

THE EFFECT OF NICARDIPINE ON MILD TO MODERATE ESSENTIAL HYPERTENSION

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SUMMARY : *Nicardipine, a slow calcium channel blocker, was administered to twenty patients for mild to moderate essential hypertension in a dose of 20 mg. t.i.d., totally 60 mg. per day. The systolic and diastolic blood pressures and the heart rates of the patients were first measured during resting in supine position and standing, and were measured again after the isometric and dynamic exercises. The electrocardiograms were taken for each stage. Biochemical laboratory analysis, complete blood analysis and urine analysis were done for each patient. At the end of the nicardipine therapy for four weeks, there was no difference between all the parameters, but blood pressures.*

The systolic and diastolic blood pressures, both, were significantly lowered at the end of the therapy than pretreatment for each measurement stage.

In conclusion, nicardipine, a new slow calcium channel blocker, alone, is effective as an antihypertensive drug for the treatment of mild to moderate essential hypertension.

Key Words : *Nicardipine, Essential Hypertension.*

INTRODUCTION

Nicardipine antagonizes the transport of calcium ions through the slow channels on the cell membrane (Eugene et al. 1987). It is reported to be effective in treatment of the stable effort angina and especially resting angina, associated with coronary spasm, and mild or moderate hypertension. Although mechanism of its action in these conditions is not clear, nicardipine, with a potent coronary and peripheral arterial dilator effect, has an important action on the oxygen demand - consumption ratio with an increase in demand and a decrease in consumption, and decreases systemic vascular resistance (Clarke et al. 1983; Eugene et al. 1987; Lambert et al. 1985).

The aim of this study was to investigate the effect of nicardipine, known as a slow calcium channel blocker, on the systolic and diastolic blood pressures and heart rates of patients with mild to moderate essential hypertension.

MATERIALS AND METHODS

Nicardipine was administered with a total daily dose of 60 mg to twenty patients between the ages of 40-67 (mean 53.8 ± 6.7), ten of them were male. The daily dose was administered as 20 mg. t.i.d. The systolic blood pressures of the patients were within the range of 140.0 - 200.0 mmHg (mean 162.2 ± 16.1 mmHg) and diastolics 100.0 -120.0 mmHg (mean 105.3 ± 6.0 mmHg).

In the control group, placebo was administered three times daily. We continued the therapy for four weeks. The systolic and diastolic blood pressures were 140.0 - 200 mm Hg (mean 158.7 ± 15.7 mm Hg) and 100.0 - 120.0 mm Hg (mean 103.6 ± 5.4 mm Hg) respectively.

After a resting period of 15 minutes, the blood pressures were examined first during supine position and then after standing for one minute and finally after the isometric and dynamic exercises. As an isometric exercise, the patients were asked to close and open their hands with a forced palmar flexion and extension for thirty times, and were asked to crouch down and stand up for thirty times as a dynamic exercise. It took 30-45 seconds for the isometric exercise and 60-75 seconds for the dynamic exercise.

None of the patients had been using antihypertensive drugs.

Complete blood count and urine examination, physical examination, blood glucose, lipids, electrolytes, bilirubin, hepatic and renal function tests, telecardiogram, electrocardiogram were checked pretreatment for all of the patients. These tests were repeated after four weeks of treatment.

20 mg. of nicardipine tablets were taken three times, totally 60 mg. per day for four weeks by the patients.

Blood pressures and heart rates were measured twice per week during the first two weeks, and once per week during the last two weeks.

Two patients were asked not to restrict the salt intake.

RESULTS

The effect of 3x20 mg / day of nicardipine on systolic and diastolic blood pressures and heart rates during resting and after standing for one minute and after isometric and dynamic exercises are shown in Tables 1, 2, Figures 1, 2, 3.

No significant changes were observed in control group.

None of the clinical and laboratory examinations were changed at the end of therapy. PR, QRS and QT intervals didn't change either.

No serious side - effects were observed during the therapy. Six of the patients complained of headache, three of them flushing and three of them palpitation during the first days of the therapy. Dating

	Pretreatment (mmHg)	After Treatment (mmHg)	p
RESTING			
Supine	104.6 ± 6.7	87.0 ± 15.5	< 0.001
Standing	105.3 ± 9.3	89.5 ± 12.4	< 0.001
EFFORT			
Isometric	106.0 ± 7.8	87.0 ± 13.6	< 0.001
Dynamic exercise	98.7 ± 9.2	84.5 ± 7.6	< 0.001

Table - 1 : The effect of nicardipine on diastolic blood pressures.

	Pretreatment (mmHg)	After Treatment (mmHg)	p
RESTING			
Supine	167.4 ± 18.0	145.0 ± 10.6	< 0.001
Standing	167.3 ± 19.3	143.5 ± 11.8	< 0.001
EFFORT			
Isometric	173.0 ± 23.9	150.5 ± 14.0	< 0.001
Dynamic exercise	179.0 ± 19.8	152.5 ± 10.9	< 0.001

Table - 2 : The effect on nicardipine on systolic blood pressures.

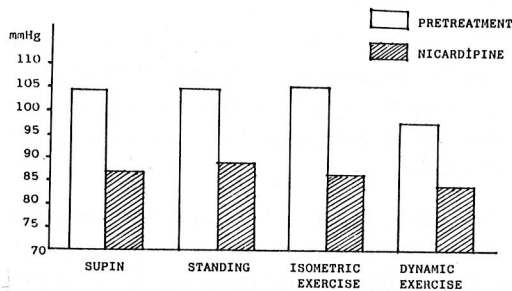


Fig. 1 : The effect of nicardipine on diastolic pressures.

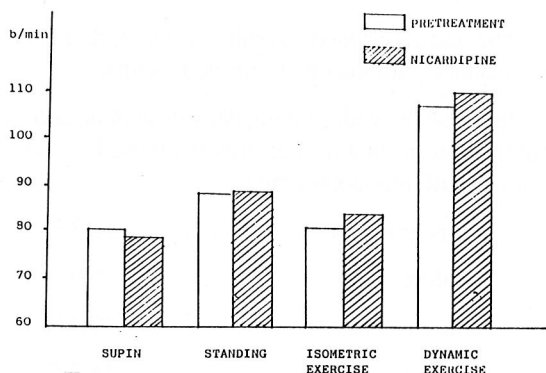


Fig. 3 : The effect of nicardipine on heart rates.

from the fifth day, these complaints were absent, although the therapy continued.

The blood pressure in seventeen of twenty patients decreased to normal limits accepted by WHO. Although the blood pressure of other three decreased, they were not within normal limits.

DISCUSSION

Clinical trials reported that nicardipine is effective in treatment of chronic stable angina pectoris and resting angina associated with coronary spasm (Rousseau et al. 1985; Scheidt et al. 1986). It is reported that nicardipine is also effective in treatment of stable angina pectoris, as much as nifedipine (Armstrong et al. 1986; Bowles et al. 1986). He-

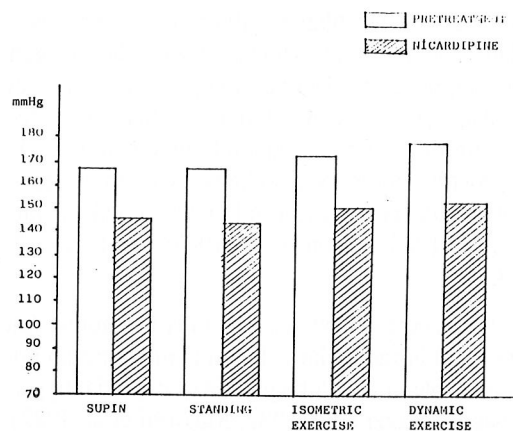


Fig. 2 : The effect of nicardipine on systolic blood pressures.

modynamic and clinical investigations have shown that nicardipine has an advantage of not suppressing myocardial conductivity and left ventricular function (Horio et al. 1983; Matsui et al. 1982; Rousseau et al. 1986). In addition, nicardipine can be used as an initial therapy or combined with other antihypertensive drugs for the treatment of mild to moderate hypertension (Bellet et al. 1985; Creyters et al. 1986; Danielsson et al. 1987; Donnelly et al. 1986). When compared with other vasodilators, it has some advantages. Nicardipine does not cause any fluid retention or increase in weight. It is reported to be effective on treatment of hypertension as much as hydrochlorothiazide, cyclopentiazide, propranolol and verapamil (Bellet et al. 1985; Creyters et al. 1986; Danielsson et al. 1987; Murray et al. 1986; Murray et al. 1986).

Agre et al. (1987) planned to investigate the antihypertensive action of nicardipine in doses of 30 - 60 - 90 - 120 mg per day and compare with placebo. They had observed that, with all these different doses, blood pressures had decreased within statistically significant limits. They had also observed that increasing the dose caused more decrease in blood pressure and no difference in antihypertensive action occurred by dividing the daily dose into two or three.

Nicardipine is a potent vasodilator, and its selective and directly vasodilator action on cerebral and coronary arteries was reported (Takenaka et al. 1979).

In fact, its mechanism of action depends on inhibiting the entrance of calcium ions to the cell. Bloc-

king of the entrance of calcium ions will delay the excitation - contraction process, and this will cause the decrease in contraction of vascular smooth muscles, and vasodilation will occur. Arterial vasodilation decreases preload and myocardial oxygen consumption. The decrease in systemic peripheral resistance, related with arterial vasodilation, decreases afterload and consequently myocardial work. Meanwhile, coronary vasodilation caused by nicardipine, increases myocardial oxygen uptake (Clarke et al. 1983; Eugene et al. 1987; Lambert et al. 1985).

It is reported in some recent investigations that increased intracellular calcium content has an important role in the pathogenesis of essential hypertension (Guazzi et al. 1982; Messerli et al. 1982). According to these reports, nicardipine decreases the intracellular concentration of calcium and can be effective in treatment of hypertension.

Naukkarinen et al. (1987) had used nicardipine in combination with beta-blockers, and had observed an antihypertensive action which was more effective than sole beta-blockers antihypertensive action.

Negative inotropic action is never observed with nicardipine (Rousseau et al. 1985).

In another study, 90 mg per day nicardipine was compared with propranolol 240 mg per day as an antihypertensive, and in conclusion no difference was observed (Danielsson et al. 1987). Considering the side effects of beta blockers, slow calcium channel blockers are preferred for antihypertensive therapy because of their lesser side effects. Although non-selective and beta-1 selective beta blockers decrease the HDL level, nicardipine has no effect on lipids. Although it was blamed to effect blood lipids in some studies the results of subsequent studies did not support this finding (Naito et al. 1984; Ohba et al. 1985). In our study, no effect on lipids was observed.

The superiority of nicardipine to other known calcium channel blockers: verapamil, diltiazem, nifedipine, is having no negative inotropic action and increasing atrioventricular conduction time (Lambert et al. 1985). As reported in other studies, nicardipine did not effect the PR, QRS and QT intervals in our study.

Young et al. (1984) blamed nicardipine and nifedipine to produce tachycardia with reflex

sympathetic activity, related with their potent vasodilator action. We did not observe any similar effect of nicardipine.

Venkata et al. (1987) compared nicardipine with different antihypertensives and observed that diuretics and beta blockers had no superiority to nicardipine.

Kolloch et al. (1985) recommended to administer low dose beta blocker if nicardipine therapy produces tachycardia. In this manner, increased reflex sympathetic activity, caused by nicardipine, would be blocked.

Generally, dizziness, headache, flashing, palpitation and feeling hot were reported as the side effects of nicardipine in the literature. These side effects of nicardipine were not severe and usually reversible (Asplund et al. 1985). It has been shown by Taylor et al. (1985) that these dose-related side effects were related with the vasodilator action of nicardipine. The side effects that we observed in this study appeared in the first days and disappeared on the fifth day of therapy.

The antihypertensive results of our study is in accordance with the other reported results.

In our study, with a 60 mg daily dose of nicardipine, diastolic blood pressures decreased as follows, in different conditions:

Supine position	16.8 %
Standing	15.0 %
Isometric exercise	17.9 %
Dynamic exercise	14.4 %

Systolic blood pressures decreased as follows :

Supine position	13.4 %
Standing	14.2 %
Isometric exercise	13.0 %
Dynamic exercise	14.8 %

In seventeen of twenty patients, blood pressures decreased in different rates but all to normal limits. Although the blood pressures fell below the pretreatment values for the other three patients, they were still within the hypertensive limits accepted by WHO. Nicardipine was successful as an antihypertensive in 85 % of our patients.

Although there are some encouraging reports about using nicardipine for the treatment of congestive heart failure and cerebrovascular diseases (Yong et al. 1981), more detailed investigations must be performed to clarify the effect of this drug.

In conclusion, nicardipine can be used for hypertension therapy with its limited and short term side effects together with its reliable antihypertensive action. It can be used solely or in combination with beta blockers. We have come to the opinion that nicardipine is sufficient with a daily dose of 60 mg in the treatment of mild to moderate hypertension.

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