A physiological comparison between idiopathic and post-hysterectomy constipation

P. Katsinelos¹, K. Christodoulou¹, A. Celic², S. Dimiropoulos¹, P. Xiarchos¹, I. Pilpilidis¹, P. Amperiadis¹, Th. Vasilidis², A. Tarpagos¹, I. Katsos¹, N. Evgenidis²

SUMMARY
In order to gain more insight into the pathophysiology of severe constipation, anorectal manometry, sphincter electromyography, whole gut transit time and a test of defaecation of a simulated stool were carried out in 22 female patients with severe idiopathic constipation, 14 patients with severe constipation after hysterectomy and 20 female normal controls. Only 1/23 patient with idiopathic constipation compared with 6/14 patients with post hysterectomy constipation showed normal transit time (p<0.01). In those with abnormal transit, the markers were in the distal colon in patients with post hysterectomy constipation but were likely to be spread along the colon in patients with idiopathic constipation. Seven patients with post hysterectomy constipation showed abnormal anal pressure oscillations [amplitude: 10-50 cmH₂O (median=25 cmH₂O); frequency: 4-10 min⁻¹ (median=8 min⁻¹)] during basal recordings, compared with only 1 patient with idiopathic constipation (p<0.01). There were no significant differences in basal and squeeze anal pressures between any of the groups, but similar percentages of patients in each constipated group showed paradoxical increases in the electrical activity of the EAS when they strained to pass a simulated stool. The lowest rectal volumes required to induce initial and sustained anal relaxation and to elicit sensations of desire to defaecate and discomfort were significantly higher (p<0.05) in both groups of patients with constipation compared with normal controls. In conclusion, though the two groups of constipation share some similarities, the defect is more localized in the anorectum in patients with post hysterectomy constipation.

Key words: Post-hysterectomy, idiopathic, constipation

INTRODUCTION
Severe constipation in middle life is a condition that is almost entirely confined to women. In most cases, the aetiology is unknown and the pathophysiology uncertain; they are said to have idiopathic constipation. There is, however, a large cohort of women who become constipated for the first time after hysterectomy, and it is suspected that these patients have sustained damage to the extrinsic nerves supplying the distal bowel.¹ This seems more likely in patients who have undergone radical Wertheim hysterectomy for cancer, in which the entire cardinal ligament including the plexus of autonomic nerves, is severed.

Physiological studies carried out a week after radical hysterectomy showed an increase in the rectal volume required to induce internal sphincter inhibition in 50% of patients and a decrease in rectal sensitivity in 80% of patients. The internal sphincter was said not to relax fully in 60% of patients.² Only a quarter of these patients developed persistent bowel dysfunction. Bowel dysfunction is less common after simple hysterectomy; in a recent prospective study, Prior and Read³ reported that constipation developed de novo in only about 5% of patients and even in these it was rated mild or moderate. Moreover, the major physiological finding in patients after simple hysterectomy was an increase, rather than a

¹Department of Gastroenterology, Theagenion Hospital, Thessaloniki, Greece, ²Gastrointestinal Motility Unit, Centre for Human Nutrition, Northern General Hospital, Sheffield S5 7AU, UK, ³Second Propedeutic Department of Internal Medicine, Ippokration Hospital, Aristotelion University, Thessaloniki, Greece

Author for correspondence:
Panagiotis Katsinelos, 14 Marathonos str., 546 36 Thessaloniki, Greece
decrease in rectal sensitivity. Thus, it seems that severe constipation following simple hysterectomy is a rare phenomenon. Only two physiological studies have been conducted on anorectal function in patients who developed constipation for the first time following simple hysterectomy. One of them found a reduction in rectal sensitivity, an increase in rectal compliance, a reversed proximal to distal motility gradient in the distal colon and supersensitivity of the rectum to carbachol; features compatible with autonomic denervation. The other did not observe reduced rectal sensation or increased compliance, but noted that 38% of patients had anismus.

The aim of this study was to gain more insight into the pathophysiology of severe constipation in women by comparing the results of detailed systematic studies of anorectal physiology and whole gut transit time in patients with post hysterectomy constipation with those from patients with constipation and normal controls.

MATERIALS AND METHODS

Subjects

There were 14 patients (aged between 29 to 53 years, median=42 years) with severe constipation that commenced for the first time after hysterectomy and 22 female patients with severe idiopathic constipation (aged between 17 and 61 years, median=24 years). All patients had suffered for at least six months with constipation that was unresponsive to dietary adjustment. Bowel frequency ranged from twice a week to once every six weeks. Patients were selected from over 200 constipated patients who had been referred to our unit for anorectal function tests over a three year period. Patients with mild constipation which was easily treated with dietary advice or severe constipation associated with some other well defined neuromuscular or surgical conditions were excluded from the study. The results of clinical investigations including sigmoidoscopy and barium enema were negative in every case. None of the patients had a megacolon.

Ten out of 22 patients with idiopathic constipation reported that their symptoms had been present since early childhood, for as long as they could remember. In the remainder (12/22), the condition commenced in adolescence (age 11 to 21). In contrast, the onset of post-hysterectomy constipation was much later and occurred within a month of the operation in every case (median=38.5 years, range=24 to 51 years).

For comparison, 20 normal female volunteers (aged between 21 and 53 years, median=43 years) were also studied. None of these subjects had a history of bowel disturbance and none of them were taking any medication known to interfere with bowel action.

Methods

Anorectal Manometry and Electrophysiology

No bowel preparation was used but subjects were invited to empty their rectum if they felt the need to do so.

With the subjects lying in the left lateral position with the hips flexed to 90°, a manometric probe, consisting of a polyvinyl 7-lumen tube with an external diameter of 4mm was inserted into the rectum. When correctly positioned, manometric side holes were situated at approximately 0.5, 1.0, 2.0, 4.5 and 15cm from the anal verge. The manometric ports were perfused with water at a rate of 0.2ml/min with the aid of a low compliance pressurized perfusion system and pressures were measured with pressure situated in each perfusion line and connected via amplifiers to a multichannel chart recorder (778A, Hewlett Packard; Waltham, Mass, USA). A high compliance latex balloon was tied 5-11cm from the anal verge and was used to distend the rectum. The pressure within the balloon was measured by a water-filled non-perfused tube linked to a transducer.

The electrical activity of the sphincter was recorded using a bipolar wire electrode inserted into the superficial EAS or into the intersphincteric groove between the EAS and IAS. The free ends of the wires were bared and attached to an amplifier which was connected via an integrator (alternating current to root mean square converter; Analog Devices AD536) to the chart recorder, which displayed both raw and integrated EMG (170-ms time constant).

Pressures and electrical activity were recorded under resting conditions for at least 20 minutes. The patient was then instructed to contract the anal sphincter maximally for a period of 30 seconds. This was repeated twice more with a gap of a minute between each effort. The patient rested for 10 minutes and then the rectal balloon was serially inflated with 10, 20, 40, 60, 100, 150, 200 and 250ml of air. Each inflation was maintained for one minute and a gap of at least 1 minute was allowed before the next inflation. All subjects were asked to report the rectal sensations induced by the balloon distension. The distension was terminated either when the subject felt discomfort or pain or after 250ml had been introduced. The tube was then withdrawn, leaving the wires in situ.
A physiological comparison between idiopathic and post-hysterectomy constipation

Simulated Defaecation
To assess defaecation, a 50ml silicon envelope, modified from an Angelchik prosthesis [George Strang Forth Medical Ltd, Berkshire, UK] and fashioned to mimic the typical size and shape of a formed stool was inserted into the rectum and pulled down into the ampulla by means of a tape. The subject was transferred to a commode and the EMG wires were connected to the recorder. The subject was then left alone while she tried to expel the simulated stool from the rectum. The time over which the subject strained to pass the object and the electrical activity of the EAS were noted. Each subject was allowed 5 minutes to pass the object. If she was unable to do so within that time, the simulated stool was withdrawn through the anus by pulling of the tape.

Whole Gut Transit Time
Whole gut transit time and the site of colonic retention of markers were assessed by asking the subject to ingest 50 radio-opaque markers (segments of polyvinyl tubing, 4mm x 2mm) at breakfast and then counting the number of radio-opaque markers in each segment on an abdominal radiograph taken 72 hours later.3,4

Statistical Analysis
The statistical significance of the differences in rectal volumes required to induce certain phenomenon was assessed using Kruskal-Wallis test and the differences in pressures was tested by using Analysis of Variance. Chi-square test with Yates’ correction was used to determine the differences between the percentages of subjects in each group, who demonstrated certain abnormalities.

RESULTS
Whole Gut Transit
All normal subjects were able to pass at least 80% of ingested markers within 72 hours.3,4 Only one patient with severe idiopathic constipation showed normal colonic transit, compared with 6/14 patients with post hysterectomy constipation (x²=6.03, p<0.01). The colonic distribution of radio-opaque markers was also different in the two groups of patients. All 8 post hysterectomy patients with slow colonic transit showed a preponderance of markers in the region of the rectum and sigmoid colon. Markers were retained in the sigmoid colon and/or rectum region in only 8/22 patients with severe idiopathic constipation (x²=7.2, p<0.001 compared with post-hysterectomy group). In the remaining 14 patients with idiopathic constipation, the markers were spread along the colon indicating a widespread disturbance of colonic propulsion or colonic interia (x²=7.2, p<0.001; compared with the post-hysterectomy group).

Anismus
Four out of the 19 patients (21%) with severe idiopathic constipation, who carried out the test, failed to expel a simulated stool from the rectum. This was associated with paradoxical increases in the electrical activity of the EAS. Another 3 patients also showed similar paradoxical increases in EAS activity but were able to pass the simulated stool. The results were similar in the post hysterectomy group. Two out of 11 (18%) patients who did this test failed to pass the simulated stool and these were the only patients in this group who showed paradoxical increases in the electrical activity of the EAS. The time over which subjects strained to pass the simulated stools was abnormally long in both groups of constipated patients, [median=24 and 25 seconds]. Normal subjects experienced no difficulty in expelling the simulated stool.

Manometric results
Basal anal pressure
After insertion of the probe, all subjects showed a reduction in anal pressure over a period of 15 minutes to reach a stable baseline, which was termed the minimum basal pressure. There were no significant differences in the minimum basal pressure (p>0.05) between each group of subjects (Table 1), though 8/22 patients with idiopathic constipation had minimum basal pressures that were lower than the normal range (<30cmH₂O) compared with only 1/14 patients with post hysterectomy constipation. Seven of the 14 patients in the post hysterectomy group showed profound regular oscillations in anal pressure with an amplitude of 15-50cmH₂O (median: 25cmH₂O) and a frequency of 4-10min⁻¹ (median: 8min⁻¹). This phenomenon was observed in only one patient with severe idiopathic constipation (p<0.01) and was not seen in the normal control group (p<0.01).

Squeeze pressures
All subjects exhibited increases in anal pressure and electrical activity of the external sphincter when they were asked to contract their anal sphincter, and the pressures recorded in each group were very similar (Table 1; p<0.05).
Table 1. Anal pressures recorded during resting conditions and during contraction of the EAS, and rectal volumes required to induce rectal sensations and sphincter responses

<table>
<thead>
<tr>
<th></th>
<th>Normal controls</th>
<th>Constipated</th>
<th>Idiopathic</th>
<th>Patients Posthysterectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anal pressure (cmH₂O)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max. basal</td>
<td>91±8</td>
<td>88±7</td>
<td>93±7</td>
<td></td>
</tr>
<tr>
<td>Min. basal</td>
<td>44±6</td>
<td>50±6</td>
<td>57±9</td>
<td></td>
</tr>
<tr>
<td>Squeeze</td>
<td>163±17</td>
<td>138±13</td>
<td>141±15</td>
<td></td>
</tr>
<tr>
<td>Rectal volumes (ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Required to induce</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perception</td>
<td>11 (10-20)</td>
<td>10 (10-100)</td>
<td>10 (10-40)</td>
<td></td>
</tr>
<tr>
<td>Wind</td>
<td>20 (10-40)</td>
<td>40 (20-100)</td>
<td>40 (20-150)</td>
<td></td>
</tr>
<tr>
<td>DD</td>
<td>40 (20-100)</td>
<td>60 (40-150)*</td>
<td>60 (40-250)*</td>
<td></td>
</tr>
<tr>
<td>Discomfort</td>
<td>100 (100-150)</td>
<td>150(100-250)*</td>
<td>150 (100-250)*</td>
<td></td>
</tr>
<tr>
<td>Initial IAS relaxation</td>
<td>10 (10-40)</td>
<td>20 (10-60)*</td>
<td>20 (10-100)*</td>
<td></td>
</tr>
<tr>
<td>Sustain IAS relaxation</td>
<td>60 (20-100)</td>
<td>100 (20-150)*</td>
<td>100 (40-200)*</td>
<td></td>
</tr>
<tr>
<td>EAS response</td>
<td>10 (10-20)</td>
<td>10 (10-60)</td>
<td>10 (10-40)</td>
<td></td>
</tr>
<tr>
<td>Rectal compliance at 100ml (ml.cmH₂O⁻¹)</td>
<td>6.5±0.1</td>
<td>6.2±0.6</td>
<td>6.9±0.9</td>
<td></td>
</tr>
</tbody>
</table>

DD: desire to defaecate;
*: significantly different from normal controls, p<0.05

Responses to rectal distension

Rectal sensation

In normal controls, intermittent distension of the rectum induced discriminative rectal sensations as the distending volumes increased, first a perception of the balloon, a feeling of wind (gas in the rectum), a desire to defaecate and finally a feeling of discomfort or pain. There were no significant differences in the rectal volumes required to induce perception and wind between normal controls and either group of constipated patients (Table 1), but the average rectal volumes required to induce a desire to defaecate and a sensation of discomfort or pain were significantly higher than controls in both groups of constipated patients (Table 1). All normal controls felt a desire to defaecate by 60ml of distending volume compared with only 7/14 patients in the hysterectomy group (x²=4.87; p<0.05) and 12/23 patients in idiopathic constipation group (x²=5.14; p<0.02). Similarly, all normal controls felt a sensation of pain by a volume of 150ml, compared with only 10/14 patients in the posthysterectomy group (x²=4.02; p<0.05) and 15/23 patients with idiopathic constipation (x²=6.36; p<0.02). There were no differences in sensory thresholds between the two groups of constipated patients.

Rectal compliance

Rectal compliance tended to be higher in both patient groups compared with normal controls, though the differences were not statistically significant.

Internal anal sphincter response

Anal relaxation was observed at a distending volume of 20ml in all normal volunteers, but the relaxation did not usually last for the full minute of rectal distension. The amplitude of relaxation became larger and the duration longer as the distending volume increased, and was sustained for the duration of rectal distension at a volume of 10ml in all normal volunteers. The threshold volumes required to induce initial and sustained relaxation were significantly higher in patients with severe idiopathic constipation and in patients with post hysterectomy constipation (Table 1) compared with normal controls.

Four patients with post hysterectomy constipation and 6 patients with idiopathic constipation failed to show any anal relaxation at any level of distension (p<0.05 compared with normal volunteers). All 4 patients in the post hysterectomy group also showed abnormal regular sphincter oscillation which was attenuated by rectal distension without any reduction in average pressure, whereas all six patients with idiopathic constipation exhibited abnormally low basal pressures [30cm H₂O], suggesting that the sphincter tone was already minimal and could not be reduced any further.

External anal sphincter response

In all subjects studied, distension of the rectum induced increases in electrical activity that became longer as the distending volumes increased. There were no sig-
nificant differences (p>0.05) in the lowest volumes required to induce increases in the electrical activity of the EAS between groups (Table 1).

**DISCUSSION**

Our results showed some important differences between the two groups of patients with severe constipation. Data obtained from patients with post hysterectomy constipation suggest that it is a disease that involves just the distal colon. None of the patients with constipation that commenced for the first time after hysterectomy showed a delay in transit involving the proximal regions of the colon, the majority showed hold-up in the rectum or sigmoid colon. In the absence of any trauma to the rectum itself, the reduction in rectal sensitivity would suggest damage to the autonomic nerves that coordinate distal colonic propulsion. The distribution of markers is very similar to those found in patients with paraplegia. The autonomic nerves may also modulate relaxation of the internal anal sphincter. Patients with diabetic autonomic neuropathy and patients with high spinal lesions show increases in the thresholds required to induce internal sphincter relaxation. Diabetic patients also demonstrated spontaneous oscillations of the sphincter occurring at a frequency of between 6 and 10 per minute, that were seen in half of our patients with constipation developing for the first time after hysterectomy. The only other group, in which this phenomenon had been observed were patients who had undergone resection of the rectum for colorectal anastomosis or reconstitutive pouch proctocolectomy. These patients may sustain damage to the autonomic nerves during section of the lateral rectal ligaments. Thus our data support the notion that the few patients with simple hysterectomy who develop severe constipation for the first time soon after the operation have sustained damage to the autonomic nerve supply to the distal colon and anal sphincter.

Patients with idiopathic constipation share some features with the posthysterectomy group; the reduction in rectal sensitivity, similar prevalence of anismus and impairment of internal sphincter relaxation. All of these might suggest a disturbance in extrinsic control, but if so, a disturbance in the extrinsic control of the whole colon must be implicated, since the majority of patients showed evidence of total colonic inertia. In addition, only one patient with idiopathic constipation showed the abnormal oscillation of the internal sphincter seen in post-hysterectomy constipation, though six more showed abnormally low basal pressures, a feature also noted in patients with low spinal or cauda equina lesions and patients with diabetic neuropathy. But, in contrast to patients with colonic inertia, patients with lesions in the low spinal cord or cauda equina do not have colonic inertia, their markers tend to hold up in the distal colon, and patients with low spinal lesions have increases in rectal compliance with faecal impaction. Thus we may argue that any disturbance in extrinsic control of the bowel in idiopathic constipation is probably exerted at a much higher level, perhaps in the brain stem.

In conclusion, our study shows that patients with severe post-hysterectomy constipation present a reduction in rectal sensation, and sigmoid motor activity, and profound regular oscillations in anal pressure which are findings suggestive of damage to the autonomic nerves supplying the distal colon and anala area.

**REFERENCES**