A COMPARATIVE EVALUATION OF NIFEDIPINE IN THE TREATMENT OF HYPERTENSIVE EMERGENCY: EFFECTS OF TWO DIFFERENT DOSES - AND ROUTES OF ADMINISTRATION

A THESIS

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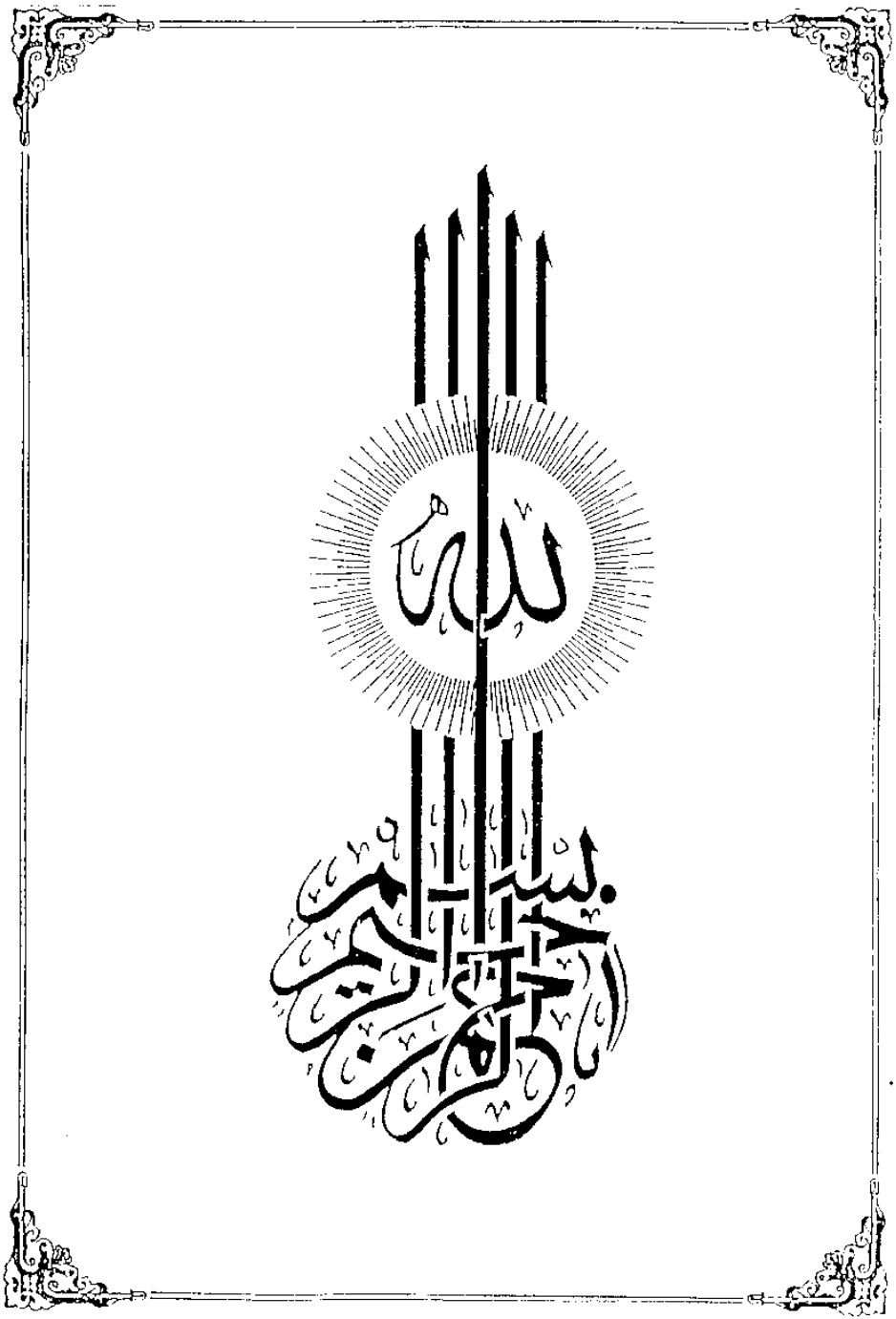
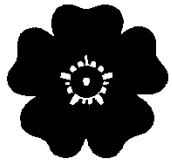
قَالُوا سُبحَانَكَ لا علم لَنا إلا مَا علمتَنا
إنكَ أنتَ العَلِيم الحَكِيم

صدق الله العظيم
البقرة ٣٢



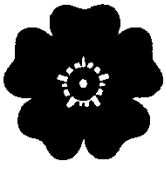


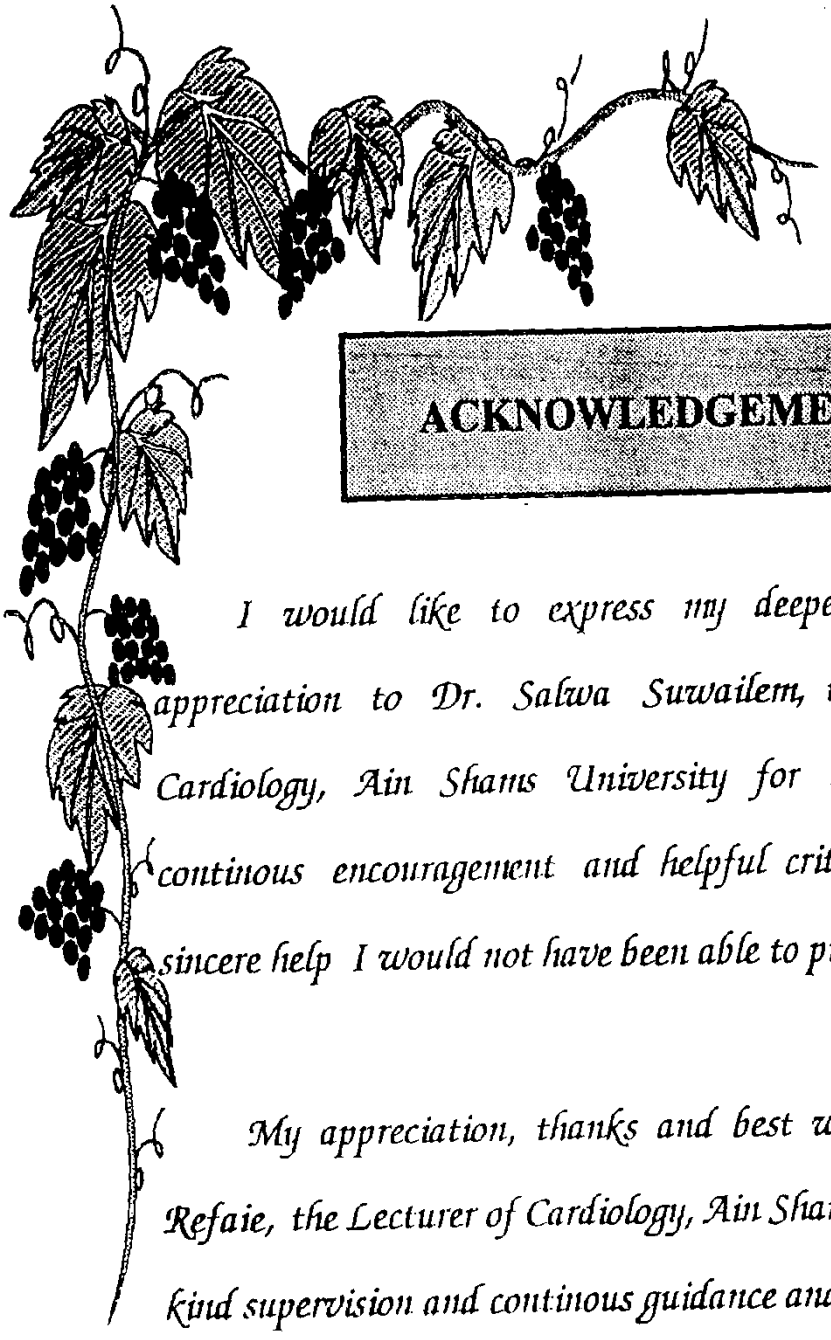
TO MY PARENTS

&

MY LOVELY CHILDREN

SHAIMA AND AHMAD





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INTRODUCTION

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Hypertensive emergencies remain a clinical problem which requires immediate reduction of blood pressure, severe blood pressure elevation (diastolic blood pressure, 120 mmHg) poses a threat to the integrity of the cardiovascular system and results in high morbidity and mortality in a short period of time (Houston, 1988), Keeping in mind that the rate at which hypertension develops is more important than the absolute level of blood pressure in producing acute end organ injury (Zeller et al., 1989).

This problem is more apparent in developing areas due to limited availability or unavailability of intensive care facilities; drugs that are usually used to treat this condition (e.g., sodium nitroprusside, labetalol and hydralazine) are given intravenously and require careful supervision and monitoring to prevent the development of marked hypotension which carries the risk of serious complications that result from a reduction in regional cerebral, retinal, renal and myocardial blood flow.

A drug that is easily administered (by either the oral or sublingual route), has a rapid onset of action, is efficacious and has a low incidence of serious adverse effects would be advantageous. Nifedipine fulfils these criteria (Maharaj and van der Byl, 1992).

Nifedipine has been used effectively to treat high levels of blood pressure quickly. Doses of 10 to 20 mg provide almost uniform reduction of blood pressure by 25 percent within 30 minutes (Jaker et al., 1989). But if a fast onset of action is desired, the bite and swallow method is preferable because higher serum levels will be achieved (van Harten et al., 1987). In spite of these favourable data about nifedipine and like any antihypertensive drug, there is an increased tendency to use the lowest possible dose of the drug whenever possible so that efficacy is maintained and adverse effects are reduced (Maharaj and van der Byl, 1992).

AIM OF THE WORK

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The aim of this study was designed to compare the acute hypotensive effects of two single doses of nifedipine (10 mg and 20 mg) administered by two different routes of administration (sublingual and oral) in severely hypertensive patients in the outpatient clinic, without the necessity for hospital admission.

REVIEW OF LITERATURE

HYPERTENSION
DEFINITION AND CLASSIFICATION

DEFINITION:

The systemic arterial pressure is the driving pressure of the capillary circulation throughout the body. Pathological increase in the arterial pressure is an abnormality which is difficult to define at present in absence of reliable criteria for normality (Rose, 1980).

Hypertension in the adult is defined by most authorities as the arterial pressure exceeding 140/90 mmHg as there is an increased risk for cardiovascular disease associated with systolic blood pressure levels above 140 mmHg and diastolic levels above 90 mmHg (Kaplan, 1992). However, there is no sharp dividing line between normal and high blood pressure (Williams, 1991).

CLASSIFICATION:

I- Classification according to the course of hypertensivestates:

1- Benign hypertension:

Occurs in old subjects in whom the pressure is not so high. The patient's condition remains relatively stable for years, but death may occur either due to heart failure or stroke. Retinopathy when present shows the picture of arteriosclerotic retinopathy and exudates which are small, sharply defined and often confined to one eye (Dollery, 1985).

2- Malignant hypertension:

Occurs at any age, but more frequently is present in the young age, here, the blood pressure is very high and it is characterized by neuroretinopathy and

rapid decline in renal function. It rarely rises de novo but commonly on top of primary or secondary hypertension (Dollery, 1985). Though a patient with malignant hypertension often has a blood pressure above 200/140 mmHg, it is papilledema, usually accompanied by retinal haemorrhage and exudates, and not the absolute pressure level, that defines this condition. Accelerated hypertension signifies a significant recent increase over previous hypertensive levels associated with evidence of vascular damage on fundoscopic examination but without papilledema (Williams, 1991). The clinical features and survival rates of those with or without papilledema are similar that there is no reason to separate the two (Ahmed et al., 1986).

II- Classification according to the level of blood pressure:

This can be shown in the following table:

Table(1):Classification of blood pressure in adults aged 18 years or older.

BP range, mmHg	Category
DBP	
< 85	Normal BP
85-89	High-normal BP
90-104	Mild hypertension
105-114	Moderate hypertension
115	Severe hypertension
SBP, when DBP<90 mmHg	
<140	Normal BP
140-159	Borderline isolated ystolic
160	Isolated systolic ypertension

This classification is based on the average of two or more readings on two or more occasions; BP, indicates blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure. (Joint National Committee, 1988).

III Therapeutic classification:

Even though they are diagnosed as hypertensive, not all persons with usual levels above 140/90 mmHg need to be treated with drugs, although all should be advised to use the various non drug therapies, Drug therapy is indicated in essentially all patients with DBP persistently above 100 mmHg, in many with DBP above 95 mmHg, and in some with DBP above 90 mmHg or an even lower level, depending on the presence of other significant risk factors which may indicate the need for reduction of levels that are below 95 mmHg. Most trials have mainly considered DBP levels, so that there is less evidence concerning the levels of systolic blood pressure that mandate therapy, elevations of systolic pressure above 170 mmHg, at any age, deserve gradual reduction by appropriate non drug and drug therapies (Kaplan, 1992).

IV Aetiological classification:

1- Systolic hypertension:

In this type the systolic pressure only is raised. It is determined by two factors :(A) Stroke volume, and (B) Compliance of the aorta ad its branches.

A) Any condition increasing the stroke volume may raise systolic pressure as in :

1- Aortic incompetence. 2- A-V fistula.

3- Thyrotoxicosis. 4- Patent ductus arteriousus

5- Paget's disease of bone. 6- Severe anaemia.

7- Fevers. 8- Pregnancy.

9- Bradycardia with complete heart block.

B) Also a decrease in compliance, i.e., Reduction in elasticity of the aorta and its branches will increase the systolic pressure as in :

- Degenerative changes of the media as seen in old age and diabetes.

- Increased thickness of the media as in atheroma.

(Pickering, 1973)

Epidemiologic studies confirm that elevated systolic blood pressure in the elderly is more highly correlated with subsequent cardiovascular morbidity and mortality than is elevation of diastolic blood pressure (Applegate, 1989). Isolated systolic hypertension as is commonly seen among the elderly, presents a risk both for stroke and myocardial infarction (Kannel, 1990). The inference that the increased risk of coronary heart disease and stroke in patients with isolated systolic hypertension can be reduced by treatment is supported by analogy with the beneficial response in clinical trials of treating diastolic hypertension in population up to age 70 years, and older, however, serious adverse effects are possible under some circumstances. The advisability of drug treatment for isolated systolic hypertension in elderly populations remains uncertain (Huely et al., 1985). To be mentioned that reduction of systolic pressure will diminish myocardial oxygen demands, improve the metabolism of the heart muscle, and lessen angina pectoris (Frohlich , 1983).

Some say that elderly patients who have isolated systolic hypertension (phase V diastolic blood pressure less than 90 mmHg) may be harmed by treatment (Coope and Warrender, 1986).