

Latanoprost and dizziness

Introduction

Since June 1997 latanoprost eye drops (Xalatan[®]) has been approved for marketing in the Netherlands. Latanoprost is a Prostaglandin F(2 α) analogue and is indicated for “*the reduction of increased ocular pressure in patients with open-angle glaucoma and ocular hypertension*”. Frequently reported local ADRs are a brownish discoloration of the iris in the first eight months of treatment, irritation of the eye and changes of the eye lashes. Rarely systemic effects may occur, like an increase of angina pectoris or aggravation of an existing asthma.

In the Quarterly Report of September 2001 the Netherlands Pharmacovigilance centre Lareb described four cases of headache associated with the use of latanoprost [1]. Since the introduction of latanoprost on the Dutch market, Lareb received seven reports on dizziness. This ADR is not mentioned in the Dutch SPC of latanoprost [2].

Reports

On December 21st 2006 the database of the Netherlands Pharmacovigilance Centre Lareb contained 190 reports of latanoprost, seven (3.7%) of these reports concern dizziness.

Table 1. Reports of dizziness associated with the use of latanoprost

Patient, Sex, age	Suspected drug	Concomitant medication	ADR	Time to onset, outcome
A, M, 60	latanoprost 1dd	tolbutamide betaxolol eyedrops acenocoumarol metformin	dizziness shortness of breath	couple of hours after start. symptoms resolved after stopping
B, F, 69	latanoprost 1dd	atorvasatin, levodopa/benserazide	dizziness tongue disorder	2 years, patient recovered after stopping
C, M, 67	latanoprost 1dd	enalapril gllimepiride	dizziness vision abnormal headache	14 days Outcome unknown
D, F, 61	latanoprost 1dd	not reported not reported	extreme dizziness	resolved after stopping drug
E, F, 39	latanoprost 1dd timolol	levocitirizine, lansoprazol, pancreatine medroxyprogesteron	dizziness headache appetite impaired nausea	6 days after starting drug. Outcome unknown
F, F, 67	latanoprost 1dd	paroxetine metoprolol	dizziness	1 day after start recovered after stopping
G, M, 39	latanoprost 1dd		dizziness nausea headache fatigue dyspnoea	resolved after stopping

A total number of 7 reports mentioning latanoprost and dizziness were received by Lareb. In four cases (A,C,E and G) additional systemic symptoms were reported. Five out of seven reports mentioned a positive dechallenge. One report (B) mentions a latency time of two years. Although the time of onset of this report may seem to long, we decided to list this report in the above mentioned table, because of the close similarities with the other reports.

Other sources of information

Literature

In a study to evaluate the safety and efficacy of the timolol/dorzolamide fixed combination versus latanoprost, 65 newly diagnosed glaucoma patients were using either latanoprost or timolol/dorzolamide fixed combination daily treatment for 2 months and subsequently crossed over to the other treatment. One patient on latanoprost had dizziness for several minutes following instillation [3]. On the other hand, latanoprost has been shown to alleviate vertigo/dysequilibrium and improved hearing after intratympanic injection [4].

SPC

In the EPAR of the related drug bimatoprost, dizziness has been mentioned as an uncommon effect ($\geq 1/1000$ to $< 1/100$) [5]. In the EPAR of the Prostaglandin F(2 α) analogue travoprost, this ADR is not mentioned. Ophthalmic use of latanoprost has not been associated with significant changes in systolic or diastolic blood pressure or heart rate which may have explained this ADR [6].

Databases

On 21 December 2006 the database of the Netherlands Pharmacovigilance Centre contained 7 reports on latanoprost. Although not reported disproportionately, (ROR 1.82, 95% CI 0.84 - 3.94), dizziness together with dyspnoea is the most reported ADR on this drug reported by health professionals. The Netherlands Pharmacovigilance Centre Lareb received one report of dizziness on bimatoprost and no reports of dizziness on travoprost.

On December 21st 2006, the database of the Uppsala Monitoring Centre (UMC) of the WHO contains 78, 15 and 8 reports on dizziness (including vertigo) associated with the use of latanoprost, bimatoprost and travoprost respectively.

Prescription data

Table 2. Number of patients treated with latanoprost, bimatoprost, and travoprost in the Netherlands.

	2002	2003	2004	2005
Latanoprost (Xalatan [®])	50,415	57,428	56,411	58,237
Bimatoprost (Lumigan [®])	,	3,554	7,968	10,776
Travoprost (Travatan [®])	,	2,356	3,984	8,049

Source: GIP/College voor zorgverzekeringen 2006 (<http://www.gipdatabank.nl>)

Conclusion

The Netherlands Pharmacovigilance Centre Lareb received seven reports of the use of latanoprost associated with dizziness. In four of these reports other systemic effects are mentioned. In literature information regarding the relationship between Prostaglandin F(2 α) analogues and dizziness is ambiguous. The number of reports and the fact that this ADR is already mentioned in the SPC of bimatoprost is suggestive for a true relationship between latanoprost and dizziness.

References

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4. Rask-Andersen H, Friberg U, Johansson M, Stjernschantz J. Effects of intratympanic injection of latanoprost in Meniere's disease: a randomized, placebo-controlled, double-blind, pilot study. *Otolaryngol. Head Neck Surg*. 2005;133(3):441-3.
5. EPAR Lumigan (date assessed 21 December 2006). (version date 2006) European Medicines Evaluation Agency.
6. Alm A, Widengard I, Kjellgren D, Soderstrom M, Fristrom B, Heijl A, Stjernschantz J. Latanoprost administered once daily caused a maintained reduction of intraocular pressure in glaucoma patients treated concomitantly with timolol. *Br J Ophthalmol*. 1995;79(1):12-6.