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Octreotide Treatment of Chemotherapy-induced Diarrhoea

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THE AIM of the present study was to investigate the efficacy of octreotide, a somatostatin analogue, in the treatment of diarrhoea caused by 5-fluorouracil (5-FU) chemotherapy.

It has been estimated that 10–15% of patients under 5-FU chemotherapy suffer from gastrointestinal toxicity, including diarrhoea and/or stomatitis, oesophagitis and gastritis [1, 2]. Diarrhoea can sometimes be so severe that not only is chemotherapy interrupted but hydration and electrolyte abnormalities of the patient also have to be corrected, requiring hospital admission. Uncontrollable diarrhoea has so far been treated with antidiarrhoeal drugs, such as loperamide and diphenoxylate but without good results [3, 4]. These drugs act mainly at the level of intestinal smooth muscle fibres causing a reduction in motility and, thus, a reduced frequency of diarrhoea. Possibly, they also play a role in the reduction of gastrointestinal excretions.

In 1990, Kennedy and associates published a study [5] reporting the successful treatment of diarrhoea by the use of octreotide. It has been well demonstrated that somatostatin analogues, especially octreotide, have antidiarrhoeal action [6, 7]. Various studies have been published on the subject of treating severe diarrhoea of patients suffering from AIDS or other syndromes [8, 9].

The exact action of octreotide remains unknown. There are many hypotheses to explain its antidiarrhoeal action [10, 11]. In general, it is known that it interferes with various cell functions resulting in a reduction of gastrointestinal system excretions. More specifically, it is suggested that it can block the adenyl cyclase system and cause reduction of the calcium ion influx into the cell. In addition, it is reported that it can decrease the gastrointestinal motility and also exert an action on the ileocaecal valve that decreases the flow of ileal contents into the caecum.

The side-effect profile of octreotide includes nausea, diarrhoea, abdominal pain and pain at the injection site. Special care should be provided to patients with diabetes, since octreotide can alter blood glucose levels.

The present clinical study was conducted under the Helsinki Principles and local regulations. As far as dosage is concerned, the existing data recommend a dose range of 100–800 μg/day s.c. divided in multiple injections. We used 300 μg/day (divided in three aliquots) for 18 ambulatory cancer patients passing up to 10 stools per day and not requiring hospitalisation for fluid and electrolyte support. 4 patients who passed more than 10 stools per day were admitted to the hospital and received rehydration, electrolyte normalisation and continuous octreotide i.v. administration of 800 μg/day. We observed that diarrhoea tended to be more severe in patients with coexisting mucusitis and leucopenia.

There were 14 male and 8 female patients included in the study, with a mean age of 58 years (range 43–75 years). Seven patients had breast cancer with hepatic and/or pulmonary metastases and received Super FAC (5-FU, doxorubicin, cisplatin) chemotherapy. 13 patients had colorectal cancer with hepatic, pulmonary or lymph node metastases. They received the following chemotherapy regimens: (a) 5-FU at a dose of 600 mg/m^2 for 5 days, (b) leucovorin (LV) at a dose of 500 mg/m^2 for the first day of treatment only and (c) interferon (IFN) alpha-2a (3 patients only) at a dose of 9×10^6 U on days 1, 3 and 5 of treatment. 2 more patients had pancreatic cancer with hepatic metastases and received FAM (5-FU, doxuribicin, mitomycin C) treatment.

Our results show that no patient to whom octreotide was administered, either by the subcutaneous (300 μg/day) or the intravenous route (800 μg/day), showed any side-effect due to octreotide, except 2 patients who had mild abdominal distension. Our treatment response criterion was either complete remission of diarrhoea or reduction to one/day. Treatment was discontinued immediately after diarrhoea resolved without relapse. Of the patients who received s.c. treatment, diarrhoea was resolved in 5 patients (4 with 1–4 bowel movements/day, and 1 with 4–7/day) on day 1, in 5 patients (1 with 1–4 bowel movements/day and 4 with 4–7/day) on day 2, in 7 patients on day 3 and 1 patient on day 4 (all 8 with 7–10 bowel movements/day). Of the patients treated with i.v. therapy, diarrhoea resolved in 1 patient on day 3, 2 patients on day 4 and 1 patient on day 1.

Our study results are similar with those reported by Cascinu and associates [12], although the authors did not mention the number of bowel movements (in comparison with the day of diarrhoea remission, a clinical parameter that we consider significant). In conclusion, the results of the present study indicate that octreotide is a promising agent for the successful control of 5-FU-induced diarrhoea.

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