

BPH

## Black box warning for tamsulosin?

New data have prompted calls for the safety information provided with tamsulosin tablets to be reassessed.

Blockade of  $\alpha_{1a}$ -adrenergic receptors in the smooth muscle of the prostate and bladder is a common first-line approach to management of symptomatic benign prostatic hyperplasia (BPH). Drugs that facilitate this blockade also interfere with  $\alpha_{1a}$ -receptor signaling in the iris. This can cause 'intraoperative floppy iris syndrome' (IFIS), a condition that is known to make ophthalmic surgery more difficult. Solid data have now confirmed that recent exposure to the alpha-blocker tamsulosin is associated with a markedly increased risk of serious adverse events immediately after cataract removal.

The ramifications of the study, published in the May issue of the *Journal of the American Medical Association*, could be far-reaching. Tamsulosin generated over US\$1 billion in sales in 2007. BPH affects almost three-quarters of 70-year-old men, and almost 2 million cataract operations are performed in the US each year.

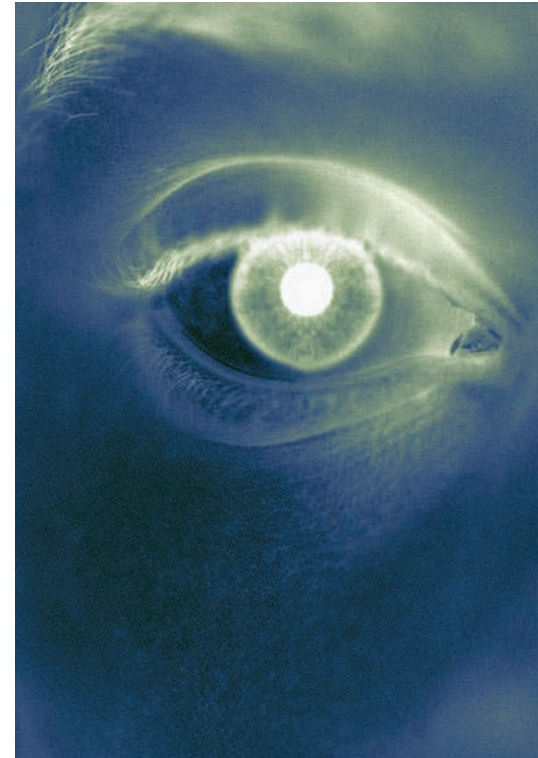
Chaim Bell from St Michael's Hospital, Toronto, and his colleagues used a nested case-control design to analyze data from several linked databases in Ontario, Canada. Of more than 96,000 men aged at least 66 years who underwent cataract surgery, 284 experienced a serious ophthalmic adverse event in the 2-week period immediately following the procedure. These complications included lens loss, retinal detachment, and inflammation—all of which can cause blindness.

Most of the 284 cases were matched to 4 controls each. The mean age of the case and control groups was 77 years. Interrogation of the prescribing database indicated that patients in both groups had taken about 10 different medications in the year prior to surgery. In the 14 days before their procedure, tamsulosin had been prescribed to 21 and 30 cases and controls, respectively.

Serious adverse events in the immediate postoperative period were more than twice as likely to affect men who had taken tamsulosin in the 2 weeks prior to surgery (adjusted odds ratio 2.33). Exposure to other alpha-blockers during the same period did not increase the risk of complications (adjusted odds ratio 0.91). That the observed effect was specific to tamsulosin may be a function of this drug's superior selectivity for  $\alpha_{1a}$ -adrenergic receptors relative to its counterparts, such as alfuzosin and doxazosin. Interestingly, the likelihood of adverse events was not elevated by less-recent use of alpha-blockers—including tamsulosin.

These findings raise several obvious questions of clinical interest. Should men discontinue tamsulosin therapy before ophthalmic surgery? Bell cautions that such a strategy could lead to acute urinary retention, and recommends weighing this risk against the estimated number needed to harm of 255. Should men switch to another alpha-blocker? As noted by Alan Friedman in an Editorial that accompanies the *JAMA* paper, IFIS can occur more than 12 months after cessation of tamsulosin, indicating the potential futility of this approach.

What, then, to do? According to Bell, emphasis needs to be given to raising awareness and improving communication among urologists, ophthalmologists, pharmacists, patients, and preoperative care teams. Bell advocates preoperative identification of patients taking tamsulosin, perhaps by including tamsulosin on the high-risk drugs checklist used to assess surgical candidates during preoperative clinics. "[If they are aware of recent tamsulosin exposure] surgeons can plan and prepare for a potentially more complicated procedure or refer to someone with more experience," Bell told *Insidermedicine* ([www.insidermedicine.com](http://www.insidermedicine.com)). Ensuring a patient's urologist receives a copy of their consult letter is another way in



which ophthalmologists can encourage a co-operative approach to clinical decision-making.

Urologists should use this new information when prescribing alpha-blockers, making a point of questioning patients about any ophthalmic issues for which they may seek future intervention and opting for a non-tamsulosin regimen in men with cataracts. Direct-to-consumer advertising in the US already advises users of tamsulosin to inform their doctor if they have this form of eye disease—Bell agrees with Friedman's suggestion that strengthening the tone of prescribing information to 'black box' warning level could also be helpful.

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**Original article** Bell, C. M. *et al.* Association between tamsulosin and serious ophthalmic adverse events in older men following cataract surgery. *JAMA* 301, 1991–1996 (2009).