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## Severe cystitis associated with tiaprofenic acid

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Cystitis, or inflammation of bladder mucosa, presents as urinary frequency, nocturia, and dysuria. Most cases of cystitis are infective, though local chemical inflammation may be responsible in some cases. We report three cases of severe cystitis associated with tiaprofenic acid.

### Case reports

#### CASE 1

An 82 year old woman was prescribed triaprofenic acid 300 mg twice a day in December 1987 for osteoarthritis. She was also taking bendrofluazide 5 mg once a day. No previous allergy or intolerances were known. Within weeks of starting treatment with tiaprofenic acid she developed symptoms of urinary frequency, dysuria, and nocturia with a sterile pyuria and microscopic haematuria. She was given multiple antibiotics and topical oestrogens but none resolved the symptoms.

An intravenous urogram and urine cytology appeared normal and a urinary culture was negative for mycobacterium. Cystoscopy showed severe global cystitis. Histological examination of multiple bladder biopsy specimens showed that most of the bladder mucosa was replaced by inflammatory cell infiltrate in the submucosa, suggestive of interstitial cystitis. Tiaprofenic acid was discontinued and within two weeks her urinary symptoms had completely resolved. Cystoscopy six weeks later showed complete resolution of cystitis.

#### CASE 2

An 81 year old woman was prescribed sustained action tiaprofenic acid in October 1988. She had taken 2.5 mg prednisolone once a day since 1973 for polyarthritis. Within a few weeks of starting tiaprofenic acid she developed cystitis with sterile pyuria. An intravenous urogram showed a partial duplex system on the left side. Analysis of blood chemistry and urine cytology gave normal results and a urine culture was negative for acid fast bacilli. Cystoscopy showed severe generalised cystitis. Four quadrant biopsy specimens showed oedematous stroma with diffuse infiltration of chronic inflammatory cells. The urothelium was completely lost, and special staining showed numerous mast cells, which suggested interstitial cystitis. Cystitis

completely resolved on stopping tiaprofenic acid.

#### CASE 3

A 69 year old woman was referred for urological consultation with a six month history of resistant cystitis. She had been taking sustained action tiaprofenic acid 300 mg/day for the past eight months. She was also receiving beclomethasone and salbutamol by inhaler, slow release theophylline 400 mg/day, and bendrofluazide 2.5 mg/day. An intravenous urogram appeared normal. Cystoscopy showed generalised cystitis. Tiaprofenic acid was stopped and a repeat cystoscopy three weeks later confirmed that the cystitis had resolved. She remained free of bladder symptoms one year later.

### Comment

Cystitis as a side effect of systemically administered drugs is rare. A Medline search from 1980 to 1990 yielded 12 reports, most of which related to cyclophosphamide. Other drugs implicated were danazol, which causes haemorrhagic cystitis in patients with hereditary angioneurotic oedema,<sup>1</sup> and tranilast, an antiallergic drug, which causes eosinophilic cystitis;<sup>2</sup> one case of cystitis with kanamycin is reported in Russian. Nineteen cases of cystitis with tiaprofenic acid are registered with the Committee on Safety of Medicines.

Tiaprofenic acid is a non-steroidal anti-inflammatory drug of the propionic acid group. It is a potent inhibitor of prostaglandin biosynthesis through inhibition of cyclo-oxygenase.<sup>3</sup> Tiaprofenic acid is metabolised in the liver, where about 5% is oxidised to phenol and alcohol derivatives. The parent compound and these metabolites are excreted in urine largely as acylglucuronides. The half life of the drug is short, and steady state is reached on the first day of the treatment.

The mechanism of tiaprofenic acid induced cystitis remains unknown. But awareness of this side effect is important as non-steroidal anti-inflammatory drugs are the most commonly prescribed drugs. In addition tiaprofenic acid induced cystitis could be confused with interstitial cystitis, the treatment of which is highly unsatisfactory and invasive.

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