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.

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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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We received completed questionnaires from 94 departments. The table shows the questions asked and replies received. There were no significant relations between the answers. Although 88 (94%) of the 94 departments dealt with bleeding in early pregnancy, only 64 (73%) of these had gynaecological staff on site. Forty one departments (47%) did not expect their doctors to perform vaginal examinations despite the fact that nine (22%) of these did not have gynaecology staff on site. Eight (20%) of the 40 departments in which doctors performed pelvic examinations did not provide an examination room with a door. Of the 86 departments with ultrasound facilities on site, 40 (47%) could not obtain an ultrasound scan outside normal working hours. Nine (56%) of the 16 departments that did not stock either ergometrine or oxytocin had no gynaecology staff on site.

Comment

This study showed that over 90% of accident and emergency departments see women with bleeding in early pregnancy. The questions referred to the minimum facilities we believed should be provided for such women. Overall, the service provided was poor.

Visualisation of the fetal heart by ultrasound scanning differentiates between a woman with a viable pregnancy, who can be discharged, and a woman with a non-viable or ectopic pregnancy, who requires admission and definitive treatment. Although access to ultrasound scanning was good, in half the departments this service was not available outside normal working hours. A similar number of departments did not have a portable Doppler ultrasound scanner (Sonicaid), a cheap and quick alternative means of detecting a fetal heart at gestations greater than 12 weeks. Bleeding in threatened abortion can lead to immunisation of a Rh negative mother with a Rh positive fetus. These women must be given anti-D immunoglobulin.^{3,4} Although most departments had access to Rh blood typing facilities, 77% had no policy for administering anti-D immunoglobulin when appropriate.

One in four units did not have gynaecology staff on site, of which 22% did not expect their doctors to perform vaginal examinations. Failure to stock either ergometrine or oxytocin in these departments was particularly worrying. Speculum examination allows the cervix to be visualised and products of conception obstructing the os to be removed, while oxytocic drugs promote uterine contraction. Both reduce blood loss

Replies to postal questionnaire by 88 accident and emergency departments managing women with bleeding in early pregnancy

	Yes	No	No answer
Are accident and emergency doctors expected to perform vaginal examinations on pregnant women with vaginal bleeding before 20 weeks?	40	41	7
Do you have an examination room with a door for such examinations?	70	16	2
Do you have on site gynaecology staff?	64	24	0
Do you have access to Rh typing?	80	6	2
Do you have access to Kleihauer testing?	55	19	14
Do you have access to anti-D immunoglobulin?	74	9	5
Do you have a policy for administering anti-D immunoglobulin?	18	68	2
Do you have a Doppler Sonicaid instrument for listening to the fetal heart in your department?	39	49	0
Do you have access to ultrasound facilities on your hospital site?	86	2	0
If yes, is this available 24 hours a day?	46/86	40/86	0
Do you have advice information sheets for women with threatened abortions?	5	83	0
Do you stock either oxytocin or ergometrine in the department?*	48/68	16/68	4

*Extra question included in 88 of 109 questionnaires sent; 74 of 88 were returned, but only 68 were from departments managing women with bleeding in early pregnancy.

and are key resuscitative measures, particularly if the patient is to be transferred to another site for surgery.

This study confirms that in many accident and emergency departments the service provided to women presenting with bleeding in early pregnancy falls short of reasonable standards. Facilities for examining women in privacy must be provided, management protocols implemented, access to basic investigations improved, and practical advice given to patients discharged home.⁵

CG-S is a Medical Research Council training fellow.

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A MEMORABLE PATIENT

A morning to remember

I joined the liner in Southampton. The nursing sister was a tall, slightly intimidating girl with the face of a thirteenth century French queen. We sailed for South Africa and some three weeks later when we arrived in Cape Town I sat in the sick bay in the early morning stricken after the previous night's farewell party. There was a commotion in the corridor and the sick bay attendant, a little leprechaun-like man, burst, ashen faced, into the consulting room. "Quick Doctor, hide, one of the greasers has just come up from the engine room. He's not sober, he has an eight inch kitchen knife, and he says he wants to stick it into you." "Why me?" I asked plaintively. "And why today of all days?" "He says that you are the only senior officer he can get at and he wants to stab a senior officer. It's nothing personal it seems. He's surrounded by the chief officer and three bosun's mates." The sister, who was standing behind my chair as she always did when we were seeing

patients, snorted. "Oh yes," she said. "Excuse me please, Doctor," and she strode out with the sick bay gnome skipping behind her. What happened was later relayed to me by the chief officer. She strode up to the group. "Pardon me please gentlemen," she said, moving between two of them. She walked up to the greaser until the point of the knife rested on her bosom. "Have you an appointment with the doctor?" The greaser looked chastened. "Er . . . er . . . no Ma'am." "Then go away and come back at half past eight and in the meantime leave this with me." She took the knife from his unresisting fingers. The four men pounced on him. "Cor, she's lovely," announced the greaser as he was led away. The sister returned to her place behind my chair and laid the knife on the desk. "Shall we see the first patient, Doctor?" she asked. Yes, dear reader, I married her.—J A M WRIGHT is a retired consultant physician