Adverse reactions to tiaprofenic acid mimicking interstitial cystitis

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Severe cystitis has been associated with tiaprofenic acid treatment for musculoskeletal pain,^{1,3} but this side effect is not well known among urologists, and the potential confusion with interstitial cystitis³ can lead to major surgery being considered or even performed.

Case reports

Case 1—A 66 year old woman had been prescribed tiaprofenic acid 300 mg twice a day for three years before referral. Other medication included bendrofluazide 2.5 mg once a day, clonidine hydrochloride 50 µg twice a day, and Codydramol (dihydrocodeine and paracetamol) as needed. She developed frequency and haematuria. Urine culture showed sterile pyuria, cystoscopy a small inflamed bladder, and biopsy interstitial cystitis. She was admitted for ileal conduit formation, but first it was decided to withdraw tiaprofenic acid. Within five months her only symptom was nocturia.

Case 2—A 69 year old woman had been taking tiaprofenic acid 600 mg at night for four years before referral. Other medication included methyldopa 250 mg three times a day and aspirin 75 mg once a day. She developed suprapubic pain and haematuria and symptoms attributed to diverticular disease. Urine culture showed sterile pyuria, cystoscopy a small inflamed bladder, and biopsy interstitial cystitis. She was admitted for urinary diversion. The operation was cancelled and the drug stopped. Within three weeks her symptoms had disappeared.

Case 3—A 64 year old man had been taking tiaprofenic acid 300 mg twice a day for five years before referral. Other medication included atenolol 100 mg once a day, lisinopril 5 mg once a day, and co-proxamol (dextropropoxyphene and paracetamol) as needed. He developed frequency, haematuria, and suprapubic pain. Investigations showed sterile pyuria with negative cultures for tuberculosis. At cystoscopy diffuse inflammation was observed and biopsy showed active chronic cystitis. He underwent subtotal cystectomy and bladder substitution. His symptoms resolved, but he had to carry out clean intermittent

self catheterisation. Tiaprofenic acid has since been stopped.

Case 4—A 59 year old woman developed increasing urinary frequency six months after starting tiaprofenic acid. Investigations showed interstitial cystitis. She underwent ileal conduit urinary diversion but continued with tiaprofenic acid for five years. She developed bilateral ureteric obstruction, which was attributed to periureteric fibrosis. She underwent pyeloplasty, and ureteric biopsy showed "interstitial cystitis." She subsequently had permanent ureteric stenting.

Comment

Previous studies have suggested that tiaprofenic acid produces a large number of adverse reactions affecting the lower urinary tract.^{1,3} Information from the Northern regional drug and therapeutics centre on non-steroidal anti-inflammatory agents showed for tiaprofenic acid 46 cases of cystitis (2.6% of all reactions to the drug), 8 of chronic cystitis, 3 of haemorrhagic cystitis, 14 of dysuria (0.8%), and 12 of haematuria (0.7%). Thus out of 1758 reactions with tiaprofenic acid there were 72 reports of cystitis, haematuria, and dysuria compared with only 133 (0.03%) among 41 159 adverse reactions with other non-steroidal anti-inflammatory drugs ($\chi^2=497$; $P<0.001$). Similar differences were found for symptoms of cystitis alone (other anti-inflammatory drugs 5; 0.012%; tiaprofenic acid 46; 2.6%; $\chi^2=941$; $P<0.001$). These data suggest that there may be a problem with tiaprofenic acid and that the drug can be stopped with subsequent clinical benefit, but we did not study control drugs which were not non-steroidal, and we have no information on rechallenging patients with the drug. Our findings extend previous reports because some patients are now being referred for major bladder reconstruction operations as a result of severe "interstitial cystitis." Recognition of this side effect may prevent surgeons from carrying out major surgery in such patients before a trial of drug withdrawal.

We thank Mr P D Ramsden for his permission to describe details of one of his patients.

- 1 Ahmed M, Davison OW. Severe cystitis associated with tiaprofenic acid. *BMJ* 1991;303:1376.
- 2 Ghose K. Cystitis and non-steroidal anti-inflammatory drugs: an anecdotal association or an adverse effect? *N Z Med J* 1993;106:501-3.
- 3 O'Neill GF. Tiaprofenic acid as a cause of non-bacterial cystitis. *Med J Aust* 1994;160:123-5.

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Management of bleeding in early pregnancy in accident and emergency departments

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Vaginal bleeding occurs in up to 20% of all pregnancies.¹ Many women present to accident and emergency departments, rather than to general practitioners or antenatal clinics, because they provide open access on a 24 hour basis. Doctors in accident and emergency receive little training, however, in the management of gynaecological emergencies. We previously showed that the use of management guidelines and the provision of advisory leaflets to patients on discharge significantly enhanced the service

provided to women with such bleeding, both by improving diagnostic accuracy and by reducing the numbers of unnecessary admissions or referrals.² We examined the facilities provided by other accident and emergency departments in such cases.

Patients, methods, and results

We sent a questionnaire to 109 accident and emergency departments in England and Wales treating more than 20 000 new patients a year. We asked them whether they saw women with bleeding in early pregnancy and, if so, to answer a further 11 questions requiring a yes or no answer on the facilities available and the management policy used. After the first 21 questionnaires had been sent, a question on the availability of ergometrine and oxytocin was added to the remaining 88 questionnaires. Consultants or senior medical or nursing staff completed the questionnaires, which were analysed with a χ^2 test.

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