

Tamsulosin antagonists and anginal complaints

Introduction

Tamsulosin (Omnice®) is a selective, competitive antagonist of post-synaptic α_1 -receptors and is approved for marketing in the Netherlands since 1995. It is indicated for *treatment of symptoms of the lower urinary tract associated with benign prostatic hyperplasia (BPH)* [1].

The effect of tamsulosin in BPH is based upon antagonism of α_1 -receptors in the bladder and in the smooth muscle of the bladder neck and the prostate. Blockade of the α_1 -receptors in the bladder and bladder neck diminishes both the increased micturition frequency and the feeling of urinary urgency. Furthermore, antagonism of the α_1 -receptors in the smooth muscle of the prostate improves the urinary outflow [2].

At least three α_1 -receptors subtypes have been identified: α_{1A} , α_{1B} and α_{1D} . Tamsulosin shows a high degree of selectivity for α_1 -receptors located in the prostate, of which 70% are of the α_{1A} - subtype [3].

Despite its high degree of selectivity for the prostate, tamsulosin also blocks α_1 -receptors in the vasculature which can lead to vasodilatation and in turn to a decrease of the peripheral vascular resistance and a decrease of blood pressure. Because of this orthostatic hypotension, dizziness, tachycardia and syncope might occur. However, due to its uroselectivity tamsulosin is less associated with these haemodynamic adverse effects than the other α_1 -receptor antagonists [2].

Reports

Until December 19 2005, the Netherlands Pharmacovigilance Centre Lareb received 13 reports of anginal complaints associated with the use of tamsulosin. The mean age of the patients was 67.1 years (range 58-81). The time to onset varies from one day to 8 months. In 7 of the 13 cases the patient recovered. Ten of the 13 patients used cardiovascular concomitant medication; in five of these cases this cardiovascular medication included a nitrate.

Table 1. reports of anginal complaints associated with the use of tamsulosin

Patient, Sex, age	Drug Indication for use	Concomitant medication	ADR	Time to onset, outcome
A M, 64	tamsulosin 0.4 mg od, hyperplasia of prostate	atenolol, carbasalate calcium	sensation of chest pressure	14 days, recovered after withdrawal of tamsulosin
B M, 70	tamsulosin 0.4 mg od	amlodipine, acetylsalicylic acid, simvastatin, atenolol	chest pain, dyspnoea, headache	1 day, not reported
C M, 64	tamsulosin 0.4 mg od, hyperplasia of prostate	salicylic acid, isosorbide-dinitrate, captopril, metoprolol	dyspnoea, sweating, chest pain	2 days, recovered after withdrawal of tamsulosin
D M, 77	tamsulosin 0.4 mg od, hyperplasia of prostate	norfloxacin, atorvastatin, acetylsalicylic acid, atenolol, enalapril	aggravation of angina pectoris	a few days, outcome not reported
E M, 81	tamsulosin 0.4 mg od	nitroglycerin	chest pain	8 months, recovered
F M, 68	tamsulosin 0.4 mg od, difficulty in micturation	enalapril, carbasalate calcium, digoxin	chest pain	10 weeks, not reported
G M, 67	tamsulosin 0.4 mg od	simvastatin, acetylsalicylic acid, metoprolol, amlodipine, nitroglycerin	unstable angina pectoris	not reported, recovered
H M, 65	tamsulosin 0.4 mg od	digoxin, enalapril, nifedipine, isosorbide-mononitrate	chest pain	not reported, not reported
I M, 67	tamsulosin 0.4 mg od	acetylsalicylic acid, digoxin, enalapril	chest pain	unknown, recovered
J M, 71	tamsulosin 0.4 mg od	bulk forming laxative, omeprazole, carbasalate calcium, isosorbide dinitrate, atorvastatin, flecainide	tachycardia, chest pain, stomach disorder	1 day, recovered after withdrawal of tamsulosin
K M, 60	tamsulosin 0.4 mg od	not reported	dizziness, headache, chest pain, sweating increased	a few days, recovered after withdrawal of tamsulosin
L M, 60	tamsulosin 0.4 mg od, hyperplasia of prostate	not reported	chest pain, dyspnoea	3 weeks, unknown
M M, 58	tamsulosin OCAS 0.4 mg od	levofloxacin, pantoprazole, acenocoumarol	somnolence, tightness of chest	unknown, not reported

Other sources of information

Literature

Chest pain and (aggravation) of angina pectoris is described in the SPCs of other alpha1-receptor antagonists [4-6]. The American SPC of tamsulosin also mentions chest pain in 4% of the patients using tamsulosin. However, chest pain also occurred in the placebo-group (3.7%) [3].

A Medline-search revealed an article in which a non-randomized, open-label, placebo-controlled study examined the influence of the concomitant use of tamsulosin (0.8mg) on the safety profile of intravenous digoxin in ten healthy volunteers. Two persons reported moderate chest pain, but this was not considered related to the use of tamsulosin or digoxin [7].

On the contrary, in a nested case control study with a study population of elderly men with a high prevalence of cardiovascular co-morbidity (220 cases and 515 controls) no evidence was found for a possible relationship between hospitalisation due ischemic heart disease and the use of alpha-blockers or finasteride[8].

Databases

On December 19 2005 the WHO database contains 1470 reports on tamsulosin. Among these reports there are 20 reports of chest pain (ROR= 0.9; 95%CI 0.6 - 1.4) and 5 reports of chest pain precordial (ROR= 18.1; 95%CI 7.5 - 43.7). Furthermore, (aggravation of) angina pectoris is reported 17 times (ROR= 6.1; 95%CI 3.8-9.8). That means that with the exception of chest pain all associations are disproportionally present in the WHO database.

Mechanism

As mentioned before, antagonism of alpha₁-receptors in the vascular bed can lead to vasodilatation, decrease of the peripheral vascular resistance and decrease of blood pressure. In patients with coronary heart disease it is possible that fast and severe hypotension can lead to (aggravation) of anginal complaints.

Prescription data

Table 2. Total number of prescriptions of alfuzosine, tamsulosin, and terazosin per year since 2000 (Source: GIP College voor Zorgverzekeringen, Diemen).

	2000	2001	2002	2003	2004
G04CA01 alfuzosin (Xatral [®])	130,800	148,380	170,140	178,890	207,880
G04CA02 tamsulosin (Omnice [®])	209,490	257,140	282,890	305,280	365,200
G04CA03 terazosin (Hytrin [®])	22,062	19,528	17,074	15,831	14,421

Conclusion

The Netherlands Pharmacovigilance Centre Lareb received 13 reports of anginal complaints associated with the use of tamsulosin. Furthermore, the database of the WHO contains 20 reports of chest pain associated with the use of tamsulosin, but this association is not disproportionally present in the database. However, precordial chest pain and (aggravation) of angina pectoris are disproportionally present in the WHO database for tamsulosin.

In literature the possible relationship between anginal complaints and the use of alpha-blockers, such as tamsulosin, has been subject to discussion. Dutch SPCs of other selective alpha₁-receptor antagonists and the American SPC of tamsulosin mention anginal complaints as possible adverse effect of tamsulosin. On the contrary, in a nested case control study with a study population of elderly men with a high prevalence of cardiovascular co-morbidity no support for this association has been found.

References

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