Lareb
Nederlands Bijwerkingen Centrum
Netherlands Pharmacovigilance Centre

Amlodipine and photosensitivity

Introduction

Since 1990 amlodipine (Norvasc®) is available in the Netherlands for the indications *essential hypertension* and *angina pectoris* [1]. Amlodipine is a calcium-channel blocker of the dihydropyridine-type and belongs to the same group as nifedipine and felodipine.
The Dutch SPC of amlodipine mentions the following skin- and subcutaneous reactions: alopecia, pruritus, rash, skin discolorations, allergic reactions, angio-edema, erythema multiforme and urticaria. Photosensitivity reactions are not mentioned in the Dutch SPC of amlodipine [1]. However, in the Dutch SPC of nifedipine, photodermatitis is mentioned [2]. The SPC of felodipine mentions photosensitivity as well [3].

Reports

Until the 31st of May 2007 Lareb received three reports of photosensitivity reactions associated with the use of amlodipine. The time to onset varied from hours to 13 days. The outcome was reported in one case, the patient recovered after cessation of amlodipine.

Table 1. reports of photosensitivity reactions associated with the use of amlodipine

Patient, Sex, age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, outcome
A F, 69	amlodipine 5 mg od hypertension	budesonide, enalapril/hydro-chlorothiazide	photosensitivity reaction, rash, only on sites of the body exposed to light (arms and legs), ankle oedema	2 weeks, outcome not reported
B F, 70	amlodipine 5 mg od hypertension	sodium cromo-glicate, desloratadine, mometasone, bisoprolol, pravastatin, chlorthalidone, pantoprazole, triamcinolone creme	photosensitivity reaction, burning faster after sun exposition, red scalp and skin, body tempertature fluctuations	hours, amlodipine was withdrawn, the patient recovered
C M, 65	amlodipine 5 mg od hypertension	hydrochloro-thiazide/valsartan	photosensitivity reaction, photodermatosis	13 days, amlodipine was withdrawn, the outcome was not reported

Other sources of information

Literature

Several case-reports describe photosensitivity caused by amlodipine, mainly presenting itself as telangiectasia.

A 57-year-old hypertensive man developed telangiectasia, initially on the forehead and rapidly extending to the upper back, shoulders and chest. The reaction occurred particularly during the summer. The reaction began one month after his antihypertensive medication had been altered from atenolol to amlodipine and diminished considerably three months after withdrawal of amlodipine [4].
A 3-year-old girl developed telangiectases on the cheeks and gingival hyperplasia while taking furosemide, captopril and amlodipine for hypertension due to hemolytic-uremic syndrome. Except for the telangiectasia there were no other signs of photosensitivity. Both adverse reactions disappeared after withdrawal of amlodipine [5].
Photodistributed telangiectasia was reported in two patients after 5 months of using nifedipine. Both were also taking atenolol, but the telangiectasia significantly improved after withdrawal of nifedipine alone. One of the patients had a positive recurrence 3 years later when he started using amlodipine. The photodistribution of the telangiectasia suggested a significant drug/light interaction according to the authors [6].
A study by *Cooper* and *Wojnarowska* assessed photo-damage (pigmentation, telangiectasia, papular changes, erythema) of the head and neck in 82 Northern European renal transplant recipients attending a dermatology clinic. Photo-damage is frequent in this population of renal transplant patients; Ninety percent had some degree of photo-damage to the skin. Fifty-three patients (65%) had received a calcium channel blocker (49 nifedipine, four amlodipine). The grade of photo-damage was strongly associated with use of calcium channel blockers as was the presence of telangiectasia and solar elastosis. It is noted that patients in this study may be expected to have more photodamage because patients with skin cancers may have been over-represented [7].

Databases

On the 31st of May 2007 the Lareb database contained three reports concerning photosensitivity reactions in association with amlodipine (ROR = 1.62; 95%CI 0.52 - 5.09). On the same date, the database of the Uppsala monitoring centre contained 87 reports of photosensitivity reactions on amlodipine (ROR= 1.3; 95%CI 1.05 - 1.61). This means that is the association is disproportionally present in the WHO database for amlodipine.

Prescription data

Table 2. Total number of users of amlodipine per year from 2002-2006 (Source: GIP College voor Zorgverzekeringen, Diemen)

	2002	2003	2004	2005	2006
Amlodipine (Norvasc ®)	193.700	211.740	233.590	247.140	310.580

Mechanism

Calcium channel blockers may provoke telangiectasia by virtue of their vasodilatory action. It is not clearly understood how they may cause photosensitivity. One theory is that the photoproducts created by UVA and visible wavelengths are somehow capable of provoking telangiectasia [7].

The calcium channel blocker nifedipine is very photolabile and when exposed to UVA or visible wavelengths undergoes photolysis that results in loss of calcium channel blocking activity. It is possible that lactam photoproducts produced *in vivo*, may be causative [8]. A similar process might be involved by photosensitivity caused by amlodipine.

Discussion and conclusion

The Netherlands Pharmacovigilance Centre Lareb received three reports of photosensitivity reactions in associated with amlodipine. A positive dechallenge was reported in one case. The outcome in the other two cases is not known. The association between photosensitivitity and amlodipine is disproportionally present in the WHO database. In the literature photosensitivity due to amlodipine is described, mainly presenting itself as telangiectasia. In the case-reports Lareb received telangiectasia is not mentioned however. The reactions reported consisted of rash, phodermatitis and increased skin burning. Photosensitivity reactions are mentioned in the SPC of closely related calcium-channel blockers nifedipine (as photodermatitis) and felodipine.

References

1. Dutch SPC Norvasc®. (version date 20-7-2005) http://www.cbg-meb.nl/IB-teksten/h13348-h13349.pdf.
2. Dutch SPC Adalat® OROS. (version date 3-11-2004) http://www.cbg-meb.nl/IB-teksten/h14794-h14795.pdf.
3. Dutch SPC Plendil®. (version date 2-3-2004) http://www.cbg-meb.nl/IB-teksten/h13693-h13694-h15580.pdf.
4. Grabczynska SA, Cowley N. Amlodipine induced-photosensitivity presenting as telangiectasia. Br J Dermatol. 2000;142(6):1255-6.
5. van der Vleuten C, Trijbels-Smeulders MA, van de Kerkhof PC. Telangiectasia and gingival hyperplasia as side-effects of amlodipine (Norvasc) in a 3-year-old girl. Acta Derm.Venereol. 1999;79(4):323-4.
6. Collins P, Ferguson J. Photodistributed nifedipine-induced facial telangiectasia. Br J Dermatol. 1993;129(5):630-3.
7. Cooper SM, Wojnarowska F. Photo-damage in Northern European renal transplant recipients is associated with use of calcium channel blockers. Clin Exp.Dermatol. 2003;28(6):588-91.
8. de VH, Beijersbergen van Henegouwen GM. Photoreactivity of nifedipine in vitro and in vivo. J Photochem.Photobiol.B 1998;43(3):217-21.