Comment

We estimate that up to 60% of the patients we treated after extending the selection criteria for treatment would otherwise have been treated by cholecystectomy. Treatment was most successful in patients with many small stones (≤ 1 cm diameter). The median time to clearance of stones in this group was seven months. This was shorter than would be expected with oral dissolution treatment alone, suggesting that lithotripsy played an important part.^{3,4}

The relative importance of extracorporeal fragmentation and oral dissolution treatment in this treatment is unclear. Sackman *et al* showed that bile salt treatment had a major influence on their results: stones were completely cleared in only 30% of their patients two months after lithotripsy compared with 93% at 18 months.¹ We added a terpene compound to the bile salts, which may have enhanced dissolution and had an important antispasmodic effect, thus

reducing biliary colic.⁵ Interestingly, only 16% of our patients had biliary colic compared with 35% reported by Sackman *et al*.¹

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- 1 Sackman M, Delius M, Sauerbruch T, *et al*. Shock wave lithotripsy of gallstones. The first 175 patients. *N Engl J Med* 1988;318:393-7.
- 2 Ell C, Kerzel W, Heyder N, *et al*. Piezoelectric lithotripsy for gallbladder stones. *Dtsch Med Wochenschr* 1988;113:1503-7.
- 3 Roehrkasse R, Fromm H, Malavolti M, Tunuguntla AK, Ceryak S. Gallstone dissolution treatment with a combination of chenodeoxycholic and ursodeoxycholic acids. Studies of safety, efficacy and effects on bile lithogenicity, bile acid pool, and serum lipids. *Dig Dis Sci* 1986;31:1032-40.
- 4 Tint GS, Salen G, Colalillo A, *et al*. Ursodeoxycholic acid: a safe and effective agent for dissolving cholesterol gallstones. *Ann Intern Med* 1982;97:351-6.
- 5 Ellis WR, Somerville KW, Whitten BH, Bell GD. Pilot study of combination treatment for gallstones with medium dose chenodeoxycholic acid and a terpene preparation. *Br Med J* 1984;289:153-6.

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Hypersensitivity vasculitis due to ofloxacin

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Since its introduction in 1985 the new fluoroquinolone antibiotic ofloxacin has gained widespread use and much information has accumulated about its possible adverse effects.¹ Skin reactions have been uncommon²; in particular, no established case of hypersensitivity vasculitis directly related to ofloxacin has been reported.¹ We report such a case.

Case report

A 67 year old man was admitted to hospital because of a rash that had developed two days earlier. For the past 15 years he had had diabetes mellitus and congestive heart failure, for which he was taking isophane insulin 40 units in the morning and 12 units in the evening and frusemide 40 mg daily. Two weeks before admission his right foot had been accidentally burnt and became infected. As povidone iodine baths were ineffective ofloxacin 200 mg twice daily had been started three days before admission. One day later a pruritic purpuric rash had developed on his feet and legs. Ofloxacin was stopped and two days later the rash cleared. On the evening before admission he had taken another tablet of ofloxacin 200 mg, and a similar rash had developed.

On admission the rectal temperature was 36.9°C. Physical examination showed an extensive papular purpuric rash on the feet and legs, swelling of the scrotum, pitting oedema of the legs, and an infected wound on the right foot. Blood cultures and cultures from the wound were sterile. The erythrocyte sedimentation rate (Westergren) was 42 mm in the first hour. A blood count yielded 11.4×10^9 leucocytes/l with 6% band forms and 2% eosinophils. Blood glucose concentration was 7.6 mmol/l, creatinine 203 μ mol/l, alanine transaminase 114 U/l, lactate dehydrogenase 407 U/l, and alkaline phosphatase 288 U/l. Blood tests for antinuclear antibody, rheumatoid factor, hepatitis B surface antigen, and cryoglobulins and the Venereal Disease Research Laboratory test yielded negative results. Serum C3 concentration was 0.56 g/l (normal 0.70-1.76 g/l) and C4 concentration normal. Urine analysis showed a protein concentration of 3 g/l, a glucose concentration of 3 g/l, and 10 red cells per high

power field. A mast cell degranulation test for ofloxacin gave a strongly positive result. A skin biopsy taken from the purpura shortly after admission showed leucocytoclastic angitis.

Ofloxacin was stopped on admission and intravenous cefoxitin sodium and oral prednisone 40 mg daily started. Insulin and frusemide were continued. The rash and the pedal and scrotal oedema resolved, and the liver and kidney functions improved. The dose of prednisone was rapidly reduced. On the 17th day in hospital the patient was discharged.

Comment

This patient had clear evidence of a hypersensitivity vasculitis characterised clinically by a diffuse papular purpuric rash and histologically by a leucocytoclastic angitis. Allergic vasculitis is a well known adverse effect of many drugs, including antibiotics and thiazide diuretics,³ and may occur with frusemide.⁴ Our patient, however, had taken frusemide for many years without adverse effects and was still taking it when the rash resolved. Thus frusemide is unlikely to have caused the hypersensitivity vasculitis in this patient. Infection can cause allergic vasculitis, but this patient's vasculitis resolved despite a worsening infection. The temporal relation between the use of ofloxacin and the development of purpura and the resolution of the purpura after the drug was stopped and its reappearance after rechallenge suggest a causal relation. The strongly positive result of the mast cell degranulation test for ofloxacin confirms hypersensitivity to the drug.

Although four cases of allergic vasculitis during ofloxacin treatment have been reported in postmarketing surveillance studies, three cases seem to have been unrelated to the drug and not enough is known to evaluate the fourth.¹ Hypersensitivity vasculitis induced by ciprofloxacin, another fluoroquinolone antibiotic, has been reported.⁵ We suggest that hypersensitivity vasculitis be added to the growing list of adverse effects of the fluoroquinolones.

- 1 Jungst G, Mohr R. Side effects of ofloxacin in clinical trials and in postmarketing surveillance. *Drugs* 1987;34 (suppl 1):144-9.
- 2 Paton JH, Reeves DS. Fluoroquinolone antibiotics. Microbiology, pharmacokinetics and clinical use. *Drugs* 1988;36:193-228.
- 3 Wintroub BU, Stern RS, Arndt KA. Cutaneous reactions to drugs. In: Fitzpatrick TB, Eisen AZ, Wolff K, Freedberg IM, Austen KF, eds. *Dermatology in general medicine*. 3rd ed. New York: McGraw Hill, 1987: 1353-66.
- 4 Lin RY. Unusual autoimmune manifestations in furosemide-associated with hypersensitivity angitis. *NY State J Med* 1988;88:439-40.
- 5 Choe U, Rothschild BM, Laitman L. Ciprofloxacin-induced vasculitis. *N Engl J Med* 1989;320:257-8.

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