SHORT REPORTS

Domperidone or metoclopramide in preventing chemotherapeutically induced nausea and vomiting

Severe and sometimes intractable nausea and vomiting are common side effects of cytotoxic chemotherapy. Most doctors prescribe an antiemetic to accompany cytotoxic chemotherapy, but little data exist on which is the most suitable agent.[1] Metoclopramide is a widely used antiemetic, but its side effects include drowsiness, extrapyramidal effects such as dystonia or oculogyric crisis, and convulsions; these are particularly common when the recommended dose is exceeded in children.[2] Domperidone is a new antiemetic[3] that hardly penetrates the blood-brain barrier, and even at doses much greater than therapeutic ones no psychotropic or neurological effects have been observed.[4] We decided to compare, using a cross-over design, the efficacy of these two antiemetics in preventing nausea and vomiting induced by cytotoxic chemotherapy.

Patients, methods, and results

We used 18 children (6 boys, 12 girls) aged 2-13 years who were selected from the paediatric oncology unit and who were receiving cyclical cytotoxic chemotherapy, which was complicated by nausea and vomiting, for a variety of malignant diseases.

Either intravenous metoclopramide (0·5 mg/kg body weight) or domperidone (up to 1 mg/kg body weight) was given in a random, cross-over design, on at least two occasions immediately before cytotoxic treatment. We did not consider it ethical to include a placebo group. Patients and parents were told that one of two drugs, both effective in controlling vomiting, would be given. Parents or nurses not participating in giving the drugs recorded prodromal symptoms, such as insomnia, anxiety, and vomiting in the 12 hours before treatment, and episodes of nausea and vomiting for a period of 36 hours after treatment.

The incidence of nausea and vomiting on the 20 occasions on which the 18 patients were treated with metoclopramide and domperidone is shown in the table. Prodromal symptoms were similar in both groups. Thirteen

Incidence of nausea and vomiting in 18 children who together received 20 cycles of cytotoxic chemotherapy after prophylaxis with metoclopramide or domperidone

	Metoclopramide	Domperidone
Median No of incidents of nausea	4·5	1·0
Median No of incidents of vomiting	4·0	0·5
No of treatment cycles with more than one incident of nausea	16	12
No of treatment cycles with more than one incident of vomiting	17	10

patients vomited less after domperidone, two vomited more, and three as often as after metoclopramide. Vomiting was significantly reduced after domperidone ($P<0·01$, McNemar test, two-tailed probability). Domperidone had a considerable effect in the first four hours after cytotoxic treatment, but little protective effect after that, suggesting that its duration of action is about four hours.

Thirteen patients had less nausea after domperidone, one had more, and four were as nauseated as after metoclopramide: a significant difference ($P<0·01$, McNemar test, two-tailed probability). Patients were followed up at three-weekly intervals, and none experienced any acute symptom that could be implicated as an unwanted effect of either domperidone or metoclopramide. No patient during the study had an unusual fluctuation in blood count or clinical evidence of jaundice, and no patient died.

Comment

Although other studies have shown few neurological side effects associated with domperidone, we decided to use a dose of domperidone that was less than the recommended maximum dose of 1 mg/kg body weight. The patients' subjective response to domperidone was favourable; no patient refused a second treatment, and six patients remarked spontaneously on the benefit gained from domperidone treatment. We think that domperidone offers considerable antiemetic benefit to children receiving cytotoxic chemotherapy, and that further studies of this type are justified.

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[1] Morran, C, *et al*, *British Medical Journal*, 1979, **1**, 1323.
[2] Robinson, O P W, *Postgraduate Medical Journal*, 1973, **49**, 77.
[3] Balyens, R, *et al*, *Postgraduate Medical Journal*, 1979, **55**, suppl No 1, p 19.
[4] Deberdt, R, *Postgraduate Medical Journal*, 1979, **55**, suppl No 1, p 48.

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Department of Child Health, Welsh National School of Medicine, Llandough Hospital, Penarth, South Glamorgan
I L SWANN, MRCP, DCH, senior registrar
E N THOMPSON, MD, FRCP, senior lecturer
K QURESHI, MB, CHB, house officer

Clindamycin-associated colonic vasculitis

Pseudomembranous colitis occurring in association with the use of the antibiotic clindamycin has been well documented. We report here what we believe to be the first record of selective colonic vasculitis developing after exposure to this drug.

Case report

A 27-year-old man presented with colicky lower abdominal pain, melaena, and bleeding per rectum. Diarrhoea was not present. He had a 10-year history of sarcoidosis, diagnosed radiologically and confirmed by lymph-node biopsy. He had had recurrent episodes of steroid-responsive hypercalcaemia and on admission was taking prednisolone 10 mg daily. Ten days before he had developed a respiratory infection, which was treated by his family doctor with clindamycin 150 mg four times daily for five days. Examination disclosed mild diffuse lower abdominal tenderness and cervical lymphadenopathy unchanged from that noted before. Haemoglobin concentration was 17·6 g/dl, packed cell volume 0·53 (53%), white cell count $11·7\times10^9$/l ($11\,700/mm^3$; neutrophils 71%, lymphocytes 15%, monocytes 13%, eosinophils 1%), and erythrocyte sedimentation rate 39 mm in first hour (Westergren). Biochemical profile and results of urine analysis were normal. Chest *x*-ray appearances were unchanged from those seen on other occasions but a plain abdominal radiograph showed slight dilatation of the stomach and proximal small bowel. Within 36 hours of admission severe, diffuse, sudden abdominal pain developed. Rectal bleeding was accompanied by fever (38·3°C), tachycardia, and a fall in blood pressure. The abdomen was rigid and bowel sounds were absent. The white cell count was $13·4\times10^9$/l with an unaltered differential. A total colectomy was performed for apparent fulminant colitis. Recovery was complicated by a psychotic state resulting from increased steroid cover. The psychosis resolved with reduced dosage.

The colon showed extensive thickening of the wall. Haemorrhagic areas were present throughout the mucosa, ranging in appearance from solitary, polypoid protuberances up to 2·5 cm diameter to confluent raised zones many centimetres long, which had a coarse, cobblestone appearance. There were no perforations. Microscopy of the affected areas showed widespread acute necrotising vasculitis affecting chiefly the small veins in all layers of the bowel wall. Arterioles were not affected. The submucosal connective tissue was oedematous and haemorrhagic and in severely affected areas there was full-thickness ischaemic necrosis of the mucosa.

Comment

Pseudomembranous enterocolitis related to the use of clindamycin is well recognised and the sigmoidoscopic and pathological features have been clearly defined.[1] Overgrowth of *Clostridium difficile* and the deleterious effect of its toxin on the bowel mucosa may be a causal mechanism in the development of antibiotic-induced enterocolitis,[2] which is supported by the observation that eradication of the organism with vancomycin often results in resolution of the condition.[3 4] The