Sexual dysfunction after gemfibrozil

Dr ANIL BHARANI (Department of Medicine, M G M Medical College, Indore, India 452001) writes: Gemfibrozil is a safe lipid lowering agent with minimal untoward effects.¹ Sexual dysfunction induced by this drug is a rare but disturbing side effect.

A 48 year old man sought consultation for lipidaemia in July 1989. He had been taking metoprolol 200 mg/day and a diuretic combination (benzthiazide 25 mg and triamterene 50 mg) for the past three years for essential hypertension. His clinical examination and laboratory findings were unremarkable, except for raised total cholesterol (7.75 mmol/l) and serum triglyceride (2.1 mmol/l) concentrations. He did not smoke or drink alcohol. He reported normal sexual activity with his wife. He was prescribed gemfibrozil 600 mg twice daily as well as his usual antihypertensive drugs and low cholesterol diet.

Within two to three weeks he developed diminished libido and difficulty in sexual intercourse. Gemfibrozil was withdrawn as this was the only new drug that could have caused impotence. His sexual performance gradually recovered over four weeks, although he continued taking metoprolol and the diuretic. With the patient's consent gemfibrozil was restarted in October 1989, and within two to three weeks his symptoms returned. Gemfibrozil was withdrawn again, and his sexual function gradually recovered over six weeks.

Although there are two reports on reversible impotence attributed to gemfibrozil,^{2,3} the Committee on Safety of Medicines has had six more such reports. Since gemfibrozil is an important drug for the primary prevention of coronary heart disease which is likely to be used in men aged 40-55 years the side effect assumes greater importance.

1 Frick MH, Elo O, Happa K, *et al.* Helsinki Heart study: Primary prevention trial with gemfibrozil in middle aged men with dyslipidemia, safety of treatment, changes in risk factors and incidence of coronary heart disease. *N Engl J Med* 1987;317:237-45.

2 Pizarro S, Bargay J, D'Agosto P. Gemfibrozil-induced impotence. *Lancet* 1990;336:1135.

3 Bain SC, Lemon M, Jones AF. Gemfibrozil induced impotence. *Lancet* 1990;336:1389.

Captopril associated lacrimation and rhinorrhoea

Drs MICHAEL BALDUF and VOLKER STEINKRAUS, and Professor JOHANNES RING (Department of Dermatology, University of Hamburg, 2000 Hamburg 20, Germany) write: The prototype angiotensin converting enzyme inhibitor, capto-

pril, has a broad pattern of adverse reactions.¹ We describe here a new one.

A 48 year old nurse had been treated for 18 months with captopril (25 mg orally 3 times daily) for arterial hypertension. She was working in an abdominal surgery unit and for eight months had suffered sudden attacks of acute lacrimation and rhinorrhoea that on each occasion occurred only on one side (though the side would vary) and lasted for two to four minutes. During an attack she had to stop all activity, including assistance during surgery. The attacks occurred irregularly during the day and night, three to five times over 24 hours. Sometimes they were preceded by minor pharyngeal paraesthesia and a mild cough. Erythrocyte sedimentation rate, red and white blood cell counts, routine laboratory investigations, and serum IgE concentrations were normal. Intracutaneous skin tests with standard inhalation and nutrition allergens evoked no positive reactions. When captopril was withdrawn the attacks stopped within 24 hours without any relapse over the next eight months.

Cases of persistent dry cough,² which occur more often in women and at low doses, have been repeatedly reported as side effects of captopril and enalapril. The pathogenesis is thought to be based on an increased sensitivity of the cough reflex due to the persistence of inflammatory mediators in the airways.³ Frequent daily attacks of lacrimation and rhinorrhoea have not been reported previously. The response to withdrawal of captopril suggests a causal relation with the drug, but the delayed onset of the reaction is difficult to explain.

- 1 Steiner JA. Antihypertensive drugs. In: Duker MNG, ed. *Meyers's side effects of drugs*. Amsterdam: Elsevier, 1988:397-415.
- 2 Morice AH, Brown MJ, Lowry R, Higgenbottom T. Angiotensin-converting enzyme and the cough reflex. *Lancet* 1987;ii:1116-8.
- 3 Fuller RW, Choudry NB. Increased cough reflex associated with angiotensin converting enzyme inhibitor cough. *BMJ* 1987;296:1025-6.

Cortical blindness after nifedipine treatment

Mrs C MORTON and Miss M HICKEY-DWYER (St Paul's Eye Hospital, Liverpool L3 9PF) write: A 59 year old man presented to his general practitioner with a four day history of slight visual disturbance likened to snow in front of both eyes. His blood pressure was 160/110 mm Hg and he was started on nifedipine tablets 20 mg twice daily (Adalat Retard). Thirty minutes after taking the first tablet he developed severe headache, right sided paraesthesia, and complete bilateral loss of vision. Six days later he presented at the eye hospital,

the headache and paraesthesia having resolved but not the visual symptoms. He was a cigarette smoker who suffered from chronic bronchitis, for which he had taken beclomethasone and salbutamol inhalers and theophylline 125 mg twice daily for several years. His visual acuity was 6/24 right and left, improving after several days to 6/9 right and left. Visual fields remained severely constricted, to within ten degrees of fixation. Slit lamp examination and funduscopy showed normal findings. He was obese with blood pressure of 140/100 mm Hg. There were no bruits and no temporal artery tenderness. Our clinical diagnosis of bilateral occipital lobe infarction resulting in cortical blindness with macular sparing was confirmed by computed tomography performed 12 days after the event.

The timing of nifedipine treatment and its mode of action suggest that it precipitated the occipital infarction. Nifedipine may have tipped the balance from mild ischaemia to complete infarction either through a local steal effect or possibly through a global reduction in cerebral blood flow associated with relative hypotension. Further, although Adalat Retard implies a slow release formulation, peak plasma concentrations occur between 1.6 and 4.2 hours after administration of the 20 mg tablet.¹

Cerebrovascular disorders after nifedipine have been described.^{2,4} The Committee on Safety of Medicines has received four other reports of blindness associated with nifedipine. A cerebral cause was suspected in two. Proved occipital infarction has not, however, been reported.

- 1 Sorkin EM, Clissold SP, Brogden RN. Nifedipine. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy, in ischaemic heart disease, hypertension and related cardiovascular disorders. *Drugs* 1985;30:182-274.
- 2 Nobile-Orazio E, Sterzi R. Cerebral ischaemia after nifedipine treatment. *BMJ* 1981;283:948.
- 3 Bulling M, Burns R. Occipital cortical 'angina' induced by nifedipine. *Med J Aust* 1988;148:266.
- 4 Schwartz M, Naschitz J, Yeshurun D, Sharf B. Oral nifedipine in the treatment of hypertensive urgency: cerebrovascular accident following a single dose. *Arch Intern Med* 1990;150:686-7.

Ventricular asystole and overdose with atenolol

Drs J STINSON, M WALSH, and J FEELY (St James's Hospital, Dublin, Ireland) write: A 34 year old man with a psychotic illness was admitted about four hours after taking an overdose of 80-130 tablets (50 mg) of atenolol. He was not taking any other medication. Emesis was induced but no tablets or residues were recovered from the gastric contents

and the patient was transferred to the coronary care unit. Initial physical examination was normal except for a blood pressure of 75/55 mm Hg (pulse rate was sustained at 70-80 beats/min sinus rhythm). The patient's 12 lead electrocardiogram was within normal limits (PR interval 150 ms). Intravenous fluid was the only treatment started. Three hours after admission episodes of ventricular standstill occurred (while he maintained an atrial rate of 70); several of these necessitated cardiac massage but none lasted more than 40 seconds, and after an hour or so a temporary pacemaker was inserted. The patient recovered uneventfully, being transferred to a psychiatric ward after five days.

Serum atenolol concentrations in samples taken at 36 and 96 hours were 849 pg/l and 564 pg/l respectively. Concentrations at these times after ingestion of 50 mg atenolol should have been about 20 pg/l and 10 pg/l. We therefore feel satisfied that this patient had taken a massive overdose of atenolol (4000-6500 mg).

There are relatively few deliberate overdoses of β adrenergic drugs despite their widespread use. Atenolol, which does not have a membrane stabilising effect, has been intentionally administered (by increments) in doses of up to 1200 mg without ill effect.¹ In cases of overdose with atenolol cardiovascular effects have included bradycardia, hypotension, syncope, cardiac failure, angina, and heart block.² Asystole has been reported as the usual cause of death in overdose with β blockers.³ Even in high doses, however, atenolol does not usually affect ventricular rate.⁴ As far as we are aware this is the first report of ventricular asystole induced by atenolol, and ICI Pharmaceuticals have no reports of this particular manifestation of overdose with atenolol. As the atrial rate was constant throughout transient periods of complete atrioventricular block were probably induced.

The fact that this patient remained relatively stable (other than moderate hypotension) and in sinus rhythm until these periods of ventricular asystole may have implications for managing patients after similar overdoses and reaffirms the serious potential in major overdoses of β adrenergic antagonists.

We thank Dr J Fallowfield, ICI Pharmaceuticals (Macclesfield, UK), for his help.

- 1 Zacharias FJ, Cowan KJ. Comparison of propranolol and atenol in hypertension. *Postgrad Med J* 1977;53 (suppl 3):111-3.
- 2 Prichard BNC, Battersby LA, Cruickshank JM. Overdosage with Beta adrenergic blocking agents. *Adverse Drug React Acute Poisoning Rev* 1984;3:91-111.
- 3 Beta-blocker poisoning. *Lancet* 1980;ii:803-4.
- 4 Critchley JA, Ungar A. The management of acute poisoning due to beta adrenoceptor antagonists. *Medical Toxicology and Adverse Drug Experience* 1989;4:32-45.