PROPRANOLOL IN THE SOUTH AFRICAN NON-WHITE HYPERTENSIVE PATIENT*

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SUMMARY

In a clinical trial of 25 Bantu and Indian patients over an average period of 6 months, control of blood pressure was obtained in 8 of the 12 Indian patients (66%) and in only 4 of the 13 Bantu patients (30%). This work shows that control of blood pressure in non-White patients on propranolol is possible provided a large dose and prolonged period of therapy are used; however, the control of blood pressure is not as effective as in White patients.

Propranolol (Inderal), an adrenergic beta-receptor antagonist, has been found to be an effective hypotensive agent in European patients.[1-4] However, Humphreys and Delvin[5] found in a double-blind cross-over trial of 18 hypertensive Jamaicans that there was no significant difference between propranolol and an inert placebo. To our knowledge, there is no confirmatory work in the literature recording the value of propranolol in the treatment of hypertension among Bantu and Indian patients living in a tropical environment. With this in mind, a trial of propranolol among Bantu and Indian patients living in this environment was initiated.

MATERIAL AND METHOD

The trial started with 28 patients. Three patients were withdrawn because of cardiac failure in one, insomnia in another and a pulse rate below 50/min in a third, leaving 25 patients who completed the trial at the end of 6 months. Thirteen patients were Bantu, of whom 5 were males and 8 females. There were 12 Indians, comprising 7 males and 5 females. Two patients were in the age-group 20 - 30 years, 13 were aged 31 - 40 years, 6 were aged 41 - 50 years and 4 were 51 - 60 years.

Twelve patients had normal fundi, 10 patients had vascular changes and 3 patients had either exudates or haemorrhages seen in the fundi. Twenty-four patients had essential hypertension and one patient had renal hypertension. Before therapy 14 patients had electrocardiographic or radiographic evidence of left ventricular hypertrophy. An additional patient had had a posterior myocardial infarction.

The blood urea level at the beginning of the trial was as follows: below 40 mg/100 ml 21 patients; 40 - 50 mg/100 ml 2 patients; 50 - 60 mg/100 ml 1 patient; and 60 - 90 mg/100 ml 1 patient.

The initial diastolic blood pressure in mmHg was 100 - 120 in 5 cases; 121 - 140 in 14 cases and 141 - 160 in 6 cases.

Patients suffering from bronchial asthma or incipient or overt manifestations of cardiac failure were excluded from the trial.

Initially, the patients received propranolol 10 mg *q.i.d.* and when this test dose was without effect, they were put on propranolol 40 mg *q.i.d.* Thereafter, the dosage was increased by 40 mg *q.i.d.* at fortnightly intervals until the desired drop in blood pressure was reached and stopped if the pulse rate dropped below 50/minute, or if side-effects which the patient could not tolerate developed. Of the 25 patients, 19 had attended the hypertension clinic regularly and 6 were new cases. In the old patients blood pressure had been successfully controlled by a variety of agents including methyldopa, guanethidine, clonidine and reserpine combined with a thiazide derivative. Two of the Indians and 9 of the Bantu patients were of the professional class.

The aim of therapy was to lower the diastolic blood pressure to a level of 110 mmHg or less and we regarded patients as having mild control of their blood pressure if their standing diastolic blood pressure was between 101 and 110 mmHg; moderate control if their standing diastolic blood pressure was between 91 and 100 mmHg and good control if their standing diastolic blood pressure was 90 mmHg or less. We define tolerance as a state in which an increase in the dosage of propranolol becomes necessary due to a rise in the blood pressure after a diastolic reading of 110 mmHg has been attained.

RESULT OF THERAPY

Using the above criteria, we found that among the Indian patients, 5 patients obtained good control, 2 patients obtained moderate control and 1 mild control of their blood pressure. Tolerance occurred in 3 Indian patients. In the Bantu patients, 2 patients obtained good control of their blood pressure, 1 patient obtained moderate control and 1 patient mild control of his blood pressure. Tolerance occurred in 4 of the Bantu patients.

Table I shows the initial blood pressure, the response to therapy on propranolol and the dosage of propranolol. The dosage of propranolol in the 12 Indian patients varied from 160 to 1 920 mg daily with an average of 760 mg. The dosage of propranolol in the 13 Bantu patients varied from 320 mg daily to 1 600 mg daily with an average of 761 mg.

In 6 of the 25 patients the diastolic blood pressure did not at any stage fall to 110 mmHg or less. Fifteen of the

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25 patients in whom a diastolic level of 110 mmHg was recorded, obtained this level within one month. Others obtained the level between 2 and 4 months. It is relevant that 19 patients were previously treated on other hypotensive agents, and of two patients who were controlled on guanethidine, one was not controlled on propranolol. The others had been effectively treated on alpha-methyldopa, clonidine or reserpine and a thiazide derivative.

In the 6 patients (5 Bantu) in whom no control was obtained, the first was treated on propranolol 640 mg daily for 6 months; the second received propranolol 1 600 mg daily for 4 months; the third had propranolol 400 mg daily for one month when marked bradycardia limited

TABLE I. INITIAL BLOOD PRESSURE, RESPONSE ON THERAPY TO PROPRANOLOL AND THE DOSAGE OF PROPRANOLOL

Case	*Race*	*Initial diastolic blood pressure (mmHg)*	*Standing diastolic blood pressure mmHg on therapy*	*Maximum dosage of propranolol (mg)*
1	Indian	150	130	1 280
2	Indian	120	90	160
3	Indian	130	100	480
4	Indian	150	90	1 280
5	Indian	140	130	600
6	Indian	140	125	1 920
7	Indian	140	130	1 640
8	Indian	120	90	240
9	Indian	150	90	320
10	Indian	140	100	400
11	Indian	140	90	640
12	Indian	140	110	160
13	Bantu	130	90	320
14	Bantu	120	110	640
15	Bantu	120	90	400
16	Bantu	130	120	400
17	Bantu	130	120	1 200
18	Bantu	140	130	400
19	Bantu	150	140	1 600
20	Bantu	160	150	1 480
21	Bantu	120	100	480
22	Bantu	130	120	400
23	Bantu	135	130	600
24	Bantu	130	120	800
25	Bantu	150	120	1 200

further increase; the fourth was given propranolol 1 920 mg daily for 5 months; the fifth 1 600 mg daily for 2 months and the sixth 1 920 mg daily for 6 months. Of the 6 patients who were resistant to propranolol 3 were new cases, 2 had previously been controlled on alpha-methyldopa 1·5 g daily and one on guanethidine 100 mg daily combined with cyclopenthiazide and reserpine.

The average gap between lying and standing blood pressure was 5 mmHg.

Side-effects observed were insomnia, vomiting, nausea, bradycardia, sleepiness and diarrhoea (once each), and 14 patients had a weight gain of 2 kg. One patient complained that the number of tablets (20) was excessive. There was no rise in the blood urea level in any patient.

DISCUSSION

This work sought to find out whether propranolol given in high dosage and over a sufficient period of time would lower the blood pressure in Bantu and Indian patients living in a subtropical climate. Humphreys and Delvin[5] in a study of 18 Jamaicans with hypertension who were not of completely negroid stock, concluded that propranolol alone up to a maximum of 360 mg given continuously for 2 - 4 months had no hypotensive effect. One of the main criticisms of this work by Prichard and Gillam[2] was that the dosage of propranolol was not high enough.

Humphreys and Delvin[5] also found that propranolol was no more effective than an inert placebo and suggested that this may have been because the 'tranquillizing' effect is unlikely to be of value in Jamaicans. Zacharias and Cowen,[4] however, found in a randomized, double-blind cross-over trial that propranolol produced a significant fall in blood pressure when compared with a placebo in 28 European patients with hypertension.

This study showed that when a high dosage of propranolol is used, control of blood pressure can be attained. Only 4 Indians and one Bantu were controlled with the maximum dose suggested by Humphreys and Delvin, viz. 360 mg daily. Among our 12 Indian patients, 5 obtained good control, 2 moderate control and 1 patient mild control of blood pressure. In the 13 Bantu, 2 obtained good control, one moderate control and one mild control. Thus there was a racial difference in the response to propranolol, used for hypertension, in that Bantu patients did not respond as effectively as Indians.

The advantage of propranolol, as noted by Prichard and Gillam,[2] was that the average gap between lying and standing blood pressure was only 5 mmHg. The other advantage was that side-effects occurred in only 6 of the 25 patients but except for one patient with bradycardia the side-effects were not serious enough to warrant discontinuing propranolol. It is important carefully to exclude those suffering from cardiac failure or bronchial asthma, as one patient in our series developed congestive cardiac failure.

We have found that propranolol, while it is an effective drug in the control of blood pressure in high dosage, is not as effective a hypotensive agent as guanethidine or methyldopa. This work is in contrast to that of Prichard and Gillam[2] who found that propranolol is at least of similar potency to bethanidine, guanethidine and methyldopa. Two patients who were previously controlled on methyldopa and one patient previously controlled on guanethidine, reserpine and a thiazide derivative were ineffectively controlled on propranolol. The disadvantage of using propranolol in hypertension is its property of exacerbating congestive cardiac failure or bronchial asthma. The average dosage of propranolol used in our series was 760 mg daily in Bantu and 761 mg in the Indian patients. With such doses the retail cost of the drug would prohibit its liberal use, especially in a tropical or subtropical environment where the cost of therapy is an important factor.

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