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Letter to the Editors

Bilateral acute angle closure glaucoma in a 50 year old female after oral administration of flavoxate

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Several classes of drugs, including sympathomimetics, anticholinergics, selective serotonin re-uptake inhibitors, tricyclic antidepressants and antihistaminics have been reported to induce or precipitate acute angle closure glaucoma, especially in predisposed individuals who have narrow angles of the anterior chamber [1]. Flavoxate, a tertiary-amine antimuscarinic, is used for its antispasmodic properties in the symptomatic treatment of many urological conditions including overactive bladder and incontinence. It increases urinary bladder capacity, possibly because of action on the detrusor muscle [2]. All anticholinergics present a risk of precipitating angle closure glaucoma [1]. However, there is no previous report of flavoxate-induced glaucoma. Here we report, for the first time, a case of bilateral acute angle closure glaucoma following flavoxate administration.

A 50 year old female with chronic right sided pyelonephritis was receiving the following oral medications: ofloxacin 200 mg twice daily, indapamide 5 mg once daily and propranolol 20 mg once daily for the past 1 year. She consulted a nephrologist because of urge incontinence and was prescribed flavoxate (Urispas) 200 mg twice daily. Nine hours after ingesting a single tablet she presented in the Emergency Department of JN Medical College, Aligarh, India with complaints of sudden painful diminution of vision in both eyes (which started as blurring of vision) with severe frontal headache, redness of eyes, nausea, vomiting and palpitations. There was no history of similar episodes of painful diminution of vision in the past or a history of similar complaints in any of her first degree relatives. There was no history of allergy to any drug.

On examination, her pulse rate was 93 beats min^{-1}, blood pressure was 132/90 mmHg, respiratory rate was 16 breaths min^{-1} and she was afebrile. Systemic examination revealed no apparent abnormality. Ocular examination revealed the following in both eyes: visual acuity of finger counting at 1 metre, projection of rays (a test for function of the peripheral retina) was accurate, circumciliary congestion, corneal oedema, shallow anterior chambers, normal iris pattern, mid-dilated, oval shaped non-reacting pupils and immature senile cataracts. The eyes were 'stony hard' on digital tonometry. On slit lamp examination, corneal epithelial and stromal oedema, shallow anterior chambers (Von Hericks grade one), mid dilated non reacting pupils and nuclear sclerosis grade 1 were noted. Schioetz tonometry showed a reading of 1/10 g i.e. 69.3 mmHg (normal range 10–21 mmHg) in both the eyes. Non contrast CT scan of the head revealed no abnormality.

She was advised to stop the suspected drug, flavoxate. She was given 60 mg pentazocine intramuscularly, 1 ounce glycerol orally, 300 ml of 20% mannitol intravenously, 500 mg acetazolamide orally stat and then 250 mg 6 hourly and 0.5% timolol topically 12 hourly. The intraocular pressure returned to normal levels (17.3 mmHg in both eyes) within 10 h of starting the above treatment. Gonioscopy showed grade II angle closure without peripheral anterior synechae.

The causal relationship between the drugs being used by the patient and the adverse event was investigated using the Naranjo ADR Probability Scale [3] and WHO Causality Categories [4]. Use of the Naranjo ADR Probability Scale indicated a 'probable' relationship between the adverse effect (bilateral acute ACG) and flavoxate therapy. Similarly, WHO Causality Categories, when evaluated, also confirmed a 'probable' link with the same drug.

Anticholinergic drugs are the most effective agents currently available to control overactive bladder symptoms. As parasympathetic cholinergically mediated innervation is the predominant stimulus for bladder contraction, anticholinergics can improve frequency, urgency and urge incontinence by blocking receptors in the detrusor muscle. Their most common side effects are dry mouth, constipation and blurred vision. They can induce angle closure glaucoma by narrowing the angle of the anterior chamber by pupillary dilatation, thereby blocking the circulation of aqueous and by forward movement of the iris/lens diaphragm (papillary block glaucoma) but the incidence of drug-induced cases is uncertain [1].

Sung *et al*. [5] reported one case of an 80 year old woman with acute angle closure glaucoma precipitated by oxybutynin which has a pharmacological profile similar to flavoxate. However, there is no previous report of flavoxate induced glaucoma and to the best of our knowledge, this may be considered the first report of flavoxate induced bilateral acute angle closure glaucoma.

Flavoxate has been widely promoted for the treatment of overactive bladder. The mechanism of action of flavoxate for urge incontinence is not entirely clear but it is reported to have anticholinergic properties [2]. Several randomized studies [6, 7] and one Cochrane review [8] have found flavoxate to be no better than placebo for urge incontinence. Given the lack of demonstrated effect of flavoxate in placebo controlled studies it is difficult to recommend its use and it is definitely not a first line treatment. Moreover, adequate efficacy/tolerability data to support its use in urge incontinence is lacking [9].

Urologists and nephrologists should be aware of patients with overactive bladder who have not been evaluated by an ophthalmologist but are at risk of developing angle closure glaucoma due to shallow anterior chambers. They should avoid both overestimating drug induced glaucoma, as this would unnecessarily restrict treatment modalities, and underestimating drug induced glaucoma, as in the worse cases this may even lead to blindness. In our case, as there was a sudden and sharp rise in the intraocular pressure, the patient was at a very high risk of losing her vision in both eyes in the first attack itself as at such high intraocular pressures the optic nerve is literally strangulated and the chances of ischaemic injury, which fortunately had not occurred, were high. It is necessary to explain symptoms of glaucoma to such patients, such as severe pain in the eyes, headache, 'red-eyes' and visual loss. Blurred vision is usually related to relaxation of the ciliary muscle and temporary impairment of visual accommodation which occurs as a side effect of anticholinergic drugs, rather than to elevated intraocular pressure [10]. When the diagnosis is uncertain, an ophthalmologist should be consulted.

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