Intracoronary papaverine and complete atrioventricular block

Drs A CHAUHAN, P A MULLINS, S T THURASINGHAM, and P M SCHOFIELD (Papworth Hospital, Cambridge CB3 8RE) write: Papaverine administered by the intracoronary route in humans produces a brief maximal hyperaemic response in the coronary circulation that has little systemic effect and is used to measure coronary flow reserve in cardiac disease.^{1,2} Intracoronary papaverine is known to produce changes in cardiac electrophysiological variables and ST-T configuration and prolongation of the QT interval.³ Isolated cases of ventricular tachycardia and ventricular fibrillation have also been described.^{4,6} We describe a case of complete atrioventricular block after intracoronary papaverine administration.

A 53 year old man was undergoing investigations for chest pain with a positive response on exercise electrocardiography and normal coronary arteries on angiography. He was readmitted for further investigations, including coronary flow reserve studies. He had been taking nifedipine for several months and this was stopped 24 hours before cardiac catheterisation. His only other medication was dipyridamole, which was continued. Baseline pulse rate, blood pressure, electrocardiogram, and serum electrolyte concentrations were normal. Resting coronary blood flow was measured with a 3F 20MHz intracoronary Doppler flow probe. Incremental doses of intracoronary papaverine were given after a 2mg test dose. After administration of a 12 mg dose the patient developed complete atrioventricular block lasting five seconds. He remained asymptomatic and was haemodynamically stable. The study was terminated because of this unexpected side effect.

This case shows that, although papaverine is a relatively safe coronary vasodilator for measuring coronary flow reserve, all patients should be closely monitored while receiving intracoronary papaverine. A temporary pacemaker should also be available as well as appropriate antiarrhythmic preparations.

Simonetti I, Kienzie MG, Marcus ML. Polymorphous ventricular tachycardia: a side effect of intracoronary papaverine. *J Am Coll Cardiol* 1990;15:275-8.

6 Vrolix M, Piessens J, De-Geest H. Torsades de pointes after intracoronary papaverine. *Eur Heart J* 1991;12:273-6.

Severe hypertension and bronchospasm during disulfiram-ethanol test reaction

Drs E ZAPATA and A ORWIN (Woodbourne Clinic, Birmingham B17 8BY) write: We report a hypertensive episode accompanied by a mild asthma attack as a feature of the disulfiram-ethanol reaction.

A 45 year old man had a seven year history of heavy drinking (100 units per week) and mild late onset asthma. Twice when intoxicated his blood pressure had measured 180/100 mmHg. Before starting disulfiram 200 mg/day his blood pressure was normal. On the sixth day of the loading dose he was challenged with three doses of 100 ml of lager (alcohol 4.1% vol) administered at 0, 10, and 20 minutes. Before the challenge his blood pressure was 140/100 mmHg. His pulse, respiratory rate, and findings on chest examination were normal. After the third dose the patient complained of lightheadedness and facial flushing. His blood pressure rose to 160/115 mmHg and during the next 10 minutes reached 270/150 mmHg. The heart rate was 100 beats/min with moderate dyspnoea and widespread wheezing. Blood pressure began to fall within five minutes but bronchospasm required two inhalations of salbutamol. Clinical signs returned to normal within 30 minutes, and no further adverse effects were detected during the following eight hours.

Bronchoconstriction during a disulfiram-ethanol reaction has not been reported before, though the Committee on Safety of Medicines has had two reports of bronchospasm with disulfiram. Apart from one case complicated by coma, meningitis, acute pulmonary oedema, and cerebromeningeal oedema,¹ hypertension has also not been reported during these circumstances. There has been one report of disulfiram causing moderate hypertension in an abstinent man taking therapeutic doses and another of slightly raised blood pressure in normal people and alcohol misusers receiving high doses of disulfiram.^{2,3} In our patient the paroxysmal onset of the symptoms, the interval between challenge and the simultaneous development of hypertension and asthma, the duration of the clinical manifestations, and their resolution all suggest a causal relation.

Severe hypertension and bronchoconstriction during a disulfiram-ethanol reaction are possible, the

first in those with risk factors for hypertension other than alcohol, the second in patients with a history of bronchospasm.

- 1 Fourrier A, Mouton YJ, Raviart B, Roger J. Une réaction paradoxale Disulfiram-alcool: Hypertension paroxystique avec convulsions et oedeme aigu pulmonaire. *Lille Médicale* 1973;18:146-9.
- 2 Volicer L, Nelson KL. Development of reversible hypertension during disulfiram therapy. *Arch Intern Med* 1984;144:1294-6.
- 3 Lake CR, Major LF, Ziegler MG. Increased sympathetic nervous system activity in alcoholic patients treated with disulfiram. *Am J Psychiatry* 1977;134:1411-4.

Beware of ciprofloxacin in acute otitis media

Drs CLAUDIO MARONE and FRANCO QUADRI (Department of Internal Medicine, Ospedale San Giovanni, 6500 Bellinzona, Switzerland) write: Fluoroquinolones have excellent activity against many Gram negative bacilli and have shown promise against Gram positive cocci.¹ However, delayed clinical and bacteriological responses have been reported in some patients with pneumonia treated with ciprofloxacin.² Therefore the manufacturer does not recommend ciprofloxacin as treatment of first choice for community acquired pneumonia. Here we report a case showing the dangers of using a quinolone derivative as first line treatment for otitis media.

A 54 year old patient was treated with ciprofloxacin 500 mg twice daily over two weeks for otitis media caused by an unknown infectious agent. After 12 days he complained of headache, pain in the neck, and mental disturbance with fever. On admission his temperature was 39°C, his white cell count 16x10⁹/l with 46% band neutrophils, and a lumbar puncture revealed a purulent fluid. Computed tomography of the brain showed moderate hydrocephalus. The patient was given 20 MU/day of intravenous benzylpenicillin, but he died 12 hours later. Cultures from blood and cerebrospinal fluid grew *S pneumoniae* sensitive to ciprofloxacin.³

Fluoroquinolones penetrate poorly into the cerebral spinal fluid.¹ Although they have been used successfully to treat Gram negative meningitis, these agents cannot be recommended for treating meningitis where the cause is unknown. Meningitis is a well known complication of ear infections, and in particular of otitis media caused by *S pneumoniae*—one of the commonest bacterial agents in acute otitis media.⁴ Thus primary otitis media caused by unknown bacteria should not be treated with fluoroquinolones.

- 1 Hooper DC, Wolfson JS. Fluoroquinolone antimicrobial agents. *N Engl J Med* 1991; 324:384-94.

- 2 Cooper B, Lawlor M. Pneumococcal bacteremia during ciprofloxacin therapy for pneumococcal pneumonia. *Am J Med* 1989; 87:475.
- 3 Bauer AW, Kirby WMM, Sherris I, Turk M. Antibiotic susceptibility testing by standardized single disc method. *Am J Clin Pathol* 1966;45:493-6.
- 4 Bates GJEM, Drake-Lee AB. Meningitis complicating acute otitis media. *BMJ* 1988;296: 532.
- 5 Bluestone CD. Otitis media and sinusitis in children. *Drugs* 1986;31(suppl 3):132-41.

Angio-oedema and urticaria associated with omeprazole

Dr M R HAENEY (Hope Hospital, Salford M6 8HD) writes: I describe a 44 year old man who developed angio-oedema and urticaria triggered by omeprazole capsules but not by the enteric coated granules devoid of the capsule shell. He was prescribed omeprazole for Barratt's oesophagitis. Two hours after ingesting the first capsule (20 mg) he developed generalised urticaria, facial angio-oedema, and bronchospasm, needing admission to hospital and intravenous hydrocortisone. Two days later he took a second omeprazole capsule, and urticaria, angio-oedema, and bronchospasm recurred within three hours. His oesophagitis was treated with cimetidine with no further episodes of urticaria or angio-oedema. Two challenges with a single capsule of omeprazole each resulted in urticaria and angio-oedema within three hours. He had previously experienced urticaria when a chest infection was treated with pseudoephedrine linctus. There was no history of allergy. Serum complement C4 and C1 inhibitor were normal and his serum IgE was 18 kU/l (normal < 120).

With his consent he was given enteric coated omeprazole granules without the capsule shell. No adverse reaction occurred, and he tolerated a full course without recurrence of his angio-oedema-urticaria.

The prevalence of rashes during treatment with omeprazole is 0.5%.^{1,2} The manufacturers know of a few unpublished cases of urticaria and a few episodes of angio-oedema.

Four episodes of urticaria and angio-oedema after single capsules of omeprazole suggest a causal relation, possibly triggered by the capsule shell, which consists of gelatin, red iron oxide, titanium dioxide, and printing ink. Since the patient declined challenge with the shell alone the triggering constituent is unknown, but it may be worth prescribing omeprazole granules without their shell in patients who develop urticaria-angio-oedema.

- 1 Solvell L. The clinical safety of omeprazole. *Scand J Gastroenterol* 1989;24 (suppl 166): 106-10.
- 2 Nelis GF. Safety profile of omeprazole. Adverse events with short-term treatment. *Digestion* 1989;44 (suppl 1):68-76.

- 1 Wilson RF, White CW. Intracoronary papaverine: an ideal coronary vasodilator for studies of the coronary circulation in conscious humans. *Circulation* 1986;73:444-51.
- 2 Wijkstra F, Serruys PW, Hugenoltz PG. Papaverine: the ideal coronary vasodilator for investigating coronary flow reserve? A study of timing, magnitude, reproducibility, and safety of the coronary hyperemic response after intracoronary papaverine. *Cathet Cardiovasc Diagn* 1986;12:298-303.
- 3 Mahomed Y, Moorthy SS, Brown JW, King RD. ECG changes with papaverine injection into coronary artery bypass grafts. *Anesthesiology* 1984;61:350-2.
- 4 Wilson RF, White CW. Serious ventricular dysrhythmias after intracoronary papaverine. *Am J Cardiol* 1988;62:1301-2.
- 5 Talman CL, Winniford MD, Rossen JD,

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