Ocular side-effects of urological pharmacy

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Summary
The increasing rate of aging population worldwide has resulted in a more frequent diagnosis of aging related urological diseases and conditions such as benign prostatic hyperplasia, urinary bladder instability and erectile dysfunction. This has subsequently led to the wider prescription of medications such as phosphodiesterase inhibitors, antimuscarinic agents and alpha-inhibitors which may induce severe ocular side effects. This review outlines potential ocular side effects of the above-mentioned drugs, provides information on their frequency and natural history and highlights their importance to the clinician.
Key words:
urological medications, ocular side effects.

Introduction

Continuous advances in the treatment of several urological diseases and conditions are associated with the development of novel drugs and the evolution of older agents as well. The above may have led to a rising number of prescriptions of urological medications by non-specialized physicians, an evolving incidence of prescriptions with irrational drug combination and an increasing rate of side effects occurrence. Actually, most of the medication currently used in the treatment of benign prostatic hyperplasia, urinary bladder instability and erectile dysfunction is safe for most of the patients, however several of them may develop ocular side effects. The last may result in a disproportionate concern both for the patients and the clinicians. In this article, we outline several ocular side effects of the most commonly prescribing urological medications and we provide information on their frequency, natural history and clinical importance.

1. 5-Phosphodiesterase inhibitors (5-PDE Inhibitors: Sildenafil, Tadalafil).

The main ocular side effect associated with phosphodiesterase inhibitors use is the non-Arteritic Anterior Ischemic Optic Neuropathy (NAION). Actually, few clinicians are aware of an unusual and yet unpleasant side effect of these agents. NAION is the most common cause of acute optic neuropathy in adults and it develops in 1.500-1.600 individuals annually in the USA [1,2,3]. Fifty NAION cases associated with phosphodiesterase inhibitors intake have been reported up-to-date [4,5]. NAION develops upon reduced arterial infiltration at the anterior lamina of the optic disc, causing sparse retinal infarcts [6]. Predisposing factors are:

- hypertension
- hyperlipidemia
- diabetes mellitus (DB) and
- ischemic heart disease (IHD).

Almost all patients developing NAION, usually manifest optic disc congestion which results in ischemia of optic nerve axes as they are compressed among them. It has been documented that the 5-PDE inhibitors may deteriorate the optic nerve ischemia and result in vision loss, by affecting the nitrogen monoxide levels in the optic nerve vascularisation [5].

It should be mentioned that 5-PDE inhibitors remain the most effective medical treatment option for the management of erectile dysfunction [7]. Recent data do not provide clear evidence indicating that the 5-PDE inhibitors use constitute an independent predisposition factor for developing NAION. However, patients should be informed of the possibility to suffer from vision loss. This should be particularly stressed to IHD or atherosclerosis
predisposed patients. Patients with pre-existing monocular NAION should not be prescribed phosphodiesterase inhibitors given that the risk of developing NAION in the other eye exceeds 20%.

2. Antimuscarinic agents (oxybutynin, tolterodine)

The bladder’s detrusor muscle is rich in innervations with muscarinic receptors. Muscarinic acetylcholine (mACH) receptor antagonists reduce the contractions of detrusor muscle and usually improve symptoms of overactive bladder syndrome (OAB) such as frequency and urgency. Intraocularly, there is a stable condition between the formation and the absorption of the aqueous humor (AqH) which is responsible for the humidification of the basic ocular structures and the maintenance of the organ’s spherical shape. Normal intraocular pressure preservation depends on the AqH outflow. Any intraocular pressure increase may be caused by the increased resistance in the AqH outflow (open-angle glaucoma – OAG) or stricture/obstruction in the anterior chamber (closed-angle glaucoma – CAG) due to trabecular meshwork (TM) dysfunction. The iris constantly changes its shape being affected by the parasympathetic (muscarinic) (PNS) and the sympathetic nervous system (SNS). The antimuscarinic agents cause mydriasis. In those patients with an anatomical “narrow” angle, this may result in acute occlusion of the drainage angle. This particular case constitutes an ocular emergency which, if not treated, may cause permanent vision loss. Vision loss cases have been reported after angle occlusion episodes induced by oxybutynin (8) and other anticholinergic agents e.g. propiverine (9). Prognosis is favoured by accurate diagnosis and early treatment.

CAG should be managed with laser iristomy during or after an acute episode. This prevents any further acute episodes by creating an alternative path for the AqH outflow and thusly preventing obstruction. When treated, the risk of an episode anew is zero. Therefore, anticholinergic treatment in patients with surgically treated CAG is safe.

Regarding clinicians, their poor update on glaucoma creates confusion over the management of OAB and glaucoma (9). Both may co-exist in the elderly. By definition, OAG bears no evidence of AqH outflow mechanical obstruction and accordingly the anticholinergic treatment is safe (10).

Prior to anticholinergic agents administration, taking a detailed history of the glaucoma patient is of vital importance. Anticholinergic agents must be avoided in patients reporting a narrow angle not surgically treated. In patients on anticholinergic medication, it must be recommended emergency medical consultation in case of painful eye redness or acute vision loss.

3. a- Blockers (e.g. tamsulosin, alfuzosin )
The main ocular side effect associated with a Blockers use is the Intra-operative floppy iris syndrome- IFIS.

Selective a1-antagonists are widely used in the improvement of lower urinary tract obstruction symptoms and micturition flow. Pharmacologically, a1-subtype presents the greatest interest in BPH treatment. On the other hand, both the iris and the protective tissue present a variety of several a-receptors subtypes\(^{(11)}\). Those of a1-subtype have an important role in the cataract surgical treatment. In fact, safe and successful cataract surgical treatment requires full and maintainable dilation of the pupil. The insufficient dilation increases the risk of intra-operative complications given that the surgical site is disturbed\(^{(12)}\). The eye is pharmacologically dilated prior to cataract surgery. In normal conditions, this dilation lasts throughout the surgery. Intra-operative cataract surgery difficulties have been reported in patients receiving tamsulosin. It has been found that, in stable intraocular conditions, the iris is pathologically mobile and tends to prolapse towards the surgical instruments. During surgery, an iris spasm has also been observed which usually does not respond to the pharmacological treatment. The spasm in question limits the surgical site and technically impedes the procedure. These intra-operative findings are known as Intra-operative floppy iris syndrome (IFIS).

Chang and Campbell\(^{(12)}\) studied over 500 patients who had been subjected to more than 700 cataract procedures over a 12-month period. They found that the total IFIS impact accounted for 2%. However, 63% of the patients on a-inhibitors developed IFIS during the cataract procedure. 94% of IFIS patients had been receiving tamsulosin on a regular basis. Traditional intra-operative techniques for the iris dilation during ocular surgery, e.g., mechanical dilation or dissection of the iris sphincter are ineffective in such cases.

Several IFIS-induced complications have been reported including iris atrophy and capsular rupture. Further studies have also shown increased impact of the complications in IFIS eyes. The complications in question were more common when on tamsulosin compared to terazosin\(^{(13)}\). Once the surgeon is informed of the tamsulosin intake, s/he may use several alternative strategies for the improvement of the surgical site\(^{(14)}\). To avoid the aforementioned complications, pre-operative interruption of the a-inhibitors for 1-2 weeks is advised\(^{(15,16,17)}\).

Results

It is a fact that a pool of urological conditions (BPH, undetected prostatic cancer, OAB, atonic bladder, genital glands infection, erectile dysfunction etc) can nowadays be safely and effectively treated with applicable pharmacy. Some of these medicines are now widely prescribed by unqualified clinicians causing great concern about ocular side-effects. It should be fully understood that the ocular complications induced by urological pharmacy administration are rare, yet manageable. Nevertheless, the appropriate cooperation and
communication between the urologist and the ophthalmologist is an undoubted prerequisite.

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