A Multicentre Evaluation of Sustained Release Oxprenolol in the Management of Hypertension in Otd-Patient Practice

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Abstract

Fifty six patients suffering from moderate essential hypertension (with supine diastolic blood pressure values between 106-120mm Hg), whose current treatment produced inadequate control, troublesome side-effects, or a combination of both were included in the study. Newly detected cases and patients who had discontinued treatment were also included in the study.

The regimen consisted of 160mg of Oxprenolol in sustained release formulation (Trasicor l60 SR.) and 25mg of Chlorthalidone (Hygroton) administered once daily in the morning, for eight weeks.

The mean duration of hypertension was five years and the mean heart rate and blood pressure on admission to the study was 93 & 177/112 mm of Hg respectively.

On conclusion of the study, the mean heart rate and blood pressure were 77 & 145/89mm of Hg respectively., a supine diastolic blood pressure equal to or less than 95mm Hg was reached in 45 of 56 patients (80%). Side effects were observed in 10 patients (17.9%) and were of mild nature; in no case did the treatment have to be prematurely withdrawn because of the side effects.

This study has shown that a combination of Oxprenolol. slow release (Trasicor 160 SR.) & Chlorthalidone 25mg (Hygroton) given once daily induces normalization.of blood pressure in approximately 80% of patients and a single morning dose of sustained release formulation of Oxprenolol improves patient compliance in moderate essential hypertension (JPMA 32.206, 1982).

Introduction

Beta-receptor antagonists are widely used in the treatment of essential hypertension. To produce a satisfactory therapeutic response they are commonly prescribed twice or thrice daily and may be combined with diuretics, vasodilators, adrenergic neurone blockers and methyldopa. Several reports (Ayd, 1974; Blackwell," 1973; Galley, 1968) indicate that compliance with therapy falls as the frequency of dosage increases.

Oxprenolol is a beta-blocking drug which possesses effective antihypertensive properties. Its duration of action is longer than its plasma concentration would suggest, but probably does not exceed 8-12 hours (Brunner et al., 1975). Oxprenolol is usually administered twice or thrice daily to achieve a therapeutic anti-hypertensive effect. The inconvenience associated with multiple daily doses is of concern when long term treatment is required, as is the case in essential hypertension. West et al. (1976) showed that 160 mg sustained-release oxprenolol produces maximum blood levels similar to those with 80 mg of con-ventional oxprenolol and almost, as quickly. Moreover, high concentrations of the compound persist much longer and are associated with a prolonged beta blocking effect that lasts up to 24 hours. Thus, with the development of a sustained-release formulation the goal of prolonging the half-life of the drug has been reached. An added advantage is the reduction of the peak concentration thereby minimizing the marked reduction in heart rate and possibly' tiredness on exercise which might occur when plasma levels are high (Owens, 1978).

Chlorthalidone is a diuretic widely used for the treatment of hypertension. Since it possesses a prolonged duration of action, once daily administration seems appropriate.

Beta-blockers have been shown to reduce cardiac output whereas diuretics lower peripheral resistance, at least on long term administration (Lund-Johansen, 1970; Simpson, 1974). Moreover beta-blockers

may blunt the renin stimulating effect of diuretics and attenuate their hypokalemic effect (Hettiarachchi et al., 1977).
Most authorities agree that beta-blockers and diursties, are groups of drugs with different modes of actions, useful in the treatment of moderate hypertension. Although it is possible to use a wide variety of dose levels, it appears that in practice 160 mg oxprenolol combined with 25 mg chlorthalidone is an effective ratio (Raftery, 1978; Elsdon Dew et al., 1978).
Hence this study was designed to examine the feasibility of substituting once-daily treatment with sustained release oxprenolol hydrochloride and chlorthalidone in group of hypertensive patients whose current treatment was giving inadequate blood pressure control, troublesome side-effects or a combination of both. This study was an open assessment under general practice conditions with individual doctors, each contributing a maximum of five patients.

Patients and Methods

Patients with moderate essential hypertension (with supine diastolic blood pressure values between 106-120 mm Hg), whose current treatment produced inadequate control, troublesome side-effects or a combination of both were included in this study. Newly detected cases and patients who had discontinued treatment were also included The regimen consisted of 160 mg of oxprenolol in sustained -release formulation (TRASI-COR 160 SR) and 25 mg of chlorthalidon: (HY-GROTON) administered once daily in the morning for eight weeks. All patients were seen regularly at intervals of two weeks. At each visit supin. and standing blood pressure and pulse rate were recorded and an assessment of tolerability was made recording the nature, duration and severity of any side-effects.

Results

There were 56 cases in the final analysis, 30 males and 26 females with an average age of 52 years (range 26-75 years). The mean duration of hypertension was five years and the mean blood pressure on admission to study was 177/112 mm Hg. The results for heart rate and blood pressure are shown in Table I.

Table I

Heart Rate and Blood Pressure During Trial

Parameter		*Pretrial*	*Week 2*	*Week 4*	*Week 6*	*Week 8*
Heart Rate b/min	Mean	93	82	79	79	77
	St. Dev.	14.3	10.9	10.2	10.2	8.5
Systolic B.P. (mm of Hg)	Mean	177	162	155	148	145
	St. Dev.	25.1	23.6	18.0	16.0	16.7
Diastolic B.P. (mm of Hg)	Mean	112	100	95	92	89
	St. Dev.	11.9	10.8	9.7	8.6	8.2

The mean heart rate at the start of the study was 93 and on its completion 77. The mean systolic and diastolic blood pressures at the start of the study were 177 and 112 mm Hg respectively and on completion of study 145 and 89 mm Hg respectively. At the end of the study, a supine diastolic blood

pressure equal to or less than 95 mm Hg was reached in 45 of the 56 (80%) patients.

Table II
Duration of Hypertension

Duration of Hypertension	*Number of Cases*
Less than 1 Year	18
1—5 Years	20
6—10 Years	5
Above 10 Years	6
Unknown	7

Table II shows the duration of the hypertension in 56 patients; the mean duration of hypertension was five years.

Table III
Preference of Therapy

Preference	*Number of Patients*	*Percentage*
Trasicor SR	43	77%
No Preference	12	21%
Original Therapy	1	2%

Table III shows preferences of therapy. On conclusion of the study each patient was questioned regarding preference of therapy. Forty-three patients (77%) preferred TRASICOR 160 SR, 12 patients had no preference and one patient preferred the original therapy.

Table IV

Absolute Reduction Expressed as Percentage

Parameter	*Pre/Trial*	*Completion of Trial*	*Absolute Reduction Expressed In %*
Pulse	93	77	17%
Systolic B.P. (mm of Hg)	177	145	18%
Diastolic B.P. (mm of Hg)	112	89	21%

Table IV shows absolute reductions of pulse rate and systolic and diastolic blood pressure. Pulse rate was reduced by 16.4%, systolic blood pressure by 182% and diastolic blood pressure by 20.55%.

Table V

Previous Therapy

1) Beta Blocker (conventional)	3
2) Methyldopa (monotherapy)	17
3) Vasodilators (monotherapy)	Nil
4) Diuretics (monotherapy)	5
5) Combination Therapy	16
6) Therapy Not Known	8
7) No Therapy	7

Table V shows details of previous therapy. 17 patients were on methyldopa monotherapy and 16 on combination therapy.

Table VI

Unwanted Effects

Symptoms	*Severity*	*No. of Patients*
Weakness	Mild	5
Dryness of Mouth	Mild	1
Headache & Nausea	Moderate	1
Drowsiness	Moderate	2
Numbness of Extremeties	Mild	1

Table VI lists unwanted effects which were observed in ten patients (17.9%); weakness was the commonest" side-effect and was observed in 5 patients.

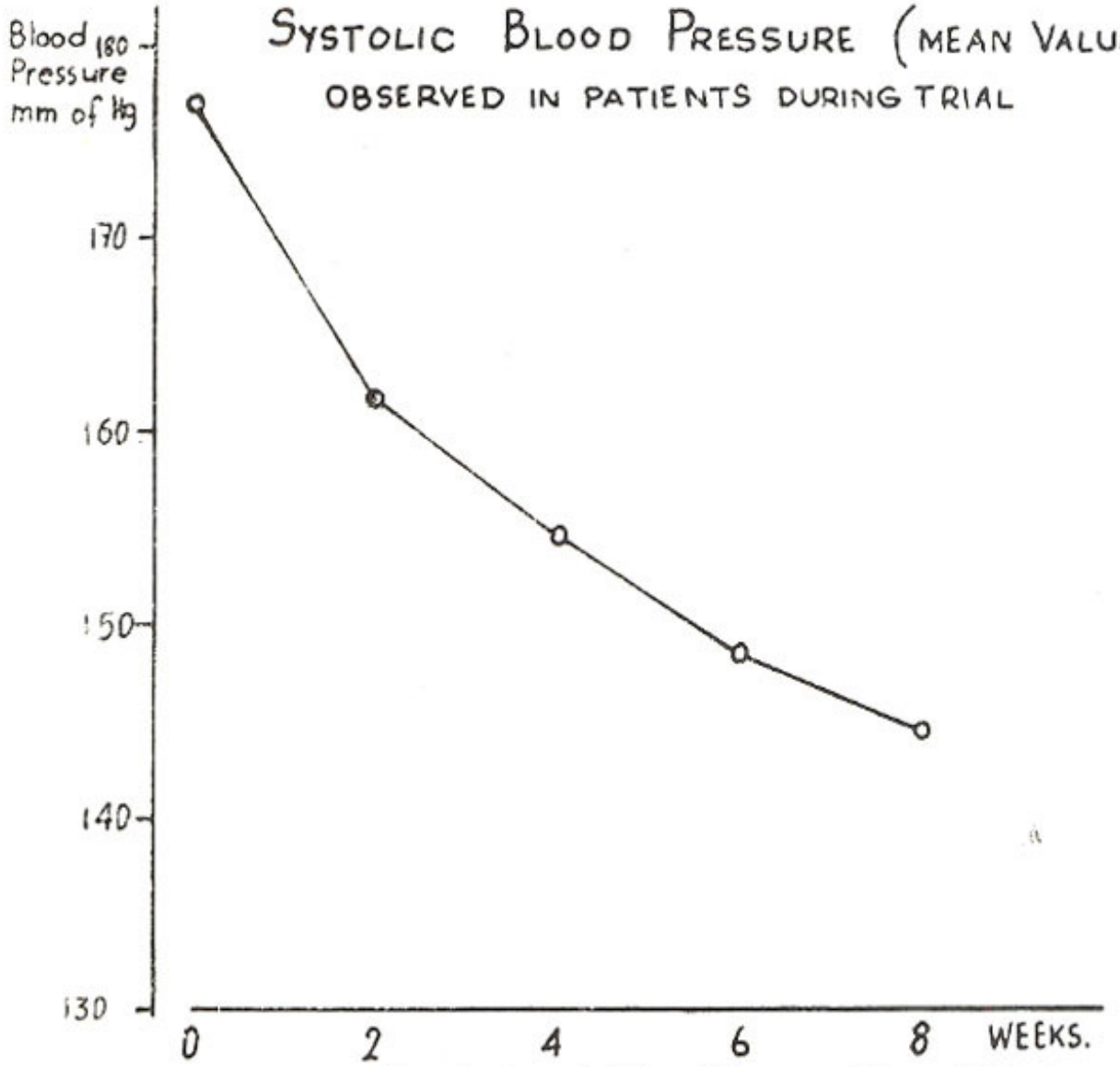


Fig. 1: Systolic Blood Pressure (Mean Values)

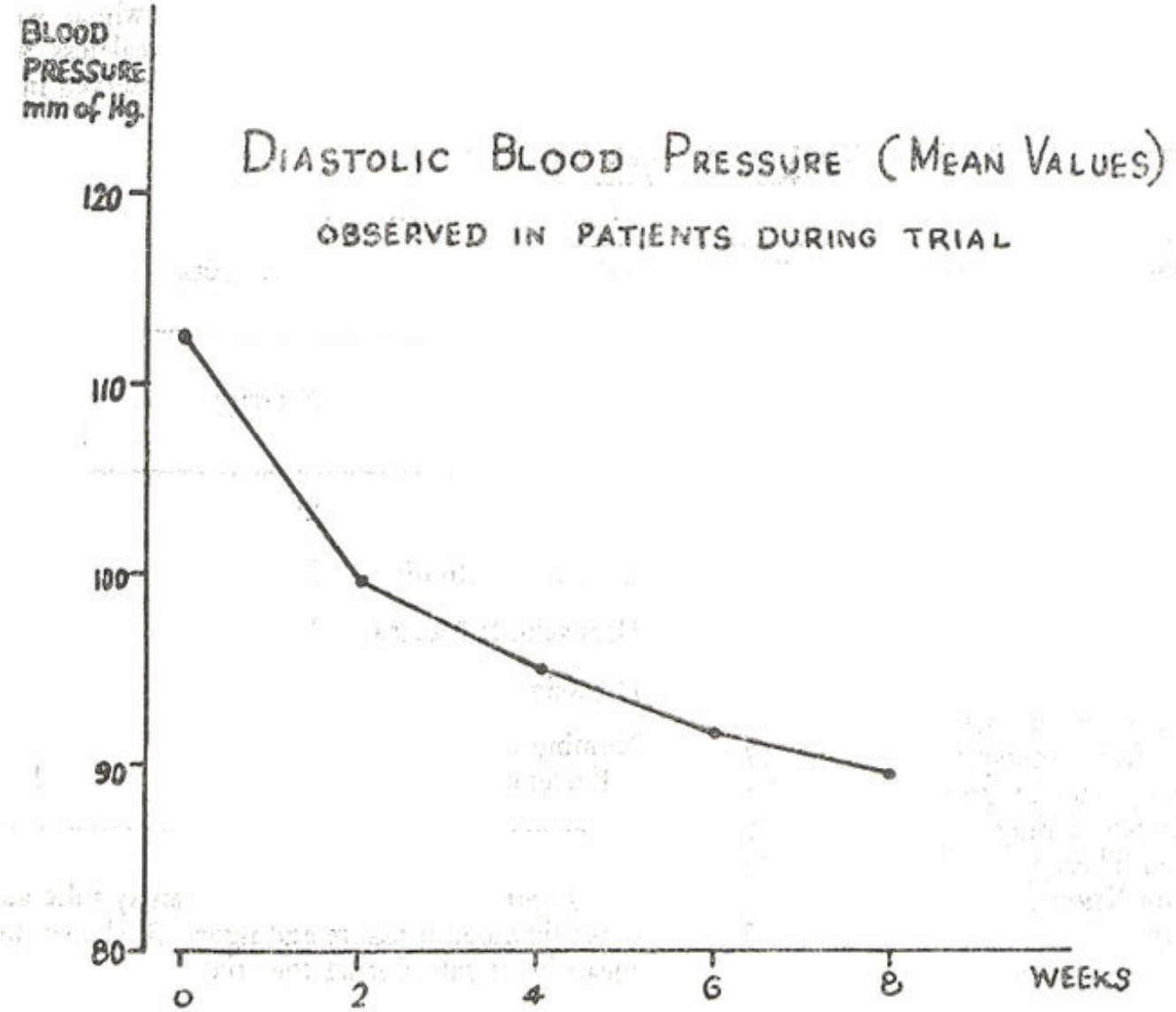


Fig. 2: Diastolic Blood Pressure (Mean Values)

Figures 1 and 2 show the mean systolic and diastolic blood pressure and figure 3 shows the mean heart rate during the trial.

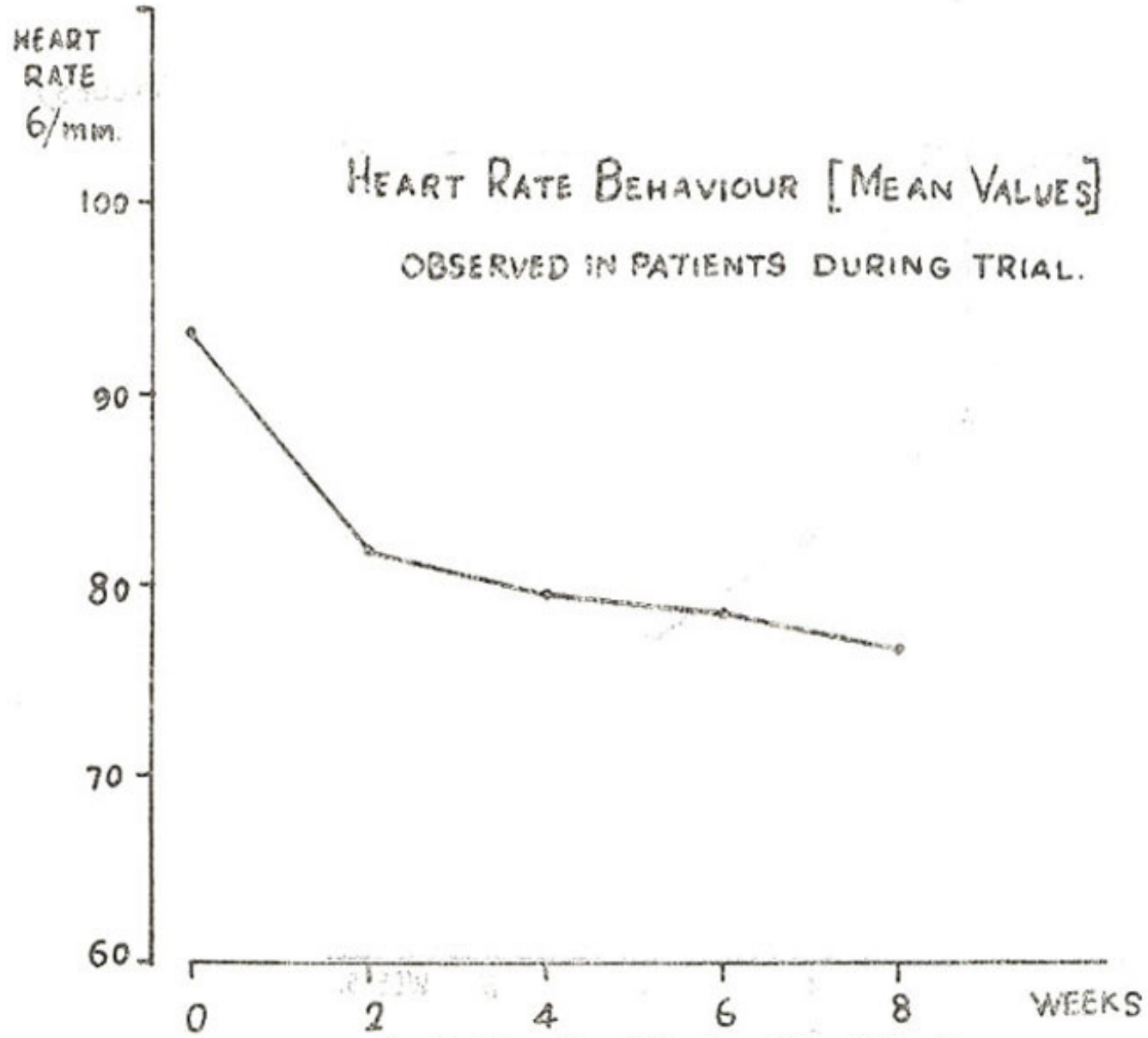
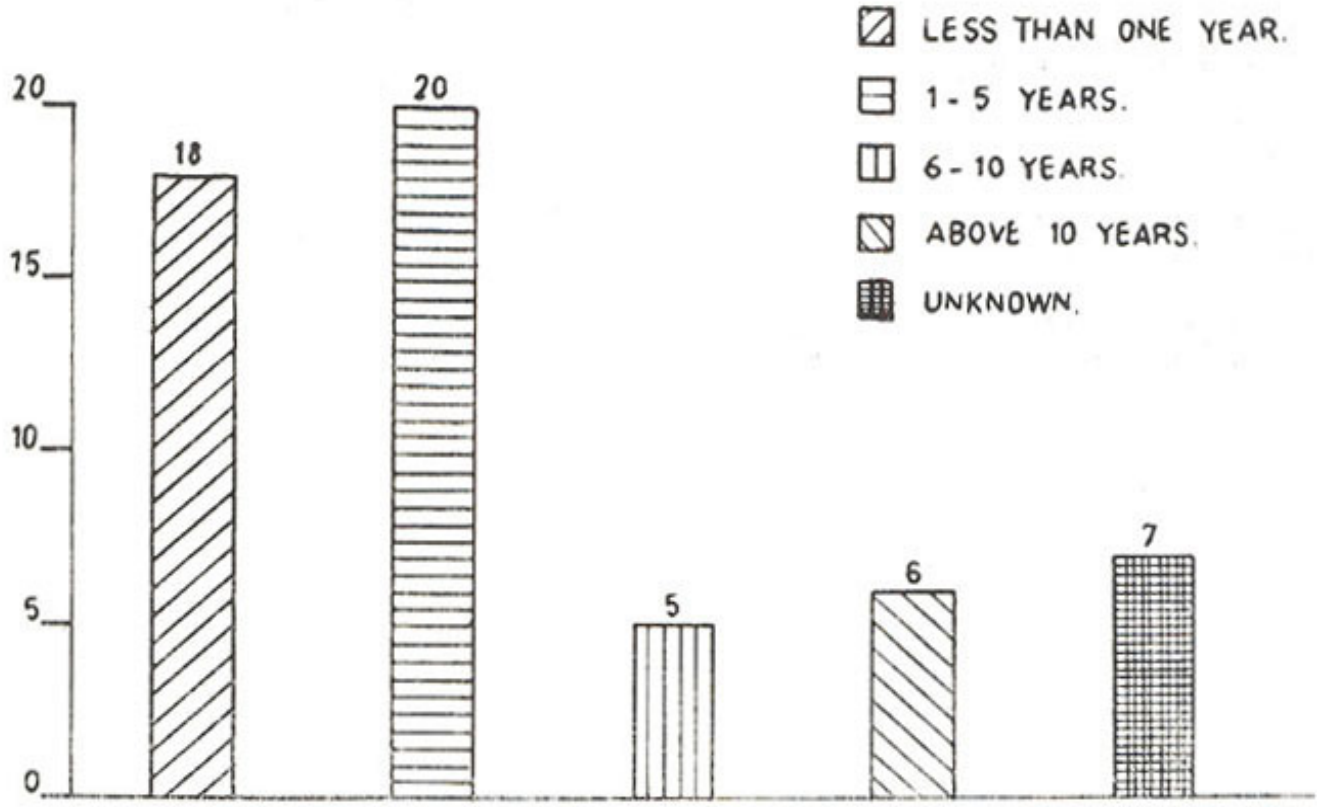
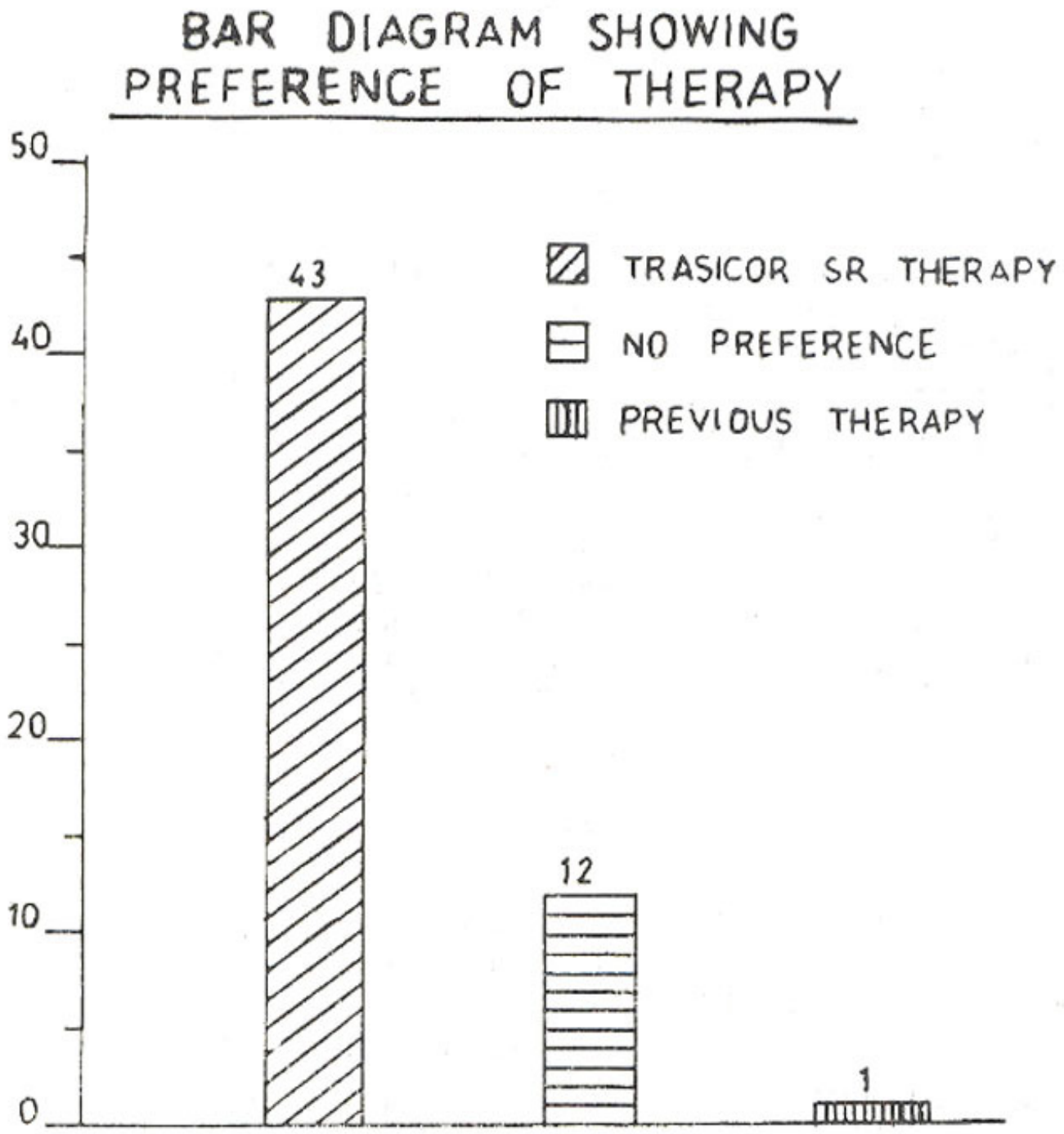


Fig. 3: Heart Rate Behaviour (Mean Values)

BAR DIAGRAM SHOWING DURATION OF HYPERTENSION





Discussion

It is well known that the prognosis of hypertension can be improved by appropriate treatment, provided that patients take the prescribed drugs regularly (Dollery and Bulpitt, 1977). In tact, in anti-hypertensive therapy, the patient's cooperation is one of the most important factors in obtaining satisfactory blood pressure control. The percentage of patients who stop taking anti-, hypertensive drugs has been shown to increase to 50% during the first year of therapy and to about: 70% over a 4 year period (Cladwell et al., 1970; Haynes and Sackctt, 1976). The need to take a number of tablets daily tor a long period very often leads to poor compliance (Havnes and Sackctt, 1976).

Our results confirm recent findings that a combination of Oxprenolol + Chlorthalidone, given daily, is well tolerated and permits normalization of diastolic blood pressure (less than 95 mm Hg) in 70% of hypertensive patients (Zan-chetti et al., 1976). This study has shown that a combination of oxprenolol slow-release and chlorthalidone, given once daily, induces normalization of blood pressure in approximately 80% of patients with moderate hypertension.

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