ORIGINAL ARTICLE

Efficacy of Amlodipine, Tolerability, Toxicity and Treatment of Essential Hypertensive patients

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ABSTRACT

To find out the efficacy and tolerability of Amlodipne in the treatment of mild to moderate hypertension. It is a case series and observational study carried out in the Department of Medicine at Social Security Hospital, Lahore during the period of seven months from 01-01-2009 to 31-07-2009. Eighty patients included in this study between 30-90 years of age with mean±SD 62.27±8.19. After the taking history they were diagnosed of mild to moderate hypertension and taking antihypertensive medicines but they were not adequately controlled the hypertension. It was defined as diastolic blood pressure between the range of 90-112mmHg in the sitting position. It is based on two different occasions separated by at least 6 days. The dose of Amlodipine 5mg was advised and given on daily basis at least 15 days. The daily dose was titrated upward to 10mg after two weeks, in those patients who did not show satisfactory reduction in blood pressure in the absence of clinically significant side effects, thought to be drug related. Patients were followed up for six weeks on outpatient basis.

Results: After the treatment of 6 weeks of patients, the reduction in systolic blood pressure was 30mmHg and reduction in diastolic blood pressure was 20mmHg. Fifty nine (76%) of these patients required 5mg while remaining 19 (24%) needed 10mg of Amlodipine. Patients did not show any significant change in heart rate at the end of the study. Over all assessment of efficacy was excellent in 78%, good in 18%, fair in 4%. As far as toleration was concerned, it was excellent in 81%, good in 15%, fair in 3% and poor in 1%. Out of 80 (14%) patients experienced adverse effects and 2 (3%) were withdrawn from the study due to adverse effects, one male patient after 2 weeks and the other one is female after 4 weeks.

Conclusion: This study concluded that Amlodipine is an effective once daily treatment of mild to moderate hypertension.

Key words: Amlodipine, Efficacy, Essential Hypertension.

INTRODUCTION

Hypertension is occasionally secondary to some distinct disease. However, most patients with persistent hypertension have essential hypertension. Few patients with persistent systemic arterial hypertension have a specific etiology (e.g. renal disease, endocrine disease, heart attack and stroke). These organs failures are the major causes of morbidity and mortality. There is strong evidence that physician's threshold for initiating medication changes or increasing dosage in approximately 5 to 10mg, currently accepted guidelines[1]. Only 31% of Americans with hypertension have their blood pressure under effective control[2].

In United States, 50 million Americans are suffering from hypertension and it is responsible for 600,000 annual cases of stroke 1.1 million annual heart attacks, 400,000 annual new chronic heart failure and nearly 1 million annual deaths from cardiovascular and kidney disease[3].

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Amlodipine is 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 mmHg upright in one representative study) with similar heart rates in the supine and standing positions[4].

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 calcium channel blockers like amlodipine are the ideal antihypertensive agents in the management of hypertensioin elderly. The calcium ion plays a critical role in vascular smooth muscle contraction and in increasing peripheral vascular coronary vasodilators and hence are useful in patients with angina[5,6].

Amlodipine with once a day dosing has a smooth onset and sustained antihypertensive effect for 24 hours and is expected to enhance patient compliance in the treatment of hypertension.

OBJECTIVES

The present study carried out to evaluate the efficacy, tolerability and toxicity of Amlodipine as monotherapy in the treatment of mild to moderate essential hypertension.

PATIENTS AND METHODS

This observational study was conducted at Nawaz Sharif Social Security Hospital/University College of Medicine, The University of Lahore during the period of seven months from 01-01-2009 to 31-07-2009. Eighty cases of essential hypertension were included in this study to see the effectiveness of amlodipine. Adults over 30 years of age who are newly diagnosed or already diagnosed to have mild to moderate HTN and taking antihypertensive medication and are not adequately controlled. Pregnant female or child bearing potential and patients who suffering for target organ damage excluded from the study. Hypertension was defined as diastolic blood pressure in the range of 95-114mmHg. The average diastolic blood pressure will be documented on two occasions separated by at least 5 days. Oral informed consent and complete medical history was obtained from each patient and physical examination was performed before entering the study. Patient's blood pressure was taken in supine, sitting and standing positions. Patients were examined on out-door basis every week. The patient who achieved the target diastolic blood pressure of <90mmHg or had a reduction of more than 5mmHg in diastolic blood pressure after initial two weeks of therapy were continued on Amlodipine 5mg once daily. The patients who did not show a satisfactory reduction in blood pressure after initial two weeks of therapy, the dose of Amlodipine was increased to 10mg/day to achieve a sitting diastolic blood pressure of <90mmHg. The patients who did not have a diastolic blood pressure decrease greater than or equal to 5mmHg or DBP <90mmHg with the maximum dose of 10mg/day of Amlodipine taken for two weeks or had clinically significant side effects thought to be drug related were withdrawn from the study.

Data analysis: The data was entered into SPSS computer software version 16 and analyzed. The quantitative variables of the study i.e. age presented as mean and standard deviation. The qualitative data sex, Amlodipine overall and toleration assessment presented as percentages and frequency.

RESULTS

The mean age of patients was 62.27±8.19 years. Out of eighty 14 (18%) patients were in age group between 30-45 years while 36 (45%) patients were in age group between 46-60 years. Most of the patients were in group 46-60 year of age. Male to female ratio was 1.16:1 (Table 1).

Table 1: Frequency distribution of demographic variables (n=80)

Age in Years	**Frequency**	**Percentage**
30 – 45	14	18.0
46 – 60	36	45.0
61 – 75	24	30.0
76 – 90	6	7.0
Gender		
Male	43	54.0
Female	37	46.0
Total	80	100.0

Table 2 shows out of total 80, 78 patients they were completed the six weeks period of therapy with Amlodipine. The average reduction in blood pressure was 30mmHg in systolic blood pressure and 20mmHg in diastolic blood from base-line. The overall assessment of 78 patients, efficacy of Amlodipine were evaluated as excellent in 61(78%) patients, good in 14 (18%) patients, fair in 2(3%) and poor in 1(1%) patients. The overall Amlodipine toleration were 63(81%) in excellent, 12(15%) in good and 3 (4%) in fair (Figure 1). The side-effects were reported by 11 (14%) patients of mild to moderate hypertension i.e. nausea 1 (1.28%), fatigue 1(1.28%), palpitation 1(1.28%), weakness 1(1.28%), headache 4(5%) and edema feet in 3(4.0%) patients. Two patients (3%) were withdrawn from the study due to side effects 1 male patient (1.28%) and also 1(1.28%) female patient. One patient developed weakness after two week of treatment and other developed severe oedema with Amlodipine after 4 weeks of treatment (Figure 2). The dosage of Amlodipine required for control of blood pressure was 5mg/day in 59(76%) patients and 10mg/day in 19(24%) patients.

Table 2: Effect of reduction in blood pressure from baseline to study end with Amlodipine

Assessment Week	=n	Mean Sitting BP (mmHg)	Reduction (mmHg)
Baseline	80	170/101	-
Week 1	80	155/97	16/6
Week 2	80	149/90	22/12
Week 3	79	142/89	25/16
Week 4	79	138/85	28/17
Week 5	78	134/83	29/18
Week 6	78	130/81	30/20

Fig. 1: Overall and toleration assessment of Amlodipine efficacy of hypertensive patient

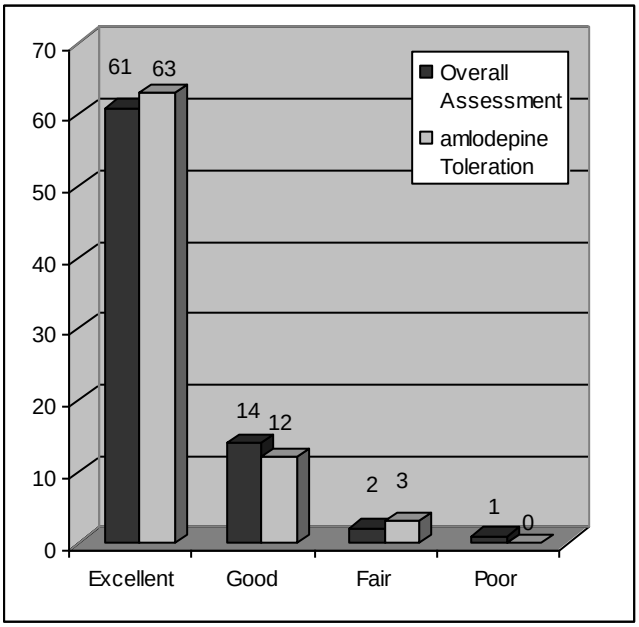
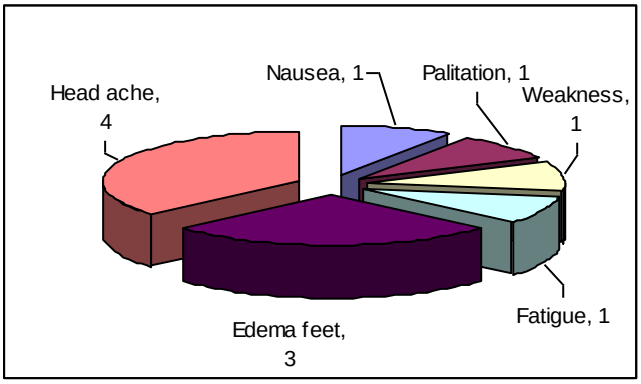


Fig. 2: Side effects of hypertension patients



DISCUSSION

Hypertension is one of the most important causes of cardiovascular disease, and treatment of hypertension leads to a significant reduction in cardiovascular mortality and morbidity. Although calcium channel blockers are regarded as an important part of the therapeutic armamentarium against cardiovascular diseases, and are among the most frequently prescribed antihypertensive medications, concern has been aroused about these drugs, particularly the short-acting dihydropyrldine derivatives. However, the value of nifedipine, the long-acting dihydropyrldine, is in need of being re-established[7].

In a study carried out by Gaba the mean age was 49.8 years who were diagnosed or had history of mild to moderate hypertension and had already been taking antihypertensive drugs but were not adequately controlled.[8] Another study done by Calhoun the mean age was 53 years[9]. In the present study the mean age of patients was 62.8 years of hypertensive patients which is which is comparable with other studies.

In a study done by Gaba the overall assessment of efficacy was excellent in 78%, good in 20% and fair in remaining 2%. As far as toleration was concerned, it was excellent in 80% good in 16% fair in 1 % and poor in 3%. Eleven of 100 (11%) patients experienced adverse effects and 2(2%) were withdrawn from the study due to adverse effects.[8] The present study showed that overall assessment of efficacy of excellent in 78%, good in 18% and fair in 3% and poor in 1% as overall assessment toleration was 81% in excellent, good in 15% and fair in 4%. Another study done by Kes[7] compared the effectiveness, safety and tolerability of once daily Nifedipine and Amlodipine treatment in mild to moderate hypertension. This was a randomized multicenter trial with an open comparison of treatment for 12 weeks, with a preceeding placebo run-in period of 2 weeks. After 12 weeks of treatment, the mean diastolic blood pressure was 83.1 and 81.9mmHg, in the Nifedipine and Amlodipine groups, respectively (P 0.436). The mean decrease in systolic blood pressure (28.5±11.9mmHg and 28.2±11.2mmHg in the Nifedipine and Amlodipine groups, respectively) and the mean decrease in diastolic blood pressure (16.47±7.0 and 17.5±6.9mmHg in the Nifedipine and Amlodipine groups, respectively) were comparable at the end of study[7].

In a study done by Ueng this multicenter, double-blind, 8-week study randomized 111 patients to fixed-dose amlodipine besylate/benazepril HCl (2.5/5 mg/day titrated to 5/10 mg/day as needed at week 4 to reach goal blood pressure (BP) <140/90 mmHg) or amlodipine besylate monotherapy (5 mg/day titrated to 10 mg/day as needed). At week 8, patients randomized to combination therapy compared with monotherapy had a comparable BP

control rate (56.0% vs. 46.2%; p = 0.32). Fixed-dose combination resulted in similar reductions in sitting systolic (SBP) and diastolic BP (DBP) compared with monotherapy (SBP 19.32±12.5 vs. 20.9±13.3 mmHg; DBP 9.2±10.4 vs. 11.3±9.3 mmHg. Safety profiles did not differ between groups, but cough was more common in the combination group (11.0% vs. 0%; p = 0.013)[10].

Langdon et al[11] undertook a study to assess the efficacy and tolerability of Amlodipine in elderly patients with mild to moderate hypertension (diastolic blood pressure 95 to 114mmHg). This was an open-label multicenter, 10 weeks general practice study involving patients >18 years of age. A total of 5135 patients received Amlodipine and were included in the tolerability analysis of these 3511 of 3628 (96.8%) <65 years and 147 of 1507 patients (97.6%) >or=65 years (including 336 of 349 (96.3%) >or=65 years were included in efficacy analysis. Significant reductions (P <0.05) in blood pressure were noted in all groups after 4 and 8 weeks of treatment.

All the international studies conducted about the efficacy and tolerability of Amlodipine show that the Amlodipine is an excellent antihypertensive with high efficacy and low incidence of side effects and provide 24 hours control of blood pressure with once daily dosing. The results of our study are comparable to the results of international and national studies.

CONCLUSION

It was concluded that Amlodipine once daily in the dose range of 5-10mg had significant anti-hypertensive effect and was well tolerated equally in the young and elderly patients either as monotherapy or as combination therapy. There was no significant change observed in the heart rate from base-line to end of the study.

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