A wide variety of disturbances of cell membrane handling of sodium have been documented in hypertension; moreover, cell membrane structure itself appears to differ, and more recently calcium affinity and extrusion have been found to be abnormal.[5] It seems most likely that a fundamental disturbance of membrane structure or function, or both, genetically determined, underlies them. Whether this is present in the cells secreting catecholamines or merely in the target organs, thereby altering their response, is uncertain. Nevertheless, the full effects of noradrenaline on cell membrane function in hypertension remain to be elucidated: in addition, the effects of catecholamines on sodium transport will have to be considered more carefully if artefactual findings are to be avoided.

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Use of a long acting somatostatin analogue in controlling life threatening ileostomy diarrhoea

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Abstract

A woman presented with persistent ileostomy diarrhoea unresponsive to conventional drug treatment and necessitating parenteral nutrition. Output was four to six litres of watery fluid per 24 hours while she was receiving oral nutrition and two to three litres when she was starved. Treatment with a long acting analogue of somatostatin (50 μg subcutaneously every 12 hours) reduced the ileostomy output to 2·0-2·5 litres/24 hours with an oral diet and the effluent became semiformed. Parenteral fluids could be stopped.

Somatostatin may have a role in the treatment of secretory diarrhoea, but prospective controlled trials are necessary.

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Introduction

Somatostatin suppresses many of the gut peptides implicated in the control of secretory and motor activity of the gastrointestinal tract. These actions no doubt contribute to its recently described efficacy in the treatment of patients with bleeding peptic ulcers, the carcinoid syndrome, and enteric fistulas. Its use in the control of diarrhoea has been virtually confined to patients with peptide secretory tumours,[1] although it has been shown to be beneficial in a few patients with profuse diarrhoea due to pseudo-obstruction[2] and the short bowel syndrome.[3] One of the main factors limiting its therapeutic use is its short half life (two to three minutes), and therefore attempts have been made to develop longer acting analogues. We report the successful use of such a drug (SMS 201-995, Sandoz Ltd) to control the output of effluent from a patient with life threatening ileostomy diarrhoea of unknown aetiology.

Case report

A 46 year old woman with Crohn's disease for which she had undergone colectomy and ileorectal anastomosis in November 1980 (35 cm of distal ileum resected) represented in December 1982 with an enterocutaneous fistula due to recurrent disease proximal to the anastomosis. Conservative treatment failed to heal the fistula, and in January 1984 she underwent resection of the fistula, ileorectal anastomosis, and distal ileum (30 cm). A new ileorectal anastomosis was fashioned and defunctioned by creating an end ileostomy. At laparotomy the rest of the small bowel was macroscopically normal.

She recovered from the operation, but during the next four months she had a persistently high ileostomy output, passing four to six litres of watery fluid per 24 hours while receiving oral nutrition and two to

three litres when starved. There was no evidence of adaptation of the ileostomy, and the diarrhoea remained unresponsive to conventional drug treatment. She required continuous parenteral nutrition, but despite treatment she continued to lose weight and developed electrolyte disturbances that prevented her from leaving hospital. Investigations failed to disclose a cause for the diarrhoea: in particular, the profile of gut hormones (including vasoactive intestinal polypeptide) was normal.

Four months after formation of the ileostomy she was given infusions of SMS 201-995 (25 μg/h) and placebo (isotonic saline 125 ml/h), each over 24 hours, on a double blind basis. During each infusion gastric emptying and transit of a standard meal through the small bowel were measured,[4] and simultaneously the amounts of nutrient and electrolyte excreted during the study period (defined as from the start of ingestion of the meal to a point when two consecutive ileostomy samples contained less than 5% of marker) were determined. Table I shows the ileostomy output, electrolyte content, and transit data. The excretion of nitrogen, fat, and glucose remained unchanged while she received the drug. In a separate study the output volume and electrolyte content over 24 hours were determined while she received a standard hospital diet during infusion with drug and placebo (table II). After the drug was stopped there was no rebound phenomenon.

TABLE I—*Results of study of transit and absorption*

	Ileostomy output (g/h)	Water and electrolyte output*			Gastric emptying time† (min)	Small bowel transit time‡ (min)
		% water	Sodium (mmol)	Potassium (mmol)		
SMS 201-995	58	86	35·5	13·5	106	134
Placebo	327	97	239·6	26·7	104	76

* Corrected for 100% marker recovery.
† Time taken for half the marker to pass through the stomach.
‡ Mouth to stoma transit time − gastric emptying time.
Conversion: SI to traditional units—Sodium and potassium: 1 mmol = 1 mEq.

TABLE II—*Twenty four hour ileostomy output with controlled diet*

	Ileostomy output (g)	Water (ml)	Sodium (mmol)	Potassium (mmol)
SMS 201-995	1600	1376	161·5	20·3
Placebo	5300	5051	655·8	47·9

Conversion: SI to traditional units—Sodium and potassium: 1 mmol = 1 mEq.

Treatment with SMS 201-995 was then started, 50 μg being given subcutaneously every 12 hours. This reduced her ileostomy output to 2·0-2·5 litres/24 hours with a normal diet, the effluent becoming semi-formed. There were no side effects. Parenteral fluids were stopped and she was discharged from hospital. One month later she was still taking SMS 201-995; she felt well, the volume of her ileostomy output remained at 2·0-2·5 litres/24 hours, and she had gained 2·5 kg in weight since the start of the treatment.

Discussion

SMS 201-995 dramatically reduced the life threatening ileostomy diarrhoea experienced by this patient and enabled her to return to a fairly normal life. The cause of the profuse output was not entirely clear. The excessive content of water and electrolytes in the effluent could not be explained entirely by the length of ileum resected or subsequent malabsorption of fat. A disturbance of the intestinal transport mechanism of fluid is partly implicated because an output of two to three litres per 24 hours persisted during starvation. Thus a combination of secretory, malabsorption, and osmotic factors appears to have been the cause. Somatostatin enhances absorption of water and electrolytes in normal ileum,[5] and presumably this was the mode of action in our patient. Interestingly, although water and electrolyte outputs were reduced during treatment, the amounts of fat and glucose excreted were not affected. Although somatostatin may slow gastric emptying, this was not the case in our patient. The prolongation of transit through the small bowel was probably secondary to the drug's effect on the transport of fluid, although a primary effect on motility cannot be ruled out.

Our results suggest that this drug might be used to treat more patients with secretory diarrhoea in addition to those with rare gastrointestinal tumours secreting hormones. This prospect is exciting, but obviously further data accrued from prospective controlled trials are required. Caution is also necessary. As the drug can inhibit secretion of a wide range of hormones including insulin and growth hormone it may have long term metabolic sequelae, and careful follow up in specialised units will be needed.

We are grateful to Professor David Johnston for allowing us to study this patient, and to Dr Roy Shentall, Sandoz Ltd, for his helpful advice. We also thank Mrs Lorna McQuade, who typed the manuscript. JCC was supported by a grant from the Yorkshire Regional Health Authority.

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ONE HUNDRED YEARS AGO

Amongst the social entertainments with which it is becoming the fashion to inaugurate the session at the various medical schools of the metropolis, we cannot call to mind any which has been more enjoyable than the *conversazione* given in St. Mary's Hospital, and the new school-buildings attached thereto, on the evening of Thursday, the 2nd instant, by the medical officers and lecturers of the school. The large new ground-floor wards of the hospital were decorated by Messrs. Gillow, and here were pictures, works of art, and other objects of interest on exhibition, lent for the occasion by various gentlemen; in the larger room, the band of the Grenadier Guards, under the direction of Mr. Dan Godfrey, played a varied selection of music during the evening. The out-patients' room was decorated in excellent taste by Mr. William Morris, and here were exhibited a loan-collection of Oriental art-manufactures, Indian curiosities, art-furniture, and pictures. The Royal Criterion Hand-bell Ringers and Glee Singers gave three short separate entertainments in this department during the evening before appreciative audiences. The medical school-buildings were decorated by Messrs. Marshall and Snelgrove; and here, in the museum, was shown the delightful method of economic electric lighting in private houses devised by Mr. Tayler Smith. The softness, steadiness, and handiness of the lights were greatly admired. Microscopes, ophthalmic instruments, portable electric lamps, and other scientific instruments, sphygmographs, a new form of spirometer, and dynamometers, were also shown. In the Board-room, Mr. Plater's Glee Union gave also three entertainments during the evening, and elicited much applause. The refreshments served to the visitors were of a *récherché* description, and included, amongst other delicacies, some £20 worth of Chinese bird's-nest soup, which had been kindly contributed for the occasion. The apartment in which refreshments were served was artistically arranged, and particularly bright with flowers in wreaths and decorations of all kinds. Over two thousand guests, ladies and gentlemen, were present; and the universally expressed opinion was that the entertainment was a great success, and reflected much credit upon those who had spared no pains to delight their guests. Foremost amongst these must, of course, be reckoned Mr. George P. Field, the energetic Dean of the School, who was ably assisted by Mr. Malcolm Morris, Mr. Noble Smith, Mr. Juler, and several other gentlemen. (*British Medical Journal* 1884;ii:722.)