Hyponatraemia has a variety of causes including renal salt wasting and inappropriate antidiuretic hormone secretion.[9] Our patient probably had drug-induced inappropriate secretion of antidiuretic hormone.

Although we used hypertonic saline, it is important to remember not to correct the patient's sodium concentration too quickly. Rapid replacement of sodium can induce the osmotic demyelination syndrome which is potentially fatal.

Conclusion

This is a rare adverse drug reaction, but it is included in the product information of omeprazole. As our patient developed hyponatraemia after three doses, this adverse reaction needs to be considered whenever there is clinical deterioration even after brief exposure to a proton pump inhibitor.

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New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may have been little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Emtricitabine

Emtriva (Gilead)

200 mg capsules

Approved indication: HIV infection

Australian Medicines Handbook section 5.4.1

The current treatment of HIV infection involves giving antiviral drugs from different classes. This may require the patient to take medications several times a day.[1] Most of the regimens include nucleoside reverse transcriptase inhibitors to prevent viral replication. This class is now expanded by the addition of emtricitabine, an analogue of cytosine.

Emtricitabine is taken once a day. It is rapidly absorbed and then phosphorylated within cells to its active form. While the elimination half-life of emtricitabine is 10 hours the intracellular half-life of emtricitabine-triphosphate is 39 hours. Most of the drug is excreted in the urine so the dose requires adjustment in patients with renal impairment.

A multinational double-blind trial studied emtricitabine in 571 patients who had not previously been treated with antiretroviral drugs. These patients were randomised to take emtricitabine or stavudine, in addition to didanosine and efavirenz. After 48 weeks 78% of the emtricitabine group and 59% of the stavudine group had fewer than 50 copies of viral RNA/mL.[2]

Another trial studied 440 patients who were already taking combinations of antiviral drugs including lamivudine. The patients were randomised to either continue lamivudine or to switch to emtricitabine. After 48 weeks 72% of the patients taking lamivudine and 67% of those taking emtricitabine had fewer than 50 copies of viral RNA/mL.

Common adverse effects are diarrhoea, nausea, abdominal pain and nightmares, but these may occur less frequently than with stavudine. Skin discolouration was observed in 3% of the previously untreated patients given emtricitabine.[2] Liver function, blood cell counts and triglyceride concentrations may be affected by emtricitabine.

Resistance can develop during treatment. In previously untreated patients, viral mutations occurred in 4% of those taking emtricitabine and 11% of those taking stavudine.[2] As emtricitabine is structurally similar to lamivudine, a virus which is resistant to lamivudine will probably be resistant to emtricitabine.

While a once-daily treatment may improve compliance, it will require further study to see if emtricitabine has a clinically significant advantage. At present, its efficacy has only been proven with surrogate end points.

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Iron sucrose

Venofer (Baxter Healthcare)

5 mL vials containing 20 mg/mL

Approved indication: iron deficiency anaemia associated with haemodialysis

Australian Medicines Handbook section 7.6

Patients who are having regular haemodialysis can develop anaemia. The patients' demand for iron will increase when they are given erythropoietin. If oral supplements of iron are unable to meet this increased demand, parenteral iron should be considered.

Iron sucrose solution is given by intravenous infusion. The molecule then dissociates with the elemental iron being taken up by iron stores and the sucrose being eliminated in the urine. When administered with erythropoietin, iron sucrose will increase the haemoglobin in reticulocytes.

A clinical trial of iron sucrose solution involved 77 patients who had dialysis-associated anaemia and had been taking erythropoietin for at least four months. The patients were given a slow injection three times a week. Seventy completed a course of 10 doses (1000 mg iron). Within five weeks of completing the course, 60 patients had a haemoglobin greater than 11 g/dL, from a baseline mean of 10.3 g/dL, on at least one occasion. There were also increases in serum ferritin and transferrin saturation. Although erythropoietin doses were reduced the change was not significant.[1]

Some patients can have an allergic reaction to iron products. In the pivotal trial there were no cases of anaphylaxis.[1] The common adverse events reported in trials of iron sucrose include hypotension, cramps, nausea, vomiting and headache.

A trial in the USA has tested iron sucrose in 23 patients who were hypersensitive to iron dextran. Most of the patients completed the course of injections and none of them withdrew because of adverse effects.[2]

While iron sucrose may have an advantage over iron dextran its safety and efficacy needs to be compared with other parenteral iron formulations such as iron polymaltose.

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Tolterodine tartrate

Detrusitol (Pfizer)

1 mg and 2 mg tablets

Approved indication: overactive bladder

Australian Medicines Handbook section 13.1.1

Incontinence is a common problem, but many cases can be helped by behavioural modification programs.[1] Some cases are caused by detrusor instability. The symptoms of urinary frequency and urgency may improve with drug treatment. Tolterodine adds to the choice of anticholinergic drugs for this problem.

Tolterodine is a competitive antagonist at muscarinic receptors. This action reduces bladder contraction. Improvements in urodynamic function can be detected after two weeks of treatment.

Patients take tolterodine twice a day. It is well absorbed but is then extensively metabolised by the liver. The active metabolite also has an antimuscarinic action. This metabolism involves cytochrome P450 2D6, an enzyme of which some people have little. Clearance is reduced in these 'poor metabolisers', but, because of the way tolterodine and its active metabolite are bound to protein, the overall effect of the drug is unchanged. The dose should be reduced in patients with liver disease. Less than 1% of the drug is excreted unchanged in the urine, but a lower dose is recommended in patients with impaired renal function.

Although tolterodine increases the volume excreted per micturition, it has not significantly reduced the frequency in all of the placebo-controlled studies. One 12-week study of 293 patients compared tolterodine, oxybutynin and placebo. At the end of the study, frequency had respectively decreased by 21%, 20% and 11%. The corresponding increases in the volume excreted per micturition were 27%, 31% and 7%. In patients with urge incontinence, tolterodine reduced the number of incontinent episodes by 47% compared to 19% in the placebo group, however there was a 71% reduction in the oxybutynin group.[2] The need for treatment should be reviewed after six months, but some studies suggest that the effect of tolterodine continues for up to a year of treatment.

The majority of patients will experience adverse effects during treatment with tolterodine. Some of these adverse effects are predictable because of the drug's action, for example dry mouth, constipation and blurred vision. Patients with narrow angle glaucoma should not take tolterodine. Other adverse effects of tolterodine include headache, dyspepsia and dry eyes. In the comparative study, oxybutynin caused more adverse effects and patient withdrawals than tolterodine.[2] This should be

interpreted with caution as the starting dose of oxybutynin in the study was higher than usual.

Tolterodine may interact with other drugs that have anticholinergic effects. There is also a potential for adverse interactions with drugs which have cholinergic effects, such as the cholinesterase inhibitors used in the treatment of dementia.

When considering drug treatment for patients with incontinence, prescribers will need to ask if the patient would prefer a drug which may be less efficacious, but might have fewer adverse effects. While tolterodine does appear to help some people with incontinence, its use for overactive bladder is more controversial.

A report from New Zealand suggests that tolterodine has been promoted for use by patients without incontinence as a strategy to expand the market for the drug.[3] While there has been a campaign to raise awareness of overactive bladder in New Zealand, a systematic review concluded that anticholinergic drugs are of questionable clinical significance for the condition. Over 48 hours, patients will have one less micturition than patients taking a placebo, but they will be more than twice as likely to complain of a dry mouth.[4]

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* At the time the comment was prepared, information about this drug was available on the web site of the Food and Drug Administration in the USA (www.fda.gov).

† At the time the comment was prepared, a scientific discussion about this drug was available on the web site of the European Agency for the Evaluation of Medicinal Products (www.emea.eu.int).

Correction

Articaine hydrochloride with adrenaline (Aust Prescr 2005;28:19)

Although the sponsor has registered both 1.7 and 2.2 mL cartridges, only the 2.2 mL cartridges have been marketed in Australia.

Answers to self-test questions

1. False	3. True	5. False	7. True
2. True	4. False	6. False	8. False

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