SHORT REPORTS

Cardiac arrest after treatment with intravenous domperidone

Domperidone (Motilium, Janssen Pharmaceuticals) is a widely used antiemetic. We report four cases of cardiac arrest after intravenous administration of this drug.

Case reports

Case 1—A 53 year old woman with inoperable ovarian carcinoma was receiving treatment with cisplatinum. Before starting treatment she had been clinically well with normal electrolyte concentrations (potassium 3·7 mmol(mEq)/l; normal 3·4-5·0 mmol/l). She was given domperidone 50 mg in one litre physiological saline over two hours just before and after the cisplatinum infusion. Treatment on day 1 proceeded uneventfully, but during the second domperidone infusion on day 2 she collapsed with apnoea, dilated and sluggishly reacting pupils, and absent circulation. She was successfully resuscitated. The plasma potassium concentration was 3·2 mmol/l.

Case 2—A 33 year old woman with stage IV non-Hodgkin's lymphoma had fever and tachycardia. Before starting chemotherapy she received domperidone 50 mg in 100 ml physiological saline over 15 minutes. Towards the end of the infusion she developed ventricular fibrillation, from which she was successfully resuscitated. Plasma potassium concentration was 2·9 mmol/l.

Case 3—A 38 year old woman with acute promyelocytic leukaemia was being treated with daunorubicin, cytarabine (cytosine arabinoside), and thioguanine. She had received 530 mg daunorubicin. She was also being treated for septicaemia with intravenous vancomycin, gentamicin, amphotericin, and metronidazole. Five minutes after receiving domperidone 20 mg and cimetidine 400 mg (slow intravenous bolus injections), and during infusion of vancomycin 500 mg (in 100 ml physiological saline over 30 minutes), she collapsed and was found to be pulseless and apnoeic with dilated pupils. She was successfully resuscitated. Plasma potassium concentration was 2·0 mmol/l. The episode was initially attributed to the vancomycin, and she received further intravenous domperidone without adverse effect.

Case 4—A 37 year old woman with acute myeloid leukaemia was being treated with daunorubicin, cytarabine, and thioguanine. She had received 240 mg daunorubicin. Treatment with amikacin and cefotaxime had been stopped 12 hours earlier. She was clinically well with no fever. After receiving a bolus of domperidone 20 mg and during administration of a bolus of cytarabine 160 mg she complained of dizziness and loss of vision. Her pulse was irregularly irregular. An electrocardiogram showed multifocal ventricular extrasystoles and salvos of ventricular tachycardia, which were abolished by lignocaine 100 mg. Plasma potassium concentration was 2·1 mmol/l and she was given a potassium chloride infusion. The arrhythmias were attributed to the cytarabine and hypokalaemia. The next evening she was given a bolus of domperidone 20 mg before chemotherapy and immediately developed multifocal ventricular extrasystoles, which were again treated with lignocaine. Despite this she developed ventricular fibrillation, from which she was resuscitated with a single direct current shock. Plasma potassium concentration was 3·1 mmol/l.

Comment

All four patients suffered cardiac arrest after receiving intravenous domperidone. None had a history of ischaemic heart disease or cardiac arrhythmia, and none had any arrhythmia subsequently.

Domperidone is a relatively new antiemetic drug that is at least as effective as metoclopramide in relieving the nausea and vomiting induced by moderately emetic chemotherapy.[1 2] Its main advantage over metoclopramide is its freedom from side effects.[1-3] Cardiac arrest has been noted previously after an intravenous bolus of 200 mg domperidone,[4] although the manufacturers disputed the drug's role in precipitating the event.[5] Six cases of cardiac arrhythmia associated with domperidone have been reported to the Committee on the Safety of Medicines (CSM). Although three of our patients had hypokalaemia at the time of their cardiac arrest, this was appreciable in only one. Hypokalaemia was noted in only two of the cases reported to the Committee on the Safety of Medicines (J C P Weber, personal communication), one of which was our case 2. We and others have found that in the low dose recommended by the manufacturers for patients receiving cytotoxic chemotherapy the antiemetic effect of domperidone is disappointing[1 2 4]: the drug is commonly used in higher doses because of the absence of side effects.

We conclude that as domperidone may cause potentially fatal cardiac arrhythmias when given in doses adequate to protect against the emetic effects of cytotoxic chemotherapy its use as an antiemetic for patients receiving such treatment is questionable.

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Prevalence of migraine in patients with diabetes

Migraine is induced in susceptible people by several factors including fasting.[1] This has led to the suggestion that blood glucose concentrations may influence the onset of an attack of migraine. If some relation exists between migraine and blood glucose concentrations the prevalence of migraine might be expected to differ between subjects with and without diabetes. Blau and Pyke studied patients with migraine and diabetes and noted that some patients either lost or showed an appreciable reduction in their migraine attacks with the onset or control of diabetes.[2]

To assess whether the prevalence of migraine differs between diabetic and non-diabetic people we asked 850 subjects to answer a questionnaire on headaches.

Subjects, methods, and results

A questionnaire based on that reported by Taylor *et al*[3] was given to 278 patients with diabetes in Southampton and 263 in Basingstoke. The patients were consecutive attenders at the outpatient diabetic clinics. Severity or duration of the disease was not assessed. The subjects completed the questionnaire themselves, with help from WKB whenever sought. Two hundred and fifty (90%) of patients in Southampton and 250 (95%) in Basingstoke completed the questionnaire.

One hundred and ninety one consecutive attenders at the fracture and general surgery clinics in Southampton and 159 at the fracture and accident and emergency clinics in Basingstoke served as controls (incidence of response 90%). They answered the same questionnaire as the diabetic patients.

Three of the most distinctive features of migraine are a unilateral distribution of headache, a warning that headache is coming, and nausea accompanying headache. For this study patients who had at least two of these features were considered to have migraine.

For statistical analysis we used logit linear models and examined the influences of sex, age, town, and whether the subject had diabetes, on the prevalence of migraine.

The figure shows the proportions of diabetic and control subjects with migraine by age and sex together with the fitted model that assumes a parallel response on the logit scale to age, sex, and whether diabetic. The most important variable in determining the prevalence of migraine was sex, with 126 (29%) of the women having migraine compared with 411 (15%) of the men ($\chi^2=26{\cdot}1$, df=1, $p<0{\cdot}001$). The proportion with migraine decreased from 44 out of 164 (27%) in the youngest subjects to 15 out of 126 (12%) in the oldest. The effect of age, adjusted for sex, was significant ($\chi^2=24{\cdot}4$, df=3, $p<0{\cdot}001$). Prevalence of migraine was similar in subjects from Basingstoke and Southampton (22·5% and 21·6% respectively).

The prevalence of symptoms of migraine was lower in diabetic patients (17%) than controls (29%). The corresponding comparison adjusted for