

## Functional bowel symptoms in diabetes – the role of autonomic neuropathy

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**Summary:** The autonomic nervous system may have a role in the pathogenesis of irritable bowel syndrome. If so, the occurrence of irritable bowel symptomatology in patients with autonomic neuropathy might indicate which, if any, of these symptoms are dependent on autonomic innervation. The prevalence of abdominal pain, abdominal distension and an abnormal bowel habit was recorded in 200 patients with diabetes, screened for autonomic neuropathy, and 200 matched controls. Constipation was significantly more common in patients with autonomic neuropathy than in those without, or controls (22.0% vs 9.2% vs 6.8%). The prevalence of abdominal pain and abdominal distension was no different in patients with and without autonomic neuropathy and their respective controls. The results of this study suggest that control of bowel habit is more dependent on the total integrity of the autonomic nervous system than the perception of pain or the production of distension.

### Introduction

The primary symptoms of irritable bowel syndrome (IBS) are abdominal pain, abdominal distension and an abnormal bowel habit. The mechanism by which these symptoms are produced or appreciated is poorly understood, but a generalized disturbance of gastrointestinal motility has been implicated.<sup>12</sup> The autonomic nervous system is intimately involved in the control of gastrointestinal motility and sensitivity and it has been suggested that a disturbance of this system may be involved in the pathophysiology of IBS.<sup>3–5</sup> If this were so, the presence or absence of particular IBS symptoms in patients with autonomic neuropathy might indicate which, if any, were dependent on autonomic innervation. Autonomic neuropathy (AN) is a well-recognized sequel of diabetes mellitus and it is generally assumed that the bowel symptoms from which these patients suffer are due to this complication.<sup>6–8</sup> However, these studies have confined themselves to bowel habit disturbances only and the prevalence of the other symptoms of IBS, namely abdominal pain and distension, have not been previously recorded. It was the purpose of this study to assess all the symptoms of IBS in diabetic patients, with and without autonomic neuropathy, and compare these with appropriately matched controls.

### Materials and methods

Two hundred patients attending a diabetic clinic and 200 individually age- and sex-matched controls were studied using a detailed questionnaire to determine the prevalence of functional bowel disease in both groups. Hospital visitors were used as controls, with diabetics being excluded. All subjects were interviewed by the same researcher over a period of one year. The prevalence of abdominal pain, abdominal distension and an abnormal bowel habit was recorded and a diagnosis of IBS was only made when all three symptoms were present on a regular basis. Abnormal bowel habit was further sub-divided into constipation, diarrhoea or alternating types. Any history of faecal incontinence was also noted.

In the diabetic subjects, data were collected relating to length of history, type of diabetes, diabetic complications and past and current treatment. Autonomic function was assessed on the sinus arrhythmia resulting from a single forced respiratory cycle as described by Smith.<sup>9</sup> The shortest R-R interval during inspiration (I) and the longest during expiration (E) was measured and the E:I ratio calculated. The values were then compared to an age-specific normal range and only those values below the lower 95th percentile considered abnormal and reflecting autonomic neuropathy.<sup>9</sup> Patients taking drugs known to influence this test, or who were unable to co-operate fully, were excluded. Statistical comparisons between groups were made by the chi-squared test with Yates correction.

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## Results

The diabetic group consisted of 106 women and 94 men with a mean age of 49.4 years; 115 were on insulin and the remainder controlled by diet or oral hypoglycaemic agents. Fifty nine had evidence of autonomic neuropathy (AN positive). This group did not differ from those without autonomic neuropathy (AN negative) except in having significantly more insulin-dependent subjects (Table I).

Table II compares the prevalence of IBS symptoms in diabetic patients, with and without AN, and their individually matched controls. Significant differences were observed with regard to bowel habit, but not abdominal pain and distension.

Constipation occurred in 22.0% of diabetics with AN which was significantly more common than in diabetics without AN (9.2%,  $P < 0.03$ ). Further, diabetics with AN complained of significantly more constipation than in their individual-

ly matched controls (22.0% vs 6.8%,  $P < 0.04$ ). In contrast, no increase in constipation was observed in diabetics with an intact autonomic nervous system compared to their controls. Indeed diarrhoea was the commonest disturbance of bowel habit in this group. However, only 2 patients, both with evidence of autonomic neuropathy, had features of nocturnal diarrhoea and faecal incontinence suggestive of 'diabetic diarrhoea'. No other patient or control complained of faecal incontinence. The prevalence of abdominal pain and distension was not significantly different either between diabetics with and without autonomic neuropathy or their controls (Table II).

## Discussion

If the IBS symptoms of either abdominal pain or distension were largely dependent on the integrity of the autonomic nervous system then they might

**Table I** Comparison of patients with (AN + ve) and without (AN - ve) autonomic neuropathy and their matched controls

	AN + ve	Controls	AN - ve	Controls
Number	59	59	141	141
M:F	30:29	30:29	64:77	64:77
Age (years)				
mean	51.6	50.3	47.7	46.8
(s.d)	(15.3)	(15.9)	(16.4)	(15.3)
Insulin:non-insulin	44:15	-	70:71*	-

\*AN + ve vs AN - ve: chi-square (1) = 9.0,  $P < 0.01$ .

**Table II** Comparison of symptoms in patients with (AN + ve) and without (AN - ve) autonomic neuropathy and their matched controls. Figures shown are number (%) (95% confidence limits for %)

	AN + ve	Controls	AN - ve	Control
Irritable bowel syndrome	5 (8.5) (2.8-18.7)	2 (3.4) (0.4-11.7)	23 (16.3) (10.6-23.5)	17 (12.1) (7.2-18.8)
Pain	11 (18.6) (9.7-30.9)	9 (15.3) (7.2-27.0)	30 (21.3) (14.9-29.1)	31 (22.0) (15.5-29.9)
Distension	14 (23.7) (13.6-36.6)	10 (16.9) (8.4-29.0)	54 (38.3) (30.2-46.9)	40 (28.4) (21.1-36.6)
Abnormal bowel habit	20 (33.9) (22.1-47.4)	7 (11.7)* (4.9-22.9)	37 (26.2) (19.2-34.4)	33 (23.4) (16.7-31.3)
Constipation	13 (22.0) (12.3-34.7)	4 (6.8)** (1.9-16.5)	13 (9.2)† (4.9-15.3)	20 (14.2) (8.9-21.1)
Diarrhoea	3 (5.1) (1.1-14.2)	2 (3.4) (0.4-11.7)	16 (11.3) (6.6-17.8)	8 (5.7) (2.5-11.0)
Alternating	4 (6.8) (1.9-16.5)	1 (1.7) (0.0-9.1)	8 (5.7) (2.5-11.0)	5 (3.5) (1.1-8.2)

\*AN + ve vs controls: chi-square(1) = 6.9,  $P < 0.01$

\*\*AN + ve vs controls: chi-square(1) = 4.4,  $P < 0.04$

†AN + ve vs AN - ve: chi-square(1) = 5.0,  $P < 0.03$ .

be expected to occur less commonly in patients suffering from autonomic neuropathy. However, there was no significant difference in the prevalence of these symptoms in either the AN positive or AN negative patients when compared to each other or their respective controls. This would suggest that a fully intact autonomic nervous system is not critical for the perception of abdominal pain or the production of distension. It seems reasonable to assume that autonomic neuropathy is not an all or none phenomenon in terms of either degree of involvement or ratio of sympathetic to parasympathetic damage. There is evidence to support this latter view and, in particular, the parasympathetic appears to be affected before the sympathetic system.<sup>10</sup> Our results suggest that gut motility, as reflected by bowel habit, may be more sensitive to autonomic denervation, possibly as a result of the two components of the autonomic nervous system being unequally affected in an early or mild neuropathy.

The results of this study show that diabetic patients with AN have a higher incidence of constipation than either those without neuropathy or their individually matched controls. This increased prevalence of constipation would not appear to be related to diabetes alone as patients without AN showed no difference from controls. It is of interest that classic 'diabetic diarrhoea' was extremely uncommon in this study, being observed in only two subjects with AN and other severe diabetic complications.

This study could have used a battery of autonomic function tests in a small number of patients or a single sensitive test in a large number of subjects. The latter design appeared preferable in

order to include as many diabetic patients with IBS as possible, taking into account a prevalence of IBS even in the normal population of only 10–20%.<sup>11</sup> Faced with the choice of a single method, the one selected is probably the most sensitive and correlates well with other techniques for detecting AN.<sup>9,12,13</sup> Further, the prevalence of autonomic neuropathy detected was in accord with the figures for comparable groups of diabetics reported by others using a variety of different tests of autonomic function.<sup>9,12,14</sup> In addition, indirect evidence that the test was accurate came from the observation that 14 of the 15 diabetics with neurological or eye complications were autonomic neuropathy positive. The differences in symptomatology observed in the patient groups identified by this test indicate that it is detecting an abnormality of the autonomic nervous system that results in a change in gut function.

Our results suggest that bowel function as opposed to abdominal pain or distension is relatively sensitive to damage of the autonomic nervous system. This usually leads to constipation rather than the classically quoted complication of diarrhoea which is relatively uncommon. Patients with diabetes complicated by AN do not appear to be protected from the symptoms of functional bowel disease.

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#### References

1. Kumar, D. & Wingate, D. The irritable bowel syndrome: a paroxysmal motor disorder. *Lancet* 1985, **ii**: 973–977.
2. Kellow, J.E. & Phillips, S.F. Altered small bowel motility in irritable bowel syndrome is correlated with symptoms. *Gastroenterology* 1987, **92**: 1885–1893.
3. Smart, H.L. & Atkinson, M. Abnormal vagal function in irritable bowel syndrome. *Lancet* 1987, **ii**: 475–478.
4. Bockus, H.L., Bank, J. & Wilkinson, S.A. Neurogenic mucous colitis. *Am J Med Sci* 1928, **176**: 813–829.
5. Camilleri, M., Malagelada, J.R., Stanghellini, V., Fealey, R.D. & Sheps, S.G. Gastrointestinal motility disturbance in patients with orthostatic hypotension. *Gastroenterology* 1985, **88**: 1852–1859.
6. Feldman, M. & Schiller, L.R. Disorder of gastrointestinal motility associated with diabetes mellitus. *Ann Intern Med* 1983, **98**: 378–384.
7. Rundles, R.W. Diabetic neuropathy: general review with respect of 125 cases. *Medicine* 1945, **24**: 111–160.
8. Mayne, N. Neuropathy in the diabetic and non-diabetic population. *Lancet*, 1965, **ii**: 1313–1316.
9. Smith, S.A. Reduced sinus arrhythmia in diabetic autonomic neuropathy: diagnostic value of an age-related normal range. *Br Med J* 1982, **285**: 1599–1601.
10. Ewing, D.J. & Clarke, B.F. Diagnosis and management of diabetic autonomic neuropathy. *Br Med J* 1982, **285**: 916–918.
11. Thompson, W.G. & Heaton, K.W. Functional bowel disorders in apparently healthy people. *Gastroenterology* 1980, **79**: 283–288.
12. Anonymous. Diagnosis of autonomic neuropathy (Editorial). *Br Med J* 1978, **ii**: 910–911.
13. Thuluvath, P.J. & Triger, D.R. Autonomic neuropathy and chronic liver disease. *Q J Med* 1989, **268**: 737–747.
14. Mackay, J.D., Page, M.McB., Cambridge, J. & Watkins, P.J. Diabetes autonomic neuropathy. The diagnostic value of heart rate monitoring. *Diabetologia* 1980, **18**: 471–478.