 (range 2–7) per week ($P < 0.03$ compared with constipated patients), and the mean time spent per episode of defaecation was 33 min (range 15–75) ($P < 0.01$ compared with constipated patients). None used laxatives, although some needed digital stimulation to initiate defaecation.

Anticholinergic and autonomically active drugs were discontinued for at least 24 h before physiological assessment.

Twenty-six healthy volunteer controls (17 female; mean age 36, range 18–61) underwent laser Doppler flowmetry studies of rectal mucosal blood flow. None had gastrointestinal, cardiovascular or respiratory diseases. The only regular medications consumed were anticonvulsants taken by two volunteers. In volunteers who smoked, all studies were performed 6 h after the last cigarette as smoking reduces gut blood flow.¹⁴

Whole gut transit

All patients underwent a radio-opaque marker transit study.¹⁸ Three sets of radiologically distinct markers were taken at 24 h intervals and an abdominal X-ray was taken 120 h after the ingestion of the first set. Retention of more than the normal range for any one of the three sets of markers was regarded as reflecting slow whole gut transit.

Rectal electrosensitivity

All patients had assessment of rectal sensation by both balloon distention and electrosensation using a bipolar ring electrode (Dantec, Skovlunde, Denmark). Total absence of rectal electrosensation was used as an indicator of completeness of injury.

Anal sphincter manometry

All patients had assessment of their maximum resting anal sphincter pressure, a reflection predominantly of internal anal sphincter smooth muscle function, and the incremental maximum voluntary contraction pressure, reflecting striated external anal sphincter function. Manometry was performed using a closed water-filled microballoon station pull-through method.

Simulated defaecation

With patients in the left lateral position, a lubricated balloon attached to a catheter was inserted into the rectum and inflated with 50 ml of water. Two EMG electrodes were placed on the anal skin over the external anal sphincter. Patients attempted to expel the balloon, a positive result being recorded as passage of the balloon within 5 min. Sustained increases in surface EMG activity on attempted defaecation were defined as inappropriate pelvic floor contraction.

Laser Doppler studies of rectal mucosal blood flow

Patients and controls were studied in a room maintained at 22 °C after 15 min acclimatisation and examined in the left

lateral position. Examinations were carried out in the fasted state and in females during the follicular phase of their menstrual cycle.¹⁴ Digital examination and rigid sigmoidoscopy confirmed the rectum to be empty. The Doppler probe was introduced through the sigmoidoscope. Recordings were made at 10 cm from the anal verge at four points circumferentially at 90 degrees to each other. Readings were taken after the trace had stabilised for 30 s.

Results

Whole gut transit

Thirty-two of the 55 SCI patients (65%) had slow whole gut transit, representing 71% (17/24) of those studied with lesions above T5 and 48% (15/31) of those with lesions below T5 ($P=0.09$, for percentage in different level SCI, chi-square test). All thirty-two of these patients were in the group with symptomatic constipation (Table 1).

With excessive retention, markers were retained throughout the colon in all patients, irrespective of the injury level. Patients with subjective constipation had significantly more retained markers than those without (mean markers counted 49 vs 22, respectively, $P=0.007$) (Table 2).

Rectal electrosensation

Transmucosal rectal electrical sensation was abnormal (normal <36 mA) in all patients, being significantly greater in those complaining of constipation compared with those without (67.3 vs 41.6, respectively, $P<0.01$). Rectal electrosensory thresholds were more abnormal in those with slow transit compared with normal transit (65.3 vs 44.1 mA, respectively, $P<0.04$). Patients with lesions above T5 had the highest rectal sensory thresholds (71.5 vs 47.2 mA, above vs below T5 SCI; $P=0.046$).

Anal sphincter manometry

Patients with lesions above or below T5 had similar resting anal pressures (94 vs 89 cm water, respectively, $P=0.31$;

normal >60 cm water). Voluntary contraction pressure was absent in all SCI patients.

Simulated defaecation

Seventy-one percent (17/24) of patients with lesions above T5 and 61% (19/31) of these with lesions below T5 were unable to expel a water-filled balloon and showed paradoxical sphincter contraction.

Patients who were unaware of balloon sensation were asked to attempt evacuation as they would during attempted defaecation. This included 34 of 35 patients complaining of constipation and 31 of 32 patients with slow whole gut transit.

Two of the 20 patients who did not report constipation had evidence of paradoxical sphincter contraction, as did five of the 23 with normal whole gut transit. The objective finding of paradoxical sphincter contraction was therefore more common in patients with the symptom of constipation and in those with slow transit.

Laser Doppler studies of rectal mucosal blood flow

Spinal cord injury patients with constipation had significantly lower mucosal blood flow than did asymptomatic SCI patients (mean 183 vs 267 FU, $n=55$, $P<0.04$). Those patients with measured slow transit had lower blood flow than did those with measured normal transit (mean 180 vs 273 FU, $n=55$, slow vs normal transit, $P<0.03$).

Compared with age-matched controls, resting blood flow was greater in volunteers with lesions above T5 (200 vs 238 FU, normal vs above T5 SCI; $P=0.056$) and similar in those with lesions below T5 (203 vs 213 FU, normal vs below T5 SCI; $P=0.345$).

In fact, six of the 23 patients with lesions below T5 had a level of injury below S1 resulting in loss of excitatory pelvic parasympathetic supply to the colon. Compared with age-sex-matched controls, these six volunteers had a tendency towards a reduction in mucosal blood flow (202 vs 171, normal vs below S1 transection, sample too small to test for statistical significance).

Discussion

Constipation is common in chronic SCI patients. In this study, 64% of unselected stable patients reported constipation symptoms. All the 35 patients who reported subjective constipation needed laxatives, enemas or digital reflex stimulation to defaecate. Even spinally injured patients

Table 1 Symptom and transit abnormalities according to level of injury (number of patients in each group in parentheses)

	SCI Above T5 (n = 24)	SCI Below T5 (n = 31)	P-value
% of patients with constipation	75 (18)	55 (17)	0.16
% using laxatives/enemas	71 (17)	42 (13)	0.06
% of patients with slow transit	71 (17)	48 (15)	0.03

Table 2 The median number of retained markers in different colonic segments in patients spinal cord injury lesions above or below T5

	Constipation (n = 35)				No constipation (n = 20)			
	Right colon	Left colon	Recto-sigmoid	Total	Right colon	Left colon	Recto-sigmoid	Total
SCI above T5 (n = 24)	13 (6–21)	13 (5–22)	20 (8–33)	47 (19–53)	7 (3–17)	6 (4–20)	11 (10–31)	23 (14–34)
SCI below T5 (n = 31)	11 (2–20)	16 (4–25)	24 (7–39)	51 (17–60)	5 (0–12)	6 (1–16)	10 (3–20)	21 (4–42)

Abbreviation: SCI, spinal cord injury.

Marker retention was usually excessive in both groups of patients with subjective constipation, and usually not in those without constipation.

who did not complain of constipation spent an average of an hour and a half a week on their defaecatory activity, and some patients with constipation spent up to 5 h a week. Studies show that SCI patients report bowel dysfunction as a major source of symptoms, ahead of urinary symptoms and limb spasm,¹⁰ and a large amount of time needs to be spent on bowel management using maneuvers, such as digitation and manual evacuation to reduce the effects of this dysfunction.⁸ Constipation was reported with similar frequency in patients with high and low level of injury.

Ninety-one percent (32 of 35) of chronic SCI patients complaining of constipation had slow transit using an objective measure of whole gut transit, and 97% (34 of 35) had difficulty evacuating a water-filled balloon from the rectum. Stratifying the patients with complete injuries according to the level of injury as above or below T5 (above and below the level of sympathetic outflow) showed a similar frequency of slow transit and defaecatory difficulty in both groups.

Gut transit delay was pancolonic. Patients with lesions above and below the level of the splanchnic sympathetic outflow had slow transit with similar frequencies, and colonic markers were distributed in a similar pattern. As the sympathetic system is inhibitory to transit, and patients with a high SCI lose splanchnic sympathetic and sacral cholinergic excitatory innervation, this would suggest that other factors such as loss of mobility may be important in the pattern of impaired colonic function. As a further complication, patients with spinal injuries lose supraspinal control of otherwise intact reflexes. Aberrant activity of these reflexes can cause left colonic hyperactivity,¹⁹ resulting in increased left-sided colonic tone with paradoxical sphincter contraction. Higher spinal injuries (above T5), which isolate the gut from its predominantly inhibitory spinal sympathetic input,²⁰ tend to be associated with variable and complex effects on gut function. In these higher SCI, slow transit in the left colon and right colon has been described. Loss of postprandial increases in colonic motility and reduction of rectal compliance have also been described.²¹ The symptoms and gut function such patients ultimately develop seem to also involve other factors such as patient mobility^{5,12} and possibly the function of the intrinsic enteric nervous system, with interaction with local spinal reflexes acting on the bowel and anal sphincters.

The sacral parasympathetic outflow to the hindgut is thought to be critical to the maintenance of colonic function and coordination. In this study, patients with high spinal injury had a similar prevalence of constipation as did those with an injury below the sympathetic outflow. Patients with injuries above T5 also had the highest rectal sensory threshold, suggesting the loss of an important component of the transmission of pain in sympathetic pathways, possibly in type C unmyelinated fibres. Rectal electrosensitivity may therefore be useful as a marker of gut dysfunction and level of injury in spinal cord injured patients. We have also shown that rectal electrosensitivity correlates with transit, such that electrosensation was most attenuated in spinal cord injured patients with slow transit. Similar, but less marked, impairment of rectal electrosensation in slow

transit is also observed in neurologically intact patients with chronic idiopathic constipation.¹⁵

We have shown earlier that rectal laser Doppler flow reflects the level of activity of extrinsic autonomic gut innervation.^{14,15} Using this technique to assess extrinsic autonomic function is based in part on the knowledge that excitatory parasympathetic nerves provide a vasodilatory drive to submucosal vessels.²² We found that patients with lesions below T5, who have lost this excitatory drive, tend to have a reduction of mucosal blood flow compared with age-sex-matched controls. This lends support to the validity of rectal mucosal blood flow measurement as an index of the activity of extrinsic autonomic innervation to the gut. Further support for the validity of blood flow measurement as an index of such innervation comes from the finding that patients with high SCI, who have isolated their gut from the splanchnic sympathetic outflow, have increased levels of blood flow compared with controls.

The proportion of males and females in the patient and control groups differed. However, basal rectal mucosal blood flow does not significantly differ between males and females.^{14,15} No cardiovascular autonomic tests were performed in this study. We have shown earlier that rectal mucosal blood flow correlates well with altered cardiovascular autonomic reflexes and is more specific.^{14,15}

In conclusion, we have shown that constipation affects approximately two out of three spinal injury patients, irrespective of the level of injury. Subjective constipation in spinal injury is almost invariably associated with slow whole gut transit. Finally, symptomatic patients with an injury above the level of sympathetic outflow to the gut have demonstrable altered autonomic innervation, identifiable using tests of sensitivity and laser Doppler flowmetry.

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