Recent concepts in the management of bowel problems after spinal cord injury

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Abstract

Bowel problems after SCI can be debilitating. Colonic inertia as a result of decreased parasympathetic (S2-4) stimulation of the left colon and rectosigmoid seems to be the principal abnormality accounting for DWE. The conventional measures used for decades have poor results in many people. Neostigmine, an anticholinesterase inhibitor, appears to be a more physiological agent for these individuals. The combination of neostigmine + glycopyrrolate infusion has shown encouraging results after intravenous administration and studies are under way to assess the efficacy of neostigmine by other routes.

Introduction

A significant number of individuals with chronic spinal cord injury (chronic SCI) have gastrointestinal (GI) symptoms due to bowel dysfunction [1]. Adequate bowel care is an important part of their management. The intent of this paper is to acquaint physicians with the pathophysiology of bowel problems after SCI and to summarize current concepts in the management of individuals who have sustained such damage.

Magnitude of the problem

According to the most recent data from the National Spinal Cord Injury (NSCI) Database, the prevalence of SCI in the US is approximately 250000 with 12000 new cases each year [2]. About 40-50% of injuries to the spinal cord are due to motor vehicle accidents [3]. The severity of the injury determines the outcome and can be classified using the American Spinal Injury Association (ASIA) impairment scale (*Tab. 1*) into five different stages [4]. The economic burden of this problem is with the direct and indirect (loss of income and productivity) annual cost of managing these individuals estimated to be at least $ 4 billion. These costs are especially high since these injuries typically occur in young males (average age of 37.6 years at the time of injury) [5].

SCI results in permanent disability in about 30-40% of cases [1,6-8]. In addition to the physical limitations due to paralysis, bowel and bladder problems are common. In terms of bladder dysfunction, use of intermittent catheterization has significantly reduced the incidence of urinary tract infections and improved the survival rate [9].

As a result, bowel dysfunction has become a more major issue [1,6-8]. To manage this problem effectively, it is first important to understand normal neuromuscular coordination of the colon and the pathophysiological changes which occur after SCI.

Neuromuscular coordination of the colon

Normal colonic and anorectal function is important for the process of defecation. The internal anal sphincter (IAS), an involuntary sphincter, is the continuation of the inner circular muscle layer of the colon. In contrast, the external anal sphincter (EAS) is made up of striated muscle layer and is under voluntary control [10]. Normal function of the EAS is important in preventing premature expulsion of feces and its integrity is a major factor in maintaining continence.

The colon is richly supplied with both autonomic (parasympathetic and sympathetic) and somatic (sensory and motor) innervation (*Fig. 1*) [11]. These different pathways are integrated by higher centers in the brain and spinal cord. The parasympathetic innervation of the colon is responsible for colonic contractions and motility. The right and proximal transverse colon are innervated through the vagus nerve while the left colon and rectum receive input from spinal segments S2-S4

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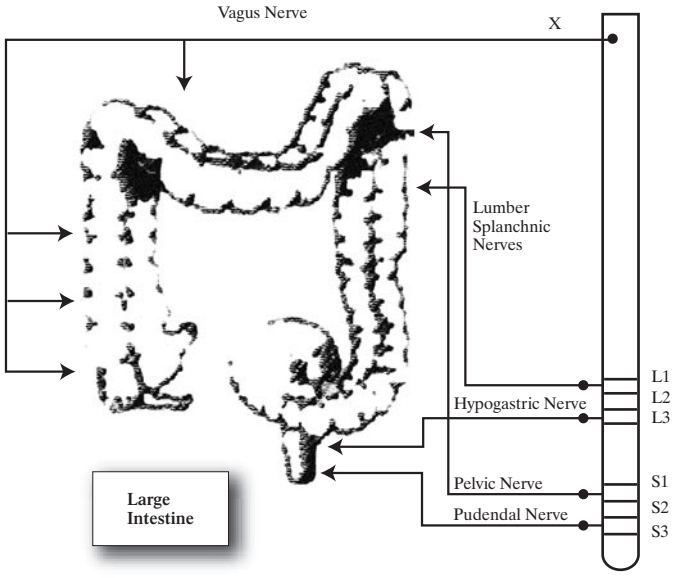


Figure 1. **Extrinsic innervation of the large intestine. The vagus nerve (X) innervates the right colon while propulsive activity in the left colon is mediated by the parasympathetic (pelvic) nerves. Sympathetic innervation (L1-3) via the splanchnic nerves and hypogastric nerves is inhibitory. The anal canal is innervated by voluntary efferent motor fibers to the external anal sphincter via the pudendal nerve from the sacral spinal cord (S2-4)**

Table 1. **American Spinal Injury Association (ASIA) impairment scale**

Grade	Description
A	Complete; no sensory or motor function preserved in the sacral segments S4-S5
B	Incomplete; sensory but not motor function preserved below the neurological level and extending through the sacral segment S4-S5
C	Incomplete; motor function preserved below the neurological level; most key muscles have a grade <3
D	Incomplete; motor function preserved below the neurological level; most key muscle have a grade >3
E	Normal motor and sensory function

via pelvic nerve or nervi erigentes [11]. The sympathetic supply originates from the lumbar splanchnic nerves and is the major pathway for carrying the sensations from the colon. The somatic fibers innervating the EAS are derived from the pudendal nerve (S2-S4). These nerves directly innervate the colon and also form Auerbach's and Meissner's plexuses within the muscle layers. Together, these plexi constitute what is termed the enteric nervous system (ENS) [10,11].

The neuromuscular innervation of the colon results in both non propulsive contractions under the control of ENS as well as high amplitude propagating contractions (HAPC) [1]. Various neurotransmitters including acetylcholine, catecholamines, and serotonin have been shown to regulate colonic motility. However, the principal autonomic neurotransmitter is acetylcholine [12].

Pathophysiological changes after SCI

Prolonged mouth to cecum transit time (MCTT) has been shown in individuals with quadriplegia using radio-opaque markers [13,14]. Segmental evaluation has also shown pro-

Figure 2. **Effect of food ingestion on the motility index (mm Hg). The motility index increased significantly in both SCI ($p<0.01$) and SI ($p<0.02$) subjects after meal ingestion, but to a lesser extent in the latter**

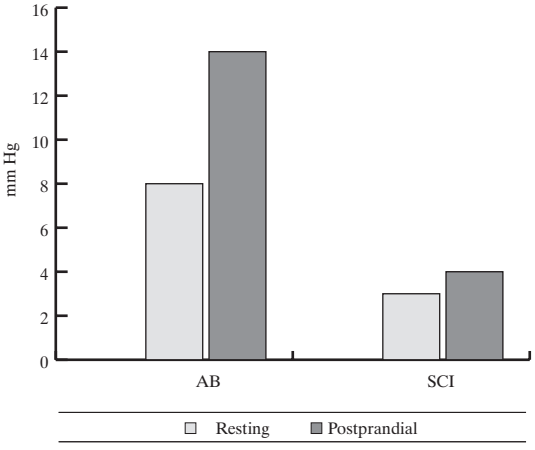


Figure 3. **Effect of food ingestion on the no. of waves per hour. There was a significant increase in the number of waves seen in SCI ($p<0.008$) as well as SI ($p<0.005$) subjects after meal ingestion**

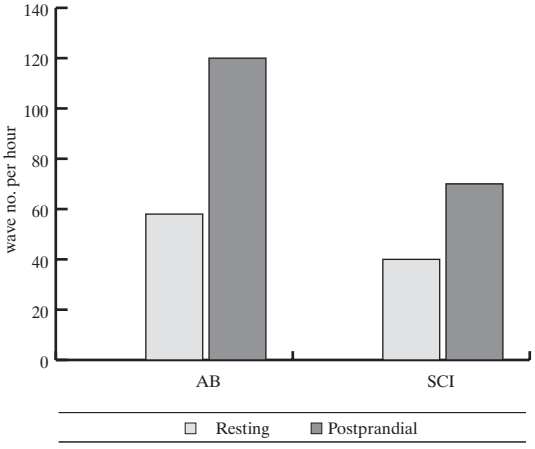


Figure 4. **The effect of food ingestion on the motility index shows regional variation in the SCI group. The increase in motility index (mm Hg) was only significant in the descending colon ($p < 0.03$) and not the rectosigmoid region**

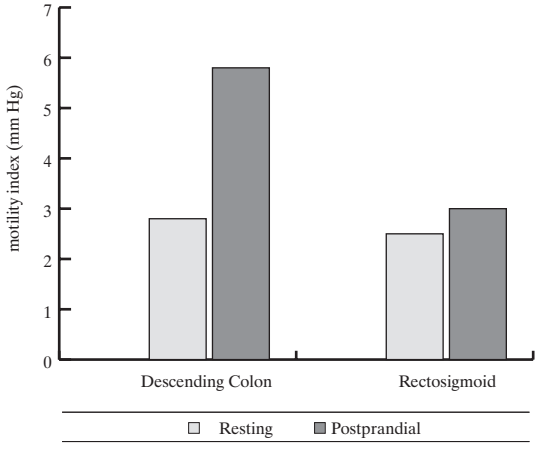


Table 2. **Clinical presentation in patients with SCI due to UMN vs LMN injury**

	UMN lesion	LMN lesion
Level of lesion	Above T10 vertebral or T12 spinal segment	Below T10 vertebral or T12 spinal segment
Transit time (Cecum to anus)	Increased	Increased
Motility of left colon	Decreased	Decreased
EAS	Spastic paralysis	Flaccid paralysis
Sympathetic output	Absent with lesions above T6 spinal segment	Retained
Symptoms	Constipation DWE Incontinence*	Constipation DWE Incontinence
Fecal impaction	Proximal colon	Rectal
Autonomic dysreflexia	Common with injuries above T6 level	Rare
Reflex defecation	Present	Not known

Constipation is <3 bowel movements per week; DWE or difficulty with evacuation is a combination of constipation with bloating, discomfort, pain, and prolonged bowel care sessions; * Patients with SCI due to UMN injury develop incontinence due to loss of sensations and development of lax sphincter later due to use of frequent laxatives and enemas

longed transit time of the left colon in subjects with paraplegia compared to able bodied (AB) individuals [15,16]. Our group has studied colonic motility in different segments of the left colon after SCI (4 subjects with paraplegia and 4 with quadriplegia). The results were compared to findings in 6 matched AB individuals [17]. Motility was evaluated for 1 h before breakfast and for 1 h during meals.

Baseline as well as meal stimulated colonic motility was reduced in SCI subjects compared to AB individuals (*Fig. 2,3*). Regional variations were noted in the SCI group with a post prandial response seen only in the descending colon and not in the rectosigmoid (*Fig. 4*).

We also studied the effect of SCI on colonic contractions in 14 male volunteers (8 with chronic SCI and 6 healthy controls) 1 h before sleep, during the entire period of sleep and 1h after sleep [18]. It was shown that HAPC are absent during sleep in both SCI and control groups. However, arousal from sleep failed to restore HAPC in subjects with SCI [18].

It appears that prolonged colonic transit time and absence of HAPC contributes to constipation and difficulty with evacuation (DWE) after SCI. As colonic motility depends on adequate colonic parasympathetic tone, these results, in part, were consistent with an absolute or relative loss of such autonomic tone.

Bowel problems with chronic SCI

Problems with defecation become more prominent as time progresses after the acute injury [1]. The clinical picture depends on whether the injury is upper motor neuron (UMN) (above vertebral T10 level) or lower motor neuron (LMN) (below vertebral T10 level) as shown in *Tab. 2*. Problems with defecation in both types of injuries have a significant impact on quality of life in individuals with chronic SCI given the prolonged amount of time spent on their bowel care [1,6-8,19].

In addition, complications such as fecal impaction and autonomic dysreflexia can occur. Fecal impaction is the most common problem often presenting with atypical symptoms such as paradoxical diarrhea, abdominal pain, nausea, vomiting, acute confusional states, urinary symptoms, and rectal bleeding due to pressure ulcerations [20]. Autonomic dysreflexia, occurs in patients with SCI above T6 spinal segment. It is due to an autonomic response to stimuli such as fecal impaction, bladder distension, catheterization, digital rectal stimulation, and colonoscopy [21,22]. Common symptoms are pounding headache, sweating, parasthesias, nasal obstruction, and goose flesh. Hypertension is the most common clinical sign and is seen in 90% of these cases [21]. Although rare, potentially fatal complications of autonomic dysreflexia include seizures and subarachnoid hemorrhage [23].

Management

Effective bowel management in individuals with SCI is of utmost importance. An adequate bowel regimen depends on many factors and will vary from patient to patient, but achieving effective evacuation and preventing incontinence is the common goal [24]. It is, therefore, important to completely evaluate the patient before designing a bowel regimen for any patient with a SCI.

Table 3. **Conventional management strategies for bowel symptoms in SCI individuals**

1.	**Dietary changes**
	a) Fiber diet
	b) High fluid intake
	c) Avoid foodstuffs which cause problems
2.	**Positioning during bowel care**
	a) Toilet seat/commode chiars
	b) Left lateral position for bowel care in bed
3.	**Stimulation**
	a) Digital stimulation of rectum
	b) Abdominal belt
4.	**Fiber**
	a) Soluble (pectin, guar, ispaghula, etc.)
	b) Insoluble (cellulose, legnin, etc.)
5.	**Laxatives**
	a) Bulk laxatives (docusate sodium, potassium)
	b) Stimulant laxatives (senna, bisacodyl, castor oil, etc.)
	c) Saline laxatives (magnesium hydroxide, sodium citrate, sodium biphosphate)
	d) Hyperosmolar laxatives (lactulose, sorbitol, polyethylene glycol)
6.	**Suppositories**
	a) Vegetable oil based bisacodyl suppository
	b) PEG based bisacodyl suppositor
	c) CO2 suppository
7.	**Enemas**
	a) Plain water enemas
	b) Fleet enema (sodium biphosphate)
	c) Therevac (TVC) mini enemas
8.	**Prokinetic drugs**
	a) Metoclopramide for short term use
	b) Cisapride not available for routine use
	c) Other agents like tegaserod require further evaluation
9.	**Surgical options**
	a) Sacral posterior rhizotomy
	b) Sacral anterior nerve root stimulation
	c) Appendicostomy and antegrade continent enema of Malone (MACE)
	d) Colostomy

History

There should be particular emphasis on duration and level of injury, bowel habits before the SCI and pre-SCI dietary habits (fluids, fiber, meal frequency, spices, amount). Medications with potential effects on bowel function should be ascertained and the social support system of the individual should be evaluated.

Physical examination

Patients with SCI may not report symptoms [1,6-8,19]. Particular emphasis should be placed on the person's nutritional and hydration status, the abdominal examination (distension, bowel sounds, tenderness, rigidity, fecal impaction, organomegaly), the rectal examination (hemorrhoids, sphincter tone, impaction, masses, stool guiac), and the neurological examination (level and nature of injury).

Laboratory evaluation

Laboratory evaluation should include a complete blood count, electrolytes, renal and liver function tests, amylase, and plain x-ray of abdomen.

Conventional measures for bowel care

Effective bowel care for individuals with SCI usually involves a number of different strategies (*Tab. 3*). Depending on the social needs and the bowel habits of the individual, frequency of bowel care can be tailored to each individual. Whenever possible, bowel care should be performed in either a normal position or the left lateral position [25]. Digital rectal stimulation (DRS) can also be useful [26]. In our own evaluation of 6 subjects with SCI (4 paraplegics and 2 with quadriplegia), use of DRS was shown to increase both the amplitude and frequency of colonic contractions of the left colon [27]. This anocolonic reflex probably involves stretch receptors in the IAS which increase the parasympathetic output to the left colon. All these patients had SCI of UMN type and whether a similar reflex is present in those with SCI of the LMN type is not known [27]. Diet has an important place in these individuals and minor changes in the diet can help these individuals tremendously. It is important for these individuals to consume adequate amounts of fiber and drink at least 2-3 liters of fluids every day [28]. Supplemental fiber may be needed if dietary intake is inadequate (<30 g/d). Fiber produces uniform stool consistency by absorbing excess water [29,30].

Laxatives are often employed as an adjunct to routine bowel care (*Tab. 3*). Bulk laxatives such as docusate and osmotic laxatives such as lactulose are the most commonly employed preparations [31,32]. Enemas are not promoted for routine use unless needed for fecal impaction.

These conventional strategies are time consuming and expensive and do not target the basic pathology of decreased colonic motility. Perhaps as a result, routine bowel care regimens do not yield satisfactory results in many patients. Hence, there is a need of more effective agents which attempt to reverse the basic pathophysiology after SCI.

Newer modalities

Cisapride, a prokinetic drug acts by increasing the release of acetylcholine from post-ganglionic nerve endings. Studies have documented a reduction in mouth-anus transit time and mouth to cecum transit time in subjects with quadriplegia using this drug [13,33]. We have shown the effect of cisapride in improving MCTT in subjects with SCI [13]. Though generally safe, cisapride has been linked to serious cardiac arrythmias (torsades de pointes) and has been withdrawn from the market [34].

Neostigmine, an inhibitor of enzyme acetylcholinesterase, results in increased levels of acetylcholine at the nerve endings and increases colonic peristalsis. It has been used successfully in patients with acute intestinal pseudo-obstruction [35]. Unfortunately, neostigmine also increases airway resistance and causes bradycardia in a significant number of patients. However, we have shown that these unwanted side effects can be prevented if neostigmine is administered together with glycopyrrolate. The latter is an anticholinergic which appears to spare the muscarinic receptors of the colon [17]. Recently, we have shown

***Figure 5*. Semi-quantitative measure (score of 0 to 4) of bowel emptying using barium oat-meal paste. Evacuation scores: a=1, b=2, c=3, and d=4**

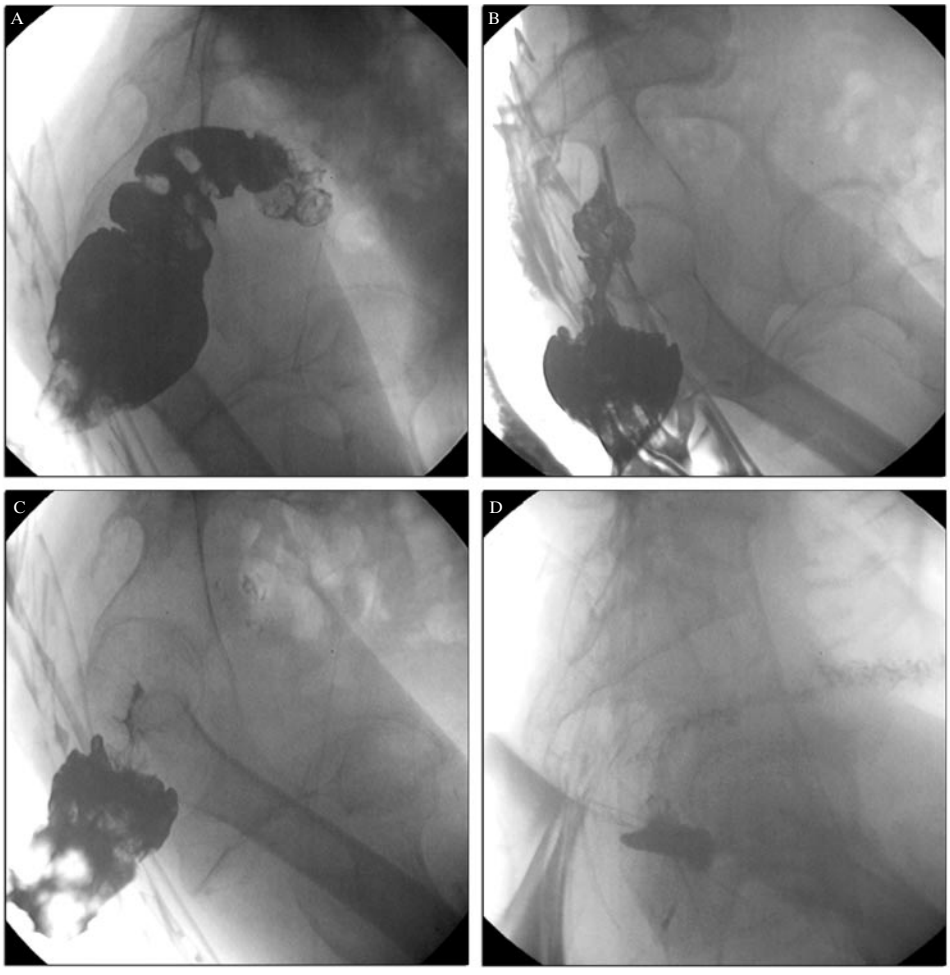


***Figure 6*. Histogram showing the effect of normal saline (control), IV neostigmine (2 mg), and IV neostigmine (2 mg) + glycopyrrolate (0.4 mg) on evacuation of oat-meal barium paste from the rectum and descending colon. The evacuation score was 3 or more in most subjects receiving neostigmine (57%) or combination of neostigmine and glycopyrrolate (64%). None of the subjects scored 2 or more after normal saline**

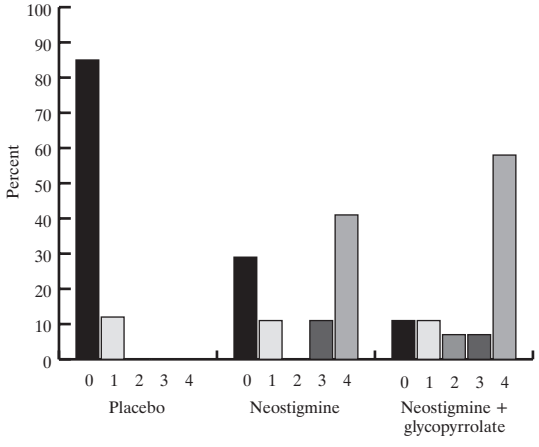
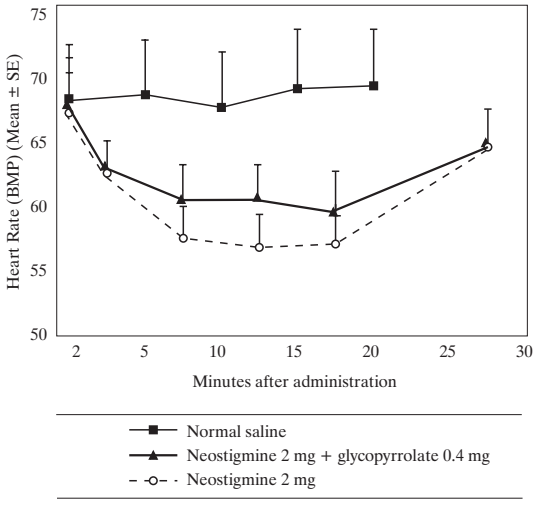


***Figure 7*. Comparison of the effect of normal saline, neostigmine, and neostigmine + glycopyrrolate on the mean heart rate at 5 min intervals**



beneficial effects of neostigmine on the gastrointestinal tract in individuals with SCI [36]. Thirteen individuals with SCI (5 with quadriplegia and 8 with paraplegia) were infused normal saline, neostigmine 2 mg, or neostigmine 2 mg with glycopyrrolate 0.4 mg on separate days. Bowel evacuation was measured by videofluoroscopy after rectal instillation of 200 ml of oat-meal paste of barium (having the consistency of soft stool). Evacuation was measured by an X-ray taken after 30 min and compared with a baseline X-ray (*Fig. 5*). In addition, airway resistance and hemodynamic parameters (pulse and blood pressure) were assessed. Both neostigmine and the combination of neostigmine with glycopyrrolate resulted in better evacuation compared with normal saline (*Fig. 6*) [36].

Although both neostigmine alone and neostigmine with glycopyrrolate resulted in bradycardia, lowest heart rates were recorded when neostigmine was given alone (*Fig. 7*). Both total and central resistance increased with neostigmine relative to normal saline, whereas, neostigmine with glycopyrrolate reversed this (+27% and +17% vs –10% and –8% respectively). The drug was well tolerated except for mild and transient (<30 min) muscle twitching (92%) and abdominal cramps (in those with injury below T10). Although intravenous infusion is not practical for routine clinical use, it remains to be established whether other routes of administration such as subcutaneous or intramuscular are effective in management of these individuals. These trials are ongoing and appear to be encouraging [37].

Tegaserod, a 5HT-4 (serotonin) receptor agonist is another agent with a potential for managing bowel symptoms in SCI. Serotonin has been documented as one of the neurotransmitters implicated in colonic motility [12,38]. Tegaserod in experimental studies has demonstrated an increase in both small bowel and colonic transit [39,40]. The drug has been successfully used in individuals with IBS, pseudo-obstruction, and habitual constipation [41-43]. There are no available data of its use in SCI and this is an area which needs to be explored.

Beneficial effect on the colonic motility of another 5-HT4 agonist, mosapride has been shown in a guinea pig model of SCI (after destruction of L1-3 and S2-4 cords) [44]. In response to rectal distension with a rectal balloon instilled with water, rectal pressures (R-R reflex) and internal anal sphincter relaxation (R-IAS reflex) were recorded at baseline and after intravenous administration of mosapride. Reflex area was derived and expressed as positive values for rectal contractions and IAS relaxations. Reflex indexes (R-R and R-IAS) were calculated as relative ratio of the reflex areas at baseline (control) and after drug administration. The authors showed that mosapride, given intravenously, increased the R-R and R-IAS indexes in a dose dependent manner. These changes could be reversed by about 50% after intravenous administration of the 5-HT4 antagonist GR-113808 [44].

Colostomy is an option in patients with severe and intractable problems [45,46]. It is also frequently advocated as an adjunct in the treatment of perineal pressure ulcers. Stone, et al. [46] showed that objective testing of the transit time can help in deciding the site of colostomy. A sigmoid colostomy is an option for those with normal colonic transit time and inability to adequately evacuate rectum. In contrast, a right transverse colostomy is useful for those with prolonged left colonic transit time. An ileostomy is generally reserved for individuals with a dilated, non-functional right colon. Stone, et al. [46], using a questionnaire, showed that colostomy simplified bowel care, relieved abdominal distension, and prevented fecal incontinence. The time spent in bowel care also decreased significantly from 98.6 min/day before colostomy to 17.8 min/day after colostomy. These individuals represent a high risk for abdominal surgery and selection of the patient is, therefore, important. In a small series, Deshmukh, et al. [47] reported a 15% mortality after colostomy in individuals with large pressure ulcers.

Moreover, Stone, et al. [46] noted postoperative complications in 10% individuals who underwent this procedure. All 27 patients in the first report had a colostomy performed for pressure ulcers whereas in the later, 13 out of 20 patients had colostomy for chronic intractable GI problems (one for rectal cancer), only 7 of 20 had this procedure for pressure ulcers. The authors in the later study performed colonic transit time and anorectal manometry in 6 patients in order to select the colostomy site. These differences could possibly explain the difference in mortality in the two reports. On the whole, it is an acceptable procedure provided it is done in a properly selected person at an appropriate time [45-47].

Surgical posterior rhizotomy and sacral anterior root stimulation are other surgical options shown to have therapeutic utility in SCI patients [48,49]. However, the high overall costs of these procedures has limited their utility. Cutaneous appendicoecostomy has been used to treat intractable incontinence in these patients.

Initially used by Malone, the technique (Malone Antegrade Colonic Enema or MACE) involves administration of enemas through the opening when required [50].

The technique has been shown to be successful in 57% of SCI patients with significant improvement in their QOL [51]. Bowel cleansing can also be accomplished in retrograde fashion using 'pulsed irrigation evacuation' (PIE) [52].

However, its efficacy remains to be determined in a controlled clinical trial.

Management of GI complications

The presenting symptoms of acute abdomen in SCI are quite variable given the sensory loss that accompanies SCI. Therefore, non-specific symptoms such as abdominal distension, vomiting, constipation always require a thorough evaluation.

An accurate diagnosis requires a careful clinical examination, laboratory evaluation, and expedited imaging studies (plain abdominal X-ray and CT scan of the abdomen).

Autonomic dysreflexia (AD) Prevention is the first step in treatment. Once recognized, however, AD should be treated as a medical emergency. If possible the stimulus should be identified and immediately removed. If needed, nifedipine and topical nitrates can be used for emergency control of the blood pressure [21].

Fecal impaction Rectal examination should always be performed if fecal impaction is suspected. If the rectum is empty, imaging is required to assess for more proximal impaction or signs of obstruction. To avoid complications, impaction

should be addressed quickly; delaying treatment for more than 3 days can be hazardous [20]. When an impaction exists, manual evacuation is the first option and requires proper lubrication and local anesthesia. When the impaction is beyond the reach of finger, sigmoidoscopic lavage can be effective. In addition, gastrograffin and golytely have been effective [53]. If these procedures fail, surgery is a last resort.

Colorectal cancer (CRC) screening

Individuals with SCI are at risk of acquiring the same degenerative conditions including cancer, as able bodied people. In a population based study in veterans, the incidence of CRC in patients with SCI similar to that in the general population [54].

The anatomic distribution of CRC was also the same as in the general population with two third of the lesions occurring on the left side or the rectum [54]. However, in contrast to able bodied population, 60% of these tumors were found to be quite advanced (stage III or IV) at the time of presentation. The inability to differentiate symptoms of colorectal carcinoma from other GI complaints in individuals with SCI probably accounts for the delay in diagnosis of colorectal cancer [54]. Even more than in able bodied individuals, early detection and cure of CRC requires regular colonoscopy as a routine measure.

Colonoscopy in individuals with SCI has unique features. Not only must the preparation of the colon be adapted to SCI, but the performance of the procedure must be modified. In this respect, we have found that a two day preparation with oral phosphosoda and golytely is often required. Moreover, we have noted that SCI patients have difficulty in retaining the insufflated air, have lower cecal intubation rate (82%) and have relatively poor colon preparation.

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