RENESE—RESERPINE FOR THE TREATMENT OF HYPERTENSION

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(Clinical trial carried out in Medical Unit II, General Hospital, Singapore)

Several hypotensives and diuretics have been used either singly or in combination for the treatment of hypertension. Reserpine has been used for many years. It is a mild hypotensive agent, the action of which is both central and peripheral. Because of its many side effects and mildness of action it has been superseded by the newer hypotensive agents like Ismelin and Aldomet, but when used in combination with either other hypotensive agents or diuretics, it still has a role to play in the treatment of hypertension. Since the introduction of Chlorothiazide, a diuretic, the use of diuretics in the treatment of hypertension has almost become a routine in most hypertension clinics. One of the disadvantages of Chlorothiazide is the urinary loss of potassium with resulting hypokalaemia. Polythiazide (Renese) which was introduced recently is claimed to be a more potent diuretic with a longer duration of action and has a more favourable sodium-potassium ratio in that the potassium loss in the urine is appreciably less. 1 (Ford, R. V.) 1961.

Polythiazide has been used for the treatment of Essential Hypertension, Essential Hypertension with Cardiac Failure, Congestive Cardiac Failure, Nephrosis, Cirrhosis and other oedema states. The response has been excellent in 80% of the cases. In the treatment of hypertension, it possesses definite blood pressure lowering properties. 2 (Klapper, M.S. and Richard, L.) 1962.

PURPOSE

A fixed combination of Polythiazide (Renese) and Reserpine has been introduced for the treatment of hypertension. In this trial this combination in one tablet was used for the treatment of hypertension. Each tablet contained 2 mg. of Polythiazide and .5 mg. of Reserpine.

METHOD AND MATERIAL

Fifteen patients were put on this drug trial. They were selected cases of mild to moderate hypertension (Diastolic pressure between 100-125 mm. of Hg.). The cases were picked from the Out-patient Clinics. Fourteen were new cases and one was an old case of hypertension which had failed to respond to therapy. There were ten males and five females in the series (Table I) and their ages ranged from 27-64 years with an average age of 48.1 years. Thirteen of the cases had essential hypertension, one had hypertension with diabetes mellitis and one had hypertension with pyelonephritis. (Table II).

TABLE I

NUMBER OF PATIENTS	:	15
MALES	:	10
FEMALES	:	5
AVERAGE AGE	:	48.1 Years (Range 27-64 Years)
AVERAGE DURATION OF TREATMENT	:	8.9 Weeks (Range 6-15 Weeks)
DOSE USED	:	1-1½ Tablets)

The systolic blood pressure (recumbent) ranged from 170-216 mm. of Hg. with an average of 196.3 mm. of Hg. The diastolic (recumbent) ranged from 100-125 mm. of Hg. with an average of 114.2 mm. of Hg. All the cases were treated as out-patients. Blood pressures were taken both in the recumbent and standing positions—each several times over a period of ten to fifteen minutes and the lowest pressure registered was recorded. The basal levels were obtained after putting the patients on sedation for one week. Only those patients with diastolic pressures between 100-125 mm. of Hg. were selected for the trial. The following investigations were carried out:—Urine examination, blood urea, X-ray chest and an E.C.G. An I.V.P. was done in the case with suspected pyelonephritis and a fasting blood sugar in the case with diabetes. Serum electrolyte levels were estimated in three cases which developed signs and symptoms of potassium deficiency while on therapy.

TABLE II

Case	Sex	Age in Years	Aetiology	Retinal grade	Blood Urea in mgm. %	X-Ray Chest	Otherons Investigati
1. M	Male	51	E.H.	Bilateral Cataract	21	Heart size. Top normal	
2. M.B.A·K.	Male	47	E.H·	Normal	47	Heart size. Top normal	
3. Y.S.S.	Female	35	E·H.	Normal	63	Enlargement of left ventricle	
4. L.C.B.	Male	64	E.H.	Grade I	40	Not done	
5. W·K.	Female	34	E.H.	Normal	15	Enlargement of left ventricle	
6. A.A.B.	Male	46	E.H.	Normal	24	Heart size. Top normal	
7. W.W.Y.	Female	51	E.H.	Normal	20	Enlargement of left ventricle	
8. L.A.B.	Female	42	E.H.	Normal	19	Enlargement of left ventricle	
9. L.H.P.	Male	54	E.H. with D.M.	Grade II	26	Normal	Fasting blood sugar 134 mgm. %
10. C.P.Y.	Female	47	E.H.	Normal	18	Enlargement of left ventricle	
11. K	Male	55	E·H.	Grade I	24	Heart size. Top normal	
12. L.A.C.	Male	59	E.H. with EMPHESEMA	Grade I	30	Normal Heart Emphesematous lungs	
13. K.C.K.	Male	27	E.H·	Normal	38	Normal	
14. L.C.L.	Male	64	Hypertension with chronic pyelonephritis	Grade I	28	Enlargement of left ventricle	Microscopic urine alb ++ RBC +++ WBC ++ Few granular casts
15. C.T.H.	Male	47	E.H.	Grade III	21	Heart size Top Normal	

E.H. — ESSENTIAL HYPERTENSION D.M. — DIABETES MELLITIS

Fundal appearances graded according to the system of Keith, Wagener and Barker.

TABLE III

Case No.	Pre-treatment		Post-treatment		Dose	Duration in weeks	Side Effects	Results	Comments
	R	S	R	S					
1.	200/125	195/115	130/80	132/80	1½	15	Giddiness Blurring of vision, Nasal congestion	G	Generally felt well
2.	190/120	170/110	170/110	150/106	1	12	Dryness of mouth Headache Insomnia	P	Felt well. Appetite increased
3.	170/100	140/100	140/90	134/90	1	7	Weakness	P	Symptoms persisted. Electrolyte studies not done.
4.	170/110	140/90	150/78	160/84	1	7	Weakness	G	Electrolytes normal. Felt well
5.	178/110	170/110	144/94	130/90	1½	13	—	S	Poor initial response
6.	194/120	194/134	128/88	128/90	1	11	Faintness	G	Felt faint during 4th week. B.P. was satisfactory 140/90 (s). Headaches less intense
7.	216/118	210/114	158/90	120/76	1	9	Sleepiness Giddiness Weakness	G	Serum Electrolyte showed low K.(3mEq/litre) during 7th week. Given K. Supplements.
8.	180/110	190/116	118/70	84/64	1	8	Faintness	G	Felt faint during 5th week. B.P. was 130/84 (s).
9.	204/106	206/108	130/80	140/85	1½	7	—	G	—

TABLE III (continued)

Case No.	Pre-treatment		Post-treatment		Dose	Duration in weeks	Side Effects	Results	Comments
	R	S	R	S					
10.	180/110	170/105	144/90	130/92	1	10	—	S	—
11.	208/120	170/122	130/90	120/90	1½	6	—	G	—
12.	224/120	210/124	160/95	150/90	1½	5	—	G	Symptoms persisted
13.	180/24	158/116	138/90	130/98	1	9	—	G	Felt well
14.	210/112	120/108	120/90	120/86	1	9	—	S	Felt well
15.	190/118	180/120	150/100	144/104	1	6	Giddiness Sleepiness Weakness Pain in eyes	S	Felt weak during the 6th week. S.K. was 3 mEq/ litre Headaches less often

R — recumbent

S — standing

1 tablet = 2 mgm. Renese + 0.5 mgm. Reserpine.

G — good

S — satisfactory

P — poor

TABLE IV

Pre-Treatment			Post-Treatment			
Recumbent			Recumbent			
No. of Cases	Mean Systolic pressure in mm. of Hg.	Mean Diastolic pressure in mm. of Hg.	Mean Systolic pressure in mm. of Hg.	M.D.P. in mm. of Hg.	M.S. fall	M.D. fall
15	196.3	114.2	142.7	89	52.3	25.2

The general symptoms complained of were headache, giddiness, dyspnoea, blurring of vision, palpitations, swelling of legs and weakness. The general condition of all the patients was satisfactory. Patients were not put on any salt or dietary restriction and were instructed to lead as normal a life as possible. Each case was started off on an initial dose of one tablet. This was increased or decreased by half a tablet at intervals of one week depending on the response shown. The maximum dose used was 1 and a half tablets.

The duration of the trial was 6-15 weeks with an average of 8.9 weeks.

RESULTS

The results were considered good if the diastolic fell by more than 25 mm. of Hg., satisfactory if it fell by 15-25 mm. of Hg. and poor if it fell by less than 15 mm. of Hg. Nine of the cases responded while on a dose of one tablet, six needed one and a half tablets. Ten cases responded within the first week of starting therapy and maintained the good response. The fall in the systolic pressure (recumbent) ranged from 20-90 mm. of Hg. with an average of 52.3 mm. of Hg. The fall in the diastolic pressure (recumbent) ranged from 0-45 mm. of Hg. with an average of 25.2 mm. of Hg. (Table IV). The response was good in nine cases (60%), satisfactory in 4 (26.7%) and poor in two (13.3%). Table III).

SIDE EFFECTS

These were either complained of or were elicited by direct questioning. Eight patients experienced side effects. These were weakness (4 cases), giddiness (3), feeling faint (2), sleepiness (2), blurring of vision (1), pain in the eyes (1), insomnia (1), dryness of mouth (1), nasal congestion (1), headache (1). (Table III). Six had side effects while on one tablet and two while taking one and a half tablets. All the side effects experienced were of a mild nature and did not cause the patients any serious inconvenience.

The two patients who had a feeling of faintness while working had a satisfactory standing blood pressure (Table III). They responded well to bed-rest. The need to stop therapy or reduce the dose did not arise. Serum electrolytes were estimated in three cases that complained of weakness, in two the potassium was low (3 mEq/litre). They were given potassium supplements. Both patients were on one tablet. Generally the patients felt very well and though some still complained of the initial symptoms, these were now milder and less frequent. It is interesting to note that one of the patients who initially had a blood pressure of 230/150 and had in the past been treated with Ismelin, Serpersil and Apresoline without satisfactory response, now had a blood pressure of 130/90 with one and a half tablets of Renese-Reserpine (Case II).

TOLERANCE

This was not noted in any of the cases The duration was short to evaluate this.

DISCUSSION

The value of treating mild to moderate hypertension, especially if this is symptomless is still an open question. It is generally accepted that persistently high blood pressure has harmful effects on the essential organs of the body. The reason for not treating symptomless hypertension of mild to moderate degree is often the lack of a suitable drug. The side effects of most hypotensive agents are sometimes more troublesome than the hypertension itself. Hypertension, or the vasoconstriction, has a morbidity and a mortality. There is a great decrease in morbidity and mortality from effective treatment with a variety of agencies which have it in common that they reduce the blood pressure. 3 (F. Horace Smirk).

Polythiazide with Reserpine as shown above is a useful hypotensive agent for cases of mild to moderate hypertension. A satisfactory fall is achieved within a short period (average 1 week) with a reasonably small dose (1-1 and a half tablets). The pressure is maintained at a satisfactory level in 67% of the cases (10). The side effects are few and tolerable. The side effects of any consequence are potassium loss, which can be corrected with potassium supplements and the feeling of faintness which appears to be of a transient nature responding well to rest. More important is the fact that the average patient feels well and satisfied.

SUMMARY

Fifteen cases were put on Polythiazide-Reserpine for a period of 6-15 weeks. The response was good in nine, satisfactory in four and poor in two. Eight patients experienced side effects. These were few and tolerable. This drug is a useful hypotensive agent for cases of mild and moderate hypertension.

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