ORIGINAL PROF-610

AMLODIPINE AS ANTI-ANGINAL;
A CLINICAL TRIAL

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ABSTRACT

OBJECTIVE: To study the effects of Amlodipine in angina pectoris patients. **DESIGN:** Prospective study. **SETTING:** Medical Unit II Allied Hospital, Punjab Medical College Faisalabad **PERIOD:** Total duration was 7 weeks. **SUBJECT & METHODS:** Twenty patients with symptomatic chest pain were included and were assessed for seven weeks. This assessment was made by the number of glyceryl trinitrate (GTN) tablets required per week. **RESULTS:** Out of 20 patients , 12 were male and 8 were female having mean age of 54.7 years. A mean height was 165.3 cm and mean weight was 71.4 kg in both sexes. The patients were followed for 7 weeks and were maintained at 10 mg amlodipine once a day. Significant reduction of anginal attacks was seen i.e. 70% from base line. Use of nitrates was also reduced as well as reduction in heart rate from 84-78 beats per minute. Amlodipine was well tolerated and effective. **CONCLUSION:** This 2nd generation dihydropyridine calcium antagonist was found to have both anti hypertensive and anti-anginal property with good safety profile and tolerance.

INTRODUCTION

In the treatment of ischemic heart disease the main therapeutic aims are to reduce myocardial ischemia, both symptomatic (angina pectoris) and asymptomatic as evidenced by electro cardiographic changes and improve the heart's pumping[1]. In the recent years, the increasing importance of circadian rhythm in cardiovascular disease has started to influence the treatment of choice in angina pectoris[2]. Studies indicate that more ischemic events occur in the early morning hours hence emphasizing the need for a drug which is effective for 24 hours.

The vasodialator action of calcium antagonists have shown to be beneficial in this regard. Among these calcium antagonists, Amlodipine is the one which belongs to dihydropyridine group and its profile is favorable for the patients having angina pectoris. Its half-life is 35-50 hours having 64% bioavailability after oral intake. Its unique pharmacokinetics make it the best choice in patients having angina pectoris covering the early morning attacks[3].

This study was conducted at MU II, Allied Hospital to assess the ability of amlodipine in reducing the ischemic events and also to study the safety profile in patients treated on outdoor basis.

METHODS OF STUDY

Twenty patients with symptomatic ischemia were

included in this study. These patients were followed on weekly basis in the outdoor till the 7th week and were evaluated at end. The daily dosage of amlodipine was 5 mg in first week and 10 mg in second week maintained onwards. Response was assessed by the number of GTN tablets required by the patient per week.

RESULTS

Out of total number of 20 patients, 12 were male and 8 were female having a mean age of 57.5 and 50.6 years respectively (table I). The mean height was 165.3 cm and mean weight was 71.4 kg in both sexes (table II). The concomitant use of drugs other than nitrates were diclofenac sodium, disprin, glibenclamide and aminopyrine (table IV).

Table-I. Age and sex distribution (n=20)

Age in years between	No of patients		
	Male	Female	Total
31-40	-	2	2
41 - 50	3	2	5
51 - 60	5	3	8
61 - 70	3	-	3
71 - 75	1	1	2
Total	12	8	20

Mean age in yrs (male) = 57.5, Total mean age in yrs = 54.7, Mean age in yrs (Female) = 50.6

At the base line the number of anginal attacks were 6.2 attacks and none of the patients were attacks free. As the treatment progressed, the number of anginal attacks reduced and by the end of 7th week 50% of patients were attack-free. In the remaining 50% of patients the anginal attacks declined to 1.5 attacks per week. There was 70% reduction from the baseline (table IX).

Table -II. Height and weight distribution

Age in years	No of pts	Mean height (cm)	Mean weight (kg)
31-40	2	157	73.5
41 - 50	5	164.8	62.6
51 - 60	8	160.8	72
61 - 70	3	183.6	82.8
71 - 75	2	165.2	71.7

Total mean height in cm(165.3) Total mean weight in kgs(71.4)

Table-III. Amlodipine daily dosage regime given to study patients

Assessment	No of patients	
Visit	5 mg	10 mg
Baseline	20	-
Week # 2	1	19
Week # 3	1	19
Week # 4	1	19
Week # 5	1	19
Week # 6	1	19
Week # 7	1	19

Table-IV. Concomitant Medication other than anti anginal taken by the patients at base line (n=20)

Medication	No of patients
Diclofenace Na	2
Disprin	7
Glibenclamide	4
Aminophylline	1
Total	14

Regarding nitrates, all the patients required sublingual glyceryl trinates tablets and number of tablets consumed were 10 per week. By the end of 7th week 10 patients did not require nitrates and the number of tablets reduced to 1.2 tablets per day in those taking nitrates (table VIII).

Table-V. Amlodipine effect on patients body weight

Sex	No of Pts	Mean baseline	Weight Kg study end
Male	12	75.6	70.2
Female	8	63.5	64.7
Total	20	71.4	68

Table-VI. Efficacy of amlodipine effect on heart rate.

Visit	Mean heart rate: beats/min	Changes from baseline: beats/min
Baseline	-	-
Week # 2	83	-1
Week # 3	81	-3
Week # 4	81	+3
Week # 5	81	+3
Week # 6	80	-4
Week # 7	78	-6

Table- VII. Effects of amlodipine reduction in blood pressure (n=20)

		Mean blood pressure	
Visit	No of patients	Ist measure	2nd measure
Baseline	20	152/85	146/84
Week # 2	20	132/85	137/85
Week # 3	20	139/84	139/84
Week # 4	20	136/82	137/82
Week # 5	20	138/81	138/81
Week # 6	20	132/80	133/81
Week # 7	20	132/79	133/79

No significant difference was seen in body weight reduction. The heart rate was reduced from 84 – 78 beats per minute (table VI).

Table-VIII. Efficacy of amlodipine reduction in GTN consumption

Visit	GTN tablets consumption	Patients requiring no GTN
Baseline	10	-
Week # 2	9.9	4
Week # 3	2.2	5
Week # 4	2.8	3
Week # 5	1.6	4
Week # 6	2.9	7
Week # 7	1.2	10

GTN= Glyceryl trinitrate

Table-IX. Efficacy of amlodipine in reducing angina attacks (n=20)

Visit	Angina attacks/weeks	Patients free of attack
Baseline	6.2	-
Week # 2	5	4
Week # 3	4.5	5
Week # 4	3.2	3
Week # 5	2.6	4
Week # 6	2.3	7
Week # 7	1.5	10

All the patients included were hypertensive as well. The mean blood pressure was initially 152/85 mm/Hg and it reduced to 132/79 by the end of trial (table VII).

Only 2 patients reported oedema and fatigue. None of them was withdrawn because of these side effects (table X).

As far as efficacy and tolerability was concerned, it was found to be very effective and tolerable (table X, XI).

Table-X. Safety of amlodipine (incidence of side effects)

Side effects	Incidence	%age	Severity		
			Mild	Moderate	Severe
Edema	1	5	1	-	-
Fatigue	1	5	1	-	-
Total	21	10	2	-	-
No of patients with side effects 2 (10%)					

Table-XI. Overall assessment of clinical efficacy of amlodipine at the end of study (n=20)

Assessment	No of patients	%age
Excellent	5	25
Good	14	70
Fair	1	5
Total	20	100

Table-XII. Overall assessment of amlodipine toleration at the end of study (n=20)

Assessment	No of patients	%age
Excellent	7	35
Good	11	55
Fair	2	10
Total	20	100

All of these 20 patients, 19 patients were maintained on 10 mg amlodipine starting from the 2nd week of the trial.

DISCUSSION

The main side effects of dihydropyridines is reflex tachycardia classically reported with Nifedipine, but the 2nd generation dihydropyridines like amlodipine having smooth 24 hours coverage free from this effect[3,4].

In the present study the diagnostic criteria used were only clinical grounds and are compatible with the studies conducted previously and clearly signifies the use of amlodipine in isolation or in combination with other anti anginal drugs[5,7,8,9,10].

Similarly its use has reduced the dosage of nitrate, thus increasing the compliance of the patients and also decreasing the hazards of nitrate tolerance[6]. In our study amlodipine reduced heart rate which is comparable to study by Yosefy et al 1999.

Despite the small number of patients and short follow up, the study shows that amlodipine improves the symptomatology of the patients and substantially reduces the anginal attacks[11].

CONCLUSION

This study shows the beneficial effects of amlodipine in reducing the number of anginal attacks, reduction in use of nitrates and fewer side effects. Its judicious use in patients of angina pectoris not controlled with nitrates exerts beneficial effects in the control of symptoms. With once daily dosage the compliance is also very good hence this is the drug of choice in hypertensive anginal patients in isolation and in combination.

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