

# A Clinic Study With Prazosin and Polythiazide (Minizide) in the Treatment of Hypertension

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Shaukat M. Malik, Zubeida Khanum, Khalid Mehmood, Shehbaz Ahmed ( Cardiology Department, Central Government Polyclinic, Islamabad. )

## Abstract

The efficacy and safety of Minizide as antihypertensive agent was evaluated in 15 hypertensive patients over a period of 12 weeks. In 80% of the cases the response was satisfactory. Dizziness, dryness of the mouth and weakness were the most common side effects. In 1 case with the exception of one, these symptoms disappeared by the 2-4 weeks of the initiation of the treatment. Minizide is a safe and effective antihypertensive drug (JPMA 3238, 1982).

## Introduction

Prazosin is a quinazoline derivative and is a new antihypertensive agent. It has a chemical structure which is quite different from other antihypertensive drugs in current use. Prazosin has established its place among the other anti-hypertensive drugs, (Boll and Simpson 1974; Cohen 1970; Hayes et al 1974; Lowenstein and Steel 1978; Lud Johansen 1974; Richardson et al 1968; Stokes and Weber 1974) and has effectively lowered the supine and standing blood pressure in majority of the patients whose blood pressure was poorly controlled by other drugs. Prazosin exerts its antihypertensive action by virtue of selective inhibition of postsynaptic  $\alpha$ -adrenergic receptors with resultant dilatation of the peripheral arterioles and veins (Jouerning et al 1978; Robinson & Collier 1978). Unlike other  $\alpha$  adrenergic antagonists which block both presynaptic and postsynaptic receptors and interfere with feedback regulation of neurotransmitter (nor epinephrine) release, Prazosin appears to inhibit smooth muscle contraction without inducing increased neuron nor-epinephrine release. It causes little or no change in the heart rate (Safer et al 1974) and increases glomerular filtration rate and renal plasma flow. It also reduces the plasma renin activity (Hayes and Graham 1976). It was suggested that a small dose of a diuretic would potentiate the effect of Prazosin. We undertook a small study in which Minizide (Prazosin 0.5 mg+Poly-thiazide 0.25 mg) was used as an antihypertensive agent.

## Patients and Methods

Fifteen patients with hypertension who attended the out patient of the cardiology department, Central Government Polyclinic, Islamabad were entered in this study. Five patients had no treatment before and the ten were poorly controlled with the other antihypertensive drugs. On the first day a thorough physical examination was made, blood pressure was recorded on the right arm both in the lying and in the standing positions by means of mercury sphygmomanometer with a standard size cuff 12x35 cm. On auscultation for recording blood pressure, Phase I and Phase V were taken as the point of recording systolic and diastolic blood pressure respectively.

A twelve lead ECG and X-ray chest were obtained. Complete blood picture, urine analysis, blood urea, serum creatinine, uric acid, electrolytes and liver function tests were estimated initially and after twelve weeks when the study was concluded. The starting dose of Minizide was 1 tablet administered in the evening. The patients were warned about the possible side effects of the drug particularly the dizziness. They were advised not to get up from the bed suddenly and to sit for a little while before standing or working. The other antihypertensive drugs and dosage used before the introduction of Minizide were

recorded and changes in the regimens were kept to a minimum. The patients visited the clinic every week when their blood pressure were recorded. If the fl in the blood pressure was not satisfactory, the dose of Minizide was increased by one tablet. The patients were asked about the side effects at each visit and were entered in a proforma.

#### **Characteristics of the Patients**

A tot of 15 patients 12 me and 3 femes were included in this study. Age distribution duration of disease, associated conditions, grades of hypertension and ocular complications are shown in Tables I-V.

### Table I

#### Age Distribution

20-29 years	1 patient
20-29 years	1 patient
30-39 years	2 patints
40-49 years	4 patients
50-59 years	8 patients

Majority of the patients were between the age of 40 and 50 years. (Table I-).

### Table II

#### Duration of Hypertension

0-1 year	8 patients
2-3 years	3 patients
3-5 years	4 patients

### Family History of Hypertension

It was positive in 6 cases.

## Table III

### Associated Conditions

Angina	1 patient
Ischaemic heart disease	3 patients

### Previous Medication

## Table IV

### Grades of Hypertension

Mild (Diastolic B.P. less than 105 mm Hg)	8 patients
Moderate (Diastolic B.P. between 105 and 114 mm Hg)	4 patients
Severe (Diastolic B.P. above 115 mm Hg)	3 patients

# Table V

## Retinopathy

Grade I	6 patients
Grade II	7 patients
Haemorrhages and exudates	2 patients

### **Previous Medication**

Five patients had no previous antihypertensive drugs while other ten patients were receiving methyldopa, beta blockers, diuretics and tranquillizers in various combinations.

### **Results**

#### **Blood Pressure**

Out of the fifteen, 12 patients achieved satisfactory response. Their diastolic blood pressure fell down to 95 mm or below. The average blood pressure fl was 26/14 mm of Hg. In three cases the diastolic blood pressure remained above 104mm of Hg.

#### **Dose of Minizide**

A maximum of four tablets daily were given in divided doses.

#### **Side Effects**

These were assessed by direct questioning.

#### **Laboratory Data**

No significant changes were noted in the blood chemistry or blood count during the period of treatment.

### **Discussion**

In 80% of our cases the response was satisfactory, our findings are in keeping with other studies (Boli and Sampson 1974; Cohen 1970; Hayes et 1974; Lowenstein & Steel 1978; Lowenstein and Steel 1979; Richardson et 1968; Stokes & Weper 1974) most of these cases had mild to moderate hypertension. The average fl of B.P. was 26/14mm of Hg. while others (Smith et 1976; Turner et 1977) have recorded greater fl in blood pressure, probably due to larger doses. Smith et (1976) have

shown in their study that Prazosin is very effective as a single drug in the management of hypertension, but its major role is in combination with other drugs like a diuretic or beta blocker. The finding that fluid retention accompanies the use of Prazosin and the evidence (Fennerty et 1970) that expansion of the plasma or extra-cellular fluid volume or both may limit the antihypertensive action of the drug provided a ration basis for the use of a diuretic in combination with Prazosin. Synergistic effect between Prazosin and a thiazide diuretic has ready been demonstrated by Brogden et (1977) and Lowenstein and Steel (1978) .In our three cases with severe hypertension the response with Minizide was poor. May be, we did not push the dose high enough.

The most common side effects noted were, dizziness, particularly! in the morning, weakness and dryness of the mouth. Spells of dizziness with occasion transient syncope is “the first dose phenomemon”. This response follows initiation of Prazosin therapy or increase in the dose, (Rosendorff 1976; Turner et 1977). Patients receiving diuretics or beta blockers are more prone to this phenomenon. The mechanism of this phenomenon is not known-probably it is due to venodilatory action of Prazosin Qouerning et 1978). In our study l the patients ‘except one’, who complained of dizziness, settled down and were free of symptoms between 2-4 weeks of the initiation of treatment. One patient was so incapacitated that he had to stay in bed for two weeks. Similarly feeling of weakness and dryness of the mouth so disappeared with the progress of the treatment.

No significant hematologic or biochemic changes were noted during the treatment.

Our conclusion, from this short term study, is that Minizide is a safe and effective drug in the control of hypertension in majority of the patients when used either single or in combination with other drugs.

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