

# Amlodipine as Monotherapy for Treating Isolated Systolic Hypertension in Elderly

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## Abstract

Amlodipine is an effective antihypertensive agent for the treatment of isolated systolic hypertension in the elderly. Among the various causes of elevated blood pressure in the elderly, isolated systolic hypertension is the commonest and its prevalence increases with age.

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## Introduction

Hypertension is a common medical problem in the elderly. Therefore, prevention and treatment of hypertension and target organ diseases remain important public health challenges. Systolic hypertension is the most common form of hypertension in people aged 60 years and above. Isolated Systolic Hypertension (ISH) is defined as systolic blood pressure of 140 mm Hg or greater and diastolic blood pressure less than 90 mm Hg. While multiple physiological changes have been described in association with ISH, the most distinctive feature is an increase in vascular stiffness resulting in decreased compliance of large arteries.

## Significance of ISH in elderly

ISH is an independent risk factor for cardiovascular disease, stroke, heart failure, end stage renal disease and all cause mortality in the elderly. Recent studies have demonstrated that it is more important to control systolic blood pressure than diastolic blood pressure.

## Treatment of ISH

Treatment of hypertension in elderly should begin with life style modifications. Antihypertensive drug therapy reduces the incidence of stroke, cardiovascular diseases, heart failure and related mortality. Thiazide diuretics can be used as monotherapy and are well tolerated by the elderly. Diuretics cause a disproportionately greater reduction in systolic blood pressure as compared with diastolic blood pressure. Long acting dihydropyridine (DHP) calcium channel blockers like amlodipine are the ideal antihypertensive agents in the management of ISH in elderly. The calcium ion plays a critical role in vascular smooth muscle contraction and in increasing peripheral vascular

resistance. Calcium channel blockers also act as coronary vasodilators and hence are useful in patients with angina.

## Role of amlodipine in ISH

The database on amlodipine, a calcium channel antagonist of 1,4- dihydropyridine class, was obtained from clinical trials in the United States, Canada and Europe. It shows that amlodipine is an effective antihypertensive drug providing smooth 24 hour blood pressure control without orthostatic hypotension and is well tolerated as monotherapy and in combination with other anti hypertensive drugs. A total of 18 clinical studies were reviewed; 1,091 patients received amlodipine whereas 805 received either placebo or another drug for comparison. Amlodipine was clearly superior to placebo and induced a clinically significant reduction in blood pressure (mean reductions 23/13 mm Hg supine, 24/12 mm Hg upright in one representative study) with similar heart rates in the supine and standing positions.

A systematic literature review by Levine et al<sup>1</sup> examined the effectiveness of amlodipine in lowering systolic blood pressure in a variety of patient subgroups and clinical settings. It was seen that in the amlodipine monotherapy arms, which included > 5000 patients, systolic blood pressure decreased by a mean of 17.5 mm Hg from baseline. The effect of amlodipine in reducing systolic blood pressure was greater in elderly patients (age  $\geq$  60 years) and patients with isolated systolic hypertension.

An open label, multicentric study<sup>2</sup> was undertaken in the United Kingdom to assess the efficacy and tolerability of amlodipine in elderly ( $\geq$  65 years of age) patients with mild to moderate hypertension ( diastolic blood pressure 95 to 114 mm Hg). Patients were given either amlodipine monotherapy or combination therapy. Amlodipine was given once daily either in the morning or in the evening. Significant reductions in blood

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pressure were noted in all groups after 4 and 8 weeks of treatment. Therapy was successful in 2,878 patients (82%) < 65 years of age, and in 1238 patients (84.2% ≥ 65 years of age and in 284 patients (84.5%) ≥ 75 years of age. The incidence of adverse events was similar in all age groups. Tolerability was rated as good or excellent in all patients with no significant differences between the groups.

These results showed that once daily amlodipine was effective in the treatment of mild to moderate hypertension in the elderly population and demonstrated a lower frequency of adverse events, a high degree of tolerability, and improved well being.

Mariani et al<sup>3</sup> of Italy studied the efficacy and safety of amlodipine in a single daily dose in the treatment of isolated systolic hypertension in the elderly. Ninety seven subjects, age range 65-85 years, with isolated systolic hypertension were randomized into two groups, similar for age, weight and height; 47 subjects submitted to active therapy and 50 subjects to placebo respectively. In the amlodipine group, at the end of third week, a significant decrease in systolic arterial pressure was reported. At the end of the follow up, a further decrease in systolic arterial pressure was observed in the active treatment group as compared to the control group. No orthostatic hypotension or reflex tachycardia was seen. Israeli study<sup>4</sup> and African study<sup>5</sup> on the safety and efficacy of amlodipine also concluded that it is an effective and well-tolerated antihypertensive suitable for elderly hypertensive patients.

A community-based study<sup>6</sup> from the US found that amlodipine produced a goal BP response ( setting diastolic BP < 90 mm Hg or 10 mm Hg decrease) in 86% of patient which was greater in those ≥ 65 years old (91.5%) than in those < 65 years old (84.1% ). Amlodipine was well tolerated, effective and safe as once a day monotherapy in these cases.

Sethi et al<sup>7</sup> from New Delhi evaluated the efficacy and safety of amlodipine in 20 patients of mild to moderate hypertension in a single blind, placebo controlled, noncomparative study. It was observed that amlodipine produced a significant (P < 0.05) reduction in mean systolic (177 mm Hg to 145 mm Hg and diastolic blood pressure (106 mm Hg to 84 mm Hg) after 4 weeks of treatment in all patients, without any significant change in heart rate or in the laboratory parameters.

In an open, non comparative, variable dose study<sup>8</sup>, 20 patients with mild to moderate essential hypertension were treated with 5-10 mg amlodipine once daily for

4 weeks after their blood pressure readings stabilized on placebo. Amlodipine produced a significant decrease in blood pressure from the initial mean of 162/100 mm Hg to 139/85 mm Hg at 4 weeks. Eighty percent of patients reached the goal diastolic blood pressure of < 90 mm Hg with a once daily dose of 5 mg amlodipine within 2 weeks. The remaining 20% also attained the goal diastolic blood pressure with in 4 weeks, with one step increase in the dose to 10 mg at 2 weeks . Amlodipine maintained blood pressure reduction throughout the 24 hours dosing interval with once daily dose. Notably, no side effects were observed and pulse rate, electrocardiogram and laboratory parameters were not significantly altered with the therapy.

## Conclusions

Isolated Systolic Hypertension (ISH) is the commonest cause of high blood pressure in the elderly. The incidence increases with age advancement. Even small reductions in BP have a substantial impact on patient outcome. In general < 140/90 mm Hg is the target for uncomplicated hypertension, < 135/85 mm Hg for those with diabetes or renal disease with proteinuria.

Long acting dihydropyridines like amlodipine is very effective antihypertensive agent in management of ISH in elderly because of its vasodilatory as well as negative inotropic effect.

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