

1.1. Tamsulosin and visual disturbances

Introduction

Tamsulosin (Omnice®) was granted marketing authorization on April 11 1995 and is indicated for the use *in lower urinary tract symptoms related to benign prostate hyperplasia (BPH)* [1].

Tamsulosin is a selective competitive postsynaptic α_1 -blocker. Tamsulosin works primarily on the receptor subtype α_{1A} and α_{1D} resulting in relaxation of smooth muscle in the prostate and urethra. This improves urinary flow. The positive effect on benign prostate hyperplasia is maintained during prolonged therapy and may delay surgery [1].

Blurred vision is the most common of visual symptoms in general. It usually refers to decreased visual acuity of gradual onset. The most common causes of blurred vision are refractive disorders [2].

Reports

On March 14th, 2011, the database of the Netherlands Pharmacovigilance Centre Lareb contained six reports of blurred vision and five reports of vision decreased associated with the use of tamsulosin, one report of visual disturbances and one of vision abnormal. The reports are listed in Table 1.

Table 1. Reports of blurred vision and vision decreased associated with the use of tamsulosin

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome
A 61447 M, 61 – 70 years	tamsulosin 0,4mg 1dd benign prostatic hyperplasia	coal tar shampoo	blurred vision, eyelid oedema	1 week, discontinued recovered positive rechallenge
B 93309 M, 71 years and older	tamsulosin 0,4mg 1dd	polyethylene glycol with electrolytes, metoprolol, finasteride, oxazepam, rosuvastatin, tiotropium, carbasalate- calcium	blurred vision	days discontinued recovered positive rechallenge
C 105317 M, 51 – 60 years	tamsulosin 0,4mg 1dd benign prostatic hyperplasia	carbasalate- calcium, alprazolam, pantoprazole, olmesartan, paroxetine, oxazepam, ciprofloxacin, mebeverine, polyethylene glycol with electrolytes	blurred vision, abnormal sputum	3 days discontinued recovered
D 66460 M, 51 – 60 years	tamsulosin 0,4mg prostate cancer NOS		blurred vision	1 month discontinued not yet recovered

Patient, Sex, Age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome
E 87476 M, 61 – 70 years	tamsulosin 0,4mg 1dd hyperplasia of prostate		blurred vision	9 weeks no change unknown
F 116053 F, 71 years and older	tamsulosin 0,4mg 1dd		blurred vision	4 days discontinued not recovered
G 30884 M, 41 – 50 years	tamsulosin 0,4mg 1dd, nifedipine 30mg 1dd, omeprazole 40mg 1dd, metoprolol 50mg 1dd	cetirizine, fluticasone nasal, nitroglycerin , carbasalate-calcium, temazepam	vision decreased	6 weeks discontinued unknown
H 70241 M, 71 years and older	tamsulosin 0,4mg 1dd, micturition disorder	bisoprolol, dutasteride, chlorambucil	vision decreased	12 hours discontinued unknown
I 73842 M, 71 years and older	tamsulosin 0,4mg 1dd, hyperplasia of prostate, digoxine 0,25mg 1dd, atrial fibrillation	hydrochloro-thiazide, dutasteride, lisinopril, isosorbide mononitrate	vision decreased	almost 4 years no change not recovered
J 79629 M, 71 years and older	tamsulosin 0,4mg 1dd		vision decreased	4 days no change not recovered
K 80627 M, 71 years and older	tamsulosin 0,4mg 1dd, hyperplasia of prostate	carbasalate-calcium, simvastatin	pneumonitis, vision decreased, angioedema	3 months discontinued not yet recovered
L 48190 M, 51 – 60 years	tamsulosin 0,4mg 1dd, benign prostatic hyperplasia		visual disturbances	3 days discontinued not yet recovered
M 96246 M, 71 years and older	tamsulosin 0,4mg 1dd, hyperplasia of prostate	amlodipine, hydrochloro-thiazide, atropine eyedrops, dorzolamide eyedrops, enalapril	vision abnormal (blurred vision, vision decreased, difficulty with contrast from light to dark)	1 day discontinued unknown

Below characteristics of some of the reports are discussed:

Patient A is a male aged 61 – 70 years who suffered from blurred vision and eyelid oedema following administration of tamsulosin for BPH with a latency of seven days after start. After withdrawal of tamsulosin the patient quickly recovered. Re-administration led to immediate return of the reaction (positive rechallenge).

Patient B suffered from blurred vision since the start of tamsulosin in April 2009 and had difficulty reading. During a re-inspection for his driver's license due to his age, a decreased vision was noticed and the patient was sent to an ophthalmologist. Tamsulosin was withdrawn and replaced by finasteride and thereafter the ophthalmologist could not find any abnormalities. The patient's

drivers license was renewed. In October 2009 tamsulosin was restarted instead of finasteride and the blurred vision returned (positive rechallenge).

Patient C suffered from blurred vision and excessive mucous in the throat with a latency of three days after start of tamsulosin. He recovered after tamsulosin was withdrawn.

The reporter in case D is an ophthalmologist. This patient was recovering from the reaction after withdrawal of tamsulosin at the time of reporting.

The reporter in case E is a patient, whose optician suspected an ADR.

Patient F is a female. Tamsulosin is used for an unknown indication. The patient had not recovered at the time of reporting. However, the reaction was reported shortly after the drug had been withdrawn. The patient was scheduled to see her specialist doctor in two days. No follow-up on the outcome of the reaction was received.

In patient G, in addition to tamsulosin nifedipine, omeprazole and metoprolol were reported as suspect drugs. The reporter in case G, a pharmacist, thought tamsulosin was the most suspected drug.

Patient I suffers from blindness of one eye. Digoxine was also reported as a suspect drug. The long latency period after start of both tamsulosin and digoxine makes a causal relationship in this case less plausible.

Patients K and L were recovering from the reaction after withdrawal of tamsulosin at the time of reporting.

Patient M only has vision in one eye, vision is normally 5-15%. He has been using atropine eyedrops since 1946 to increase his pupil. Ten years prior to the present reaction, the patient also used tamsulosin and at that time also suffered from abnormal vision.

Other sources of information

SmPC

In the Dutch SmPC of tamsulosin, blurred vision or other visual disturbances are not described. The only ocular ADR which is described is 'Intra-operative Floppy Iris Syndrome' [1,3].

The US SmPC of tamsulosin mentions the following: "In a pooled analysis from 2 multicenter, double-blind, placebo-controlled, 13-week studies in men with benign prostatic hyperplasia, blurred vision occurred in 0.2% and 2% of patients who received tamsulosin 0.4 mg/day (n=502) and 0.8 mg/day (n=492), respectively, compared with 0.4% of patients who received placebo (n=493)" [4].

In the Dutch SmPC of another alpha-1 adrenergic antagonist, alfuzosin (Xatral®), visual disturbances are described [5].

Literature

Other than 'Intra-operative Floppy Iris Syndrome' [6,7], no other descriptions of visual disturbances were found for tamsulosin. Li *et al.* [6] mention in their review article that tamsulosin does not seem to affect vision or eye health.

Databases

On March 12th, 2011, the database of the Netherlands Pharmacovigilance Centre Lareb contained six reports of the MedDRA Preferred Term (PT) vision blurred and five reports of the MedDRA Preferred Term (PT) Visual acuity reduced associated with the use of tamsulosin. The reporting odds ratio (ROR) is disproportional for both associations.

The two cases with visual disturbances and vision decreased are categorized under different MedDRA PTs and were not taken into account for the calculation of the ROR.

Table 2. Reports of blurred vision and visual acuity reduced in the Lareb database

Drug	Number of reports	ROR (95% CI)
Vision blurred	5	2.2 (1.0 – 5.0)
Visual acuity reduced	6	3.0 (1.2 – 7.2)

On March 12th, 2011, the WHO database of the Uppsala Monitoring Centre contained 132 reports of the MedDRA Preferred term blurred vision associated with the use of tamsulosin and 42 of the MedDRA Preferred term Visual acuity reduced. Both associations are disproportional.

Table 3. Reports of blurred vision and visual acuity reduced in the WHO database

PT name	Number of reports	ROR (95% CI)
Vision blurred	132	3.6 (3.1 – 4.3)
Visual acuity reduced	42	4.3 (3.2 – 5.8)

On April 20, 2011, the Eudravigilance database contained 48 reports of blurred vision or reduced visual acuity associated with the use of tamsulosine which was reported disproportionally (combined ROR = 2.7, 95% CI: 2.1 – 3.4). The reports concern two females and 46 males. The median age of the patients was 74.5 years (range 55 - 91). For six patients the age was not reported. Of these reports, 39 were considered to be serious.

Prescription data

The number of patients using tamsulosin in the Netherlands is shown in table 4.

Table 4. Number of users of tamsulosin in the Netherlands between 2006 and 2009 [8]

Drug	2006	2007	2008	2009
Tamsulosin	131,810	146,670	162,100	172,910

Mechanism

The mechanism by which tamsulosin induces blurred vision or visual disturbances is unknown, although tamsulosin's properties as a potent and selective α_{1a} -antagonist could play a role [6,9]. Iris dilator smooth muscle contraction occurs via mainly postsynaptic α_{1a} -adrenergic receptor [6,9].

A study investigating the effects of two alpha₁-adrenergic blockers, tamsulosin and alfuzosin, on pupil diameter (PD) found that with tamsulosin treatment, both mesopic (the size of the pupil of the eye under medium light conditions for example in daylight) and scotopic (the size a patient's pupils dilate to in a dark room) PD decreased. However, the difference in dilated PD was not significant. In the alfuzosin group, PD did not differ significantly from the baseline except for the scotopic measurements. Compared to baseline values, small but statistically significant decreases were detected in mesopic and scotopic illumination in patients treated with tamsulosin and in scotopic PD in patients treated with alfuzosin. The clinical significance of these differences needs further evaluation [9]. The 'Intra-operative Floppy Iris Syndrome' is also thought to be caused by an effect of tamsulosin on α_{1a} -adrenergic receptors in the iris [7].

Discussion and conclusion

Lareb received six reports of blurred vision associated with the use of tamsulosin, three with a positive dechallenge and two of these with a positive rechallenge. Another seven cases describe decreased vision, visual disturbances and abnormal vision. Blurred vision is described in the US SmPC and the associations between tamsulosin and vision blurred and visual acuity reduced are disproportionately present in the WHO and Lareb database. Tamsulosin's properties as a potent and selective α_{1a} -antagonist could play a role in the mechanism for causing this reaction. Visual disturbances are described in the SmPC of alfuzosin. For alfuzosin Lareb received three reports of abnormal vision, two reports of decreased vision and one report of blurred vision. Lareb received no reports about visual disturbances in association with the use of terazosin. It should be considered to mention visual disturbances in the Dutch SmPC of tamsulosin.

- It should be considered to mention visual disturbances in the SmPC of tamsulosin

References

1. Dutch SmPC Omnic[®]. (version date: 8-9-2008, access date: 14-3-2011) <http://db.cbg-meb.nl/IB-teksten/h27135.pdf>.
2. The Merck Manual. Blurred vision. (version date: 2011, access date: 14-3-2011) <http://www.merckmanuals.com/professional/sec09/ch098/ch098d.html>.
3. Dutch SmPC Mapelcor[®]. (version date: 2-9-2008, access date: 14-3-2011) <http://db.cbg-meb.nl/IB-teksten/h19720.pdf>.
4. US SmPC Flomax[®]. (version date: 22-12-2009, access date: 16-3-2011) http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020579s0261bl.pdf.
5. Dutch SmPC Xatral[®]. (version date: 1-9-2009, access date: 14-3-2011) <http://db.cbg-meb.nl/IB-teksten/h13689.pdf>.
6. Li J, Tripathi RC, Tripathi BJ. Drug-induced ocular disorders. Drug Saf 2008;31(2):127-41.
7. De Langen J. Selectieve α_1 -blokkers en het 'Intraoperative Floppy Iris Syndrome' (IFIS). Geneesmiddelenbulletin 2006;40(9):105-6.
8. College for Health Insurances. GIP database. (version date: 9-6-2009, access date: 16-3-2011) <http://www.gipdatabank.nl/index.asp?scherms=tabellenFrameSet&infoType=g&tabel=01-basis&item=J01FF>.
9. tan-Yaycioglu R, Yaycioglu O, Gul U, Pelit A, Adibelli FM, Akova YA. The effects of two systemic α_1 -adrenergic blockers on pupil diameter: a prospective randomized single-blind study. Naunyn-Schmiedeberg's Arch Pharmacol 2007;375(3):199-203.

This signal has been raised on July 2011. It is possible that in the meantime other information became available. For the latest information please refer to the website of the MEB www.cbgmeb.nl/cbg/en/default.htm or the responsible marketing authorization holder(s).