

Double-Blind Comparative Trial of Abana and Methyldopa for Monotherapy of Hypertension in Indian Patients

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SUMMARY

Abana is a herbomineral medicinal preparation with a property of down-regulation of beta-adrenergic receptors. A double-blind, parallel group study was conducted in 43 Indian men and women suffering from hypertension to evaluate the antihypertensive effect of Abana and compare it with that of methyldopa (M-DOPA). Twenty one patients received 800 mg tds of Abana and 22 patients received 250 mg tds of M-DOPA for 4 weeks. Blood pressure and pulse rate were recorded at weekly intervals. Relevant clinical and biochemical investigations were carried out before and after treatment.

In patients treated with Abana, there was a significant fall both in systolic B.P. (from 167 ± 3.73 to 145 ± 6.11 mmHg) and in diastolic B.P. (from 110 ± 1.86 to 91 ± 3.04 mmHg) at the end of 4 weeks. Similarly in patients treated with M-DOPA, systolic blood pressure was significantly reduced from 165 ± 4.92 to 146 ± 4.9 mmHg and diastolic blood pressure was reduced from 106 ± 2.74 to 96 ± 2.67 mmHg after 4 weeks. The onset of antihypertensive effect was earlier and there was a higher percentage of responders (80%) in the Abana-treated group. None of the patients had clinically or biochemically significant side effects. The results of this study suggest that therapy with Abana proved highly effective in hypertensive patients.

Additional Indexing Words:

Abana Methyldopa (M-DOPA) Hypertension Monotherapy

In recent years, there has been an alarming increase in cardiovascular diseases in man, so the search for a relatively safe and clinically useful drug is the need of the hour. Abana is a compound preparation of medicinal plants and mineral complexes¹. It contains a number of ingredients described in ancient Ayurvedic literature, having action on the cardiovascular system. Some of the important ingredients are listed in Table I. Experimental and clinical studies have shown that this preparation possesses the property of down-regulation of beta-adrenergic receptors^{2,3}. It has been found to be safe in patients with bronchial asthma (no aggravation of respiratory symptoms) and in diabetic patients (no aggravation of insulin-mediated hypoglycaemia)⁴. A few of the earlier studies have indicated that it has no effect in normotensives but reduces blood pressure in patients with mild or moderate hypertension⁵. These observations prompted us to undertake a double-blind, parallel study to evaluate the effects of Abana in all grades of hypertension and to compare these effects with those of M-DOPA, one of the most widely used antihypertensive agents.

Table I: Composition of Abana Capsule (400 mg)

Terminalia arjuna (Arjun)	30 mg
Withania somnifera (Ashwagandha)	20 mg
Tinospora cordifolia (Giloe)	10 mg
Boerhaavia diffusa (Punarnava)	10 mg
Nardostachys jatamansi (Jatamansi)	10 mg

These ingredients were processed approximately as per Ayurvedic principles by incorporating some other herbomineral ingredients.

MATERIAL AND METHODS

The patients included in the trial were those reporting to the Medical Outpatient Department. They were thoroughly examined for clinical signs and symptoms. Their blood pressure and pulse rates were recorded. Patients with all grades of hypertension, that was either newly detected or resistant to previous drug therapy were informed about the trial and were enrolled after signing a consent form. A chest film, ECG, fundoscopy and serum sodium, potassium, creatinine, cholesterol, SGOT, glucose, haemoglobin, total WBC count and urine analysis were performed.

Patients with satisfactory results for these studies were considered for drug therapy. Patients with recent history of myocardial ischaemia, congestive cardiac failure, left ventricular failure, renal failure or cerebrovascular accidents were excluded from the study.

Forty three patients (aged 35-70 years) were randomized to receive Abana or M-DOPA in the double-blind, parallel group trial. In the beginning, identical placebos were given for 2-3 weeks to wash out previous antihypertensive drugs, if any. Then the patients received either 2,400 mg of Abana or 750 mg of M-DOPA orally daily in 3 equally divided doses for 4 weeks. Selection of doses was on the basis of our clinical practice and doses were adjusted whenever necessary.

Blood pressure and pulse rate were recorded in the supine position by the same doctor at the same time of the day at weekly intervals, using the same sphygmomanometer. The mean of three readings was noted.

At the end of 4 weeks of drug therapy chest X-ray, ECG and laboratory investigations were repeated, drug therapy was tapered off and patients' numbers were decoded. Results are expressed as mean \pm SEM.

A patient was categorized as a 'responder' if his or her diastolic blood pressure at the end of the study period was less than 95 mmHg (accepted by WHO) or if there was a fall of 20 mmHg or more in diastolic blood pressure as compared to the initial value.

For comparison of the antihypertensive activity of these 2 agents, reduction in diastolic B.P. from 0 to 4 weeks was calculated as the area under the curve (AUC) using the trapezoidal rule. For statistical analysis, paired t-test and one-way analysis of variance followed by Duncan's multiple range test, were employed.

RESULTS

All patients completed 4 weeks of drug therapy. On decoding it was found that 21 patients received Abana and 22 patients received M-DOPA. The mean age of patients in the Abana-treated group was 54 years (range, 38 to 67 years) while the mean age of patients receiving M-DOPA was 57 years (range, 35 to 70 years). The age and sex distributions in both groups were similar.

In patients treated with Abana, the initial systolic blood pressure (week 0) was 167 ± 3.73 mmHg and diastolic blood pressure was 110 ± 1.86 mmHg. After 4 weeks of therapy, the respective pressures were reduced to 145 ± 6.11 and 91 ± 3.04 mmHg. A significant fall in both systolic and diastolic B.P. was evident within 1 week; there was a further fall for up to 3 weeks and then it was maintained. The heart rate at week 0 was 92 ± 3 per minute and at the end of 4 weeks of therapy it was 84 ± 4 per minute. Though there was an apparent reduction in the heart rate, it did not reach statistical significance (Fig. 1). In patients treated with M-DOPA over a period of 4 weeks the systolic B.P. was brought down from 165 ± 4.92 (week 0) to 146 ± 4.9 mmHg and diastolic blood pressure was brought down from 106 ± 2.74 (week 0) to 96 ± 2.67 mmHg. In this group, significant falls in both systolic and diastolic B.P. were observed only after 2 weeks and it was maintained thereafter. The heart rate was not significantly affected by treatment with this agent (week 0, 85 ± 2 and at the end of 4 weeks 87 ± 2) (Fig. 2).

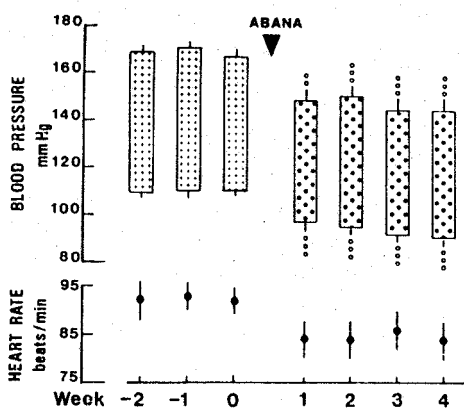


Fig. 1: Effect of Abana (800 mg tds) on blood pressure and heart rate in hypertensive patients (n=21). ∞∞ p<0.005, ∞∞∞ p<0.001.

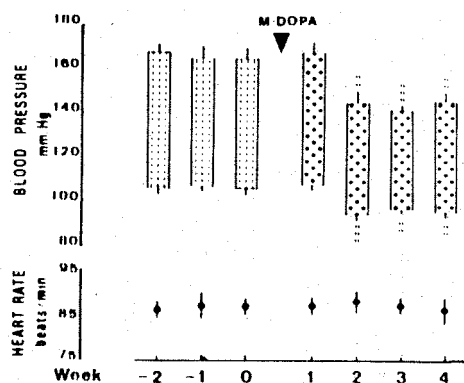


Fig. 2: Effect of M-DOPA (250 mg tds) on blood pressure and heart rate in hypertensive patients (n=22) ∞∞ p<0.005, ∞∞∞ p<0.001.

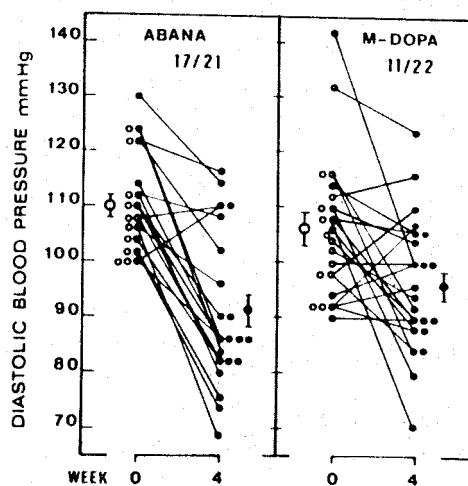


Fig. 3: Diastolic blood pressure changes following treatment with Abana and M-DOPA in individual hypertensive subjects. Abana (n=21) and M-DOPA (n=22).

The extent of the fall in diastolic B.P. in individual subjects treated with these agents is shown in Fig. 3. It was evident in 14 patients treated with Abana that diastolic B.P. was brought down to 95 mmHg or less, while in 3 patients the fall in diastolic B.P. was more than 20 mmHg in the 4-week period. Thus 17 of 21 (nearly 80%) showed a satisfactory response to therapy. Of 22 patients treated with M-DOPA, diastolic blood pressure was brought down to 95 mmHg or less in 10 patients and in 1 patient the fall in diastolic blood pressure was more than 20 mmHg in the 4 week period. Thus 11 of the 22 patients, i.e. 50% showed satisfactory response as judged by the above

mentioned criteria. Though the number of responders to Abana therapy appeared to be higher as compared to those receiving M-DOPA, the difference in response rates was not statistically significant (Chi² value 3.27). However, the fall in diastolic B.P. expressed as AUC (0-4 weeks) was significantly greater with Abana (54 ± 7.7) as compared to M-DOPA (24 ± 7.1).

Since the fall in blood pressure on treatment with Abana was earlier in onset and greater in magnitude as compared to M-DOPA, the effect of withdrawal of Abana after 4 weeks' treatment was studied in a few subjects. Placebo was substituted during this period. Here again, it was observed that there was no rebound hypertension, though the extent of the fall in diastolic B.P. was less (Fig. 4).

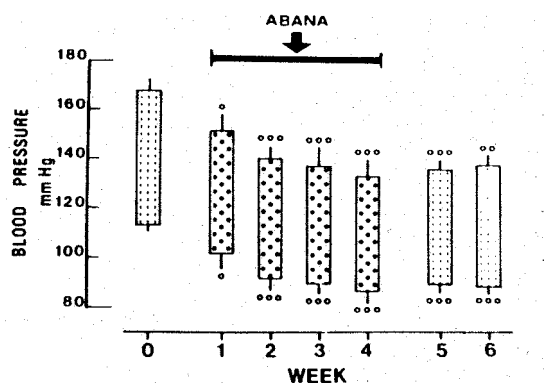


Fig. 4: Effect of discontinuation of Abana (800 mg tds) after 4 weeks of therapy (n=10).
^{oo} $p < 0.005$, ^{ooo} $p < 0.001$.

Regarding side effects, none of the patients complained of giddiness and there was no evidence of skin rash. All biochemical and clinical investigations remained within physiological limits at the end of therapy (Table II).

Table II: Effect of Abana and M-DOPA on Biochemical Parameters, Urinary Electrolytes and Selected Hematological Parameters				
Parameter	Abana		M-DOPA	
	Initial	After 4 weeks	Initial	After 4 weeks
Blood sugar (mg%)	112 ± 4.05	111 ± 4.93	107 ± 3.01	118 ± 5.43
SGOT (units)	12 ± 1.35	14 ± 1.52	16 ± 1.54	14 ± 1.11
Serum Creatinine (mg%)	1.30 ± 0.09	1.50 ± 0.08	1.40 ± 0.07	1.30 ± 0.10
Serum Cholesterol (mg%)	184 ± 7.09	192 ± 9.24	207 ± 11.00	201 ± 10.00
Serum Alk. Phosphatase (K. units)	10.00 ± 0.92	9.30 ± 0.79	8.80 ± 0.90	8.90 ± 0.68
Urine Sodium (meg/lit)	90 ± 11.90	112 ± 9.76	101 ± 6.51	95 ± 8.83
Urine Potassium (meg/lit)	33 ± 5.32	42 ± 4.66	30 ± 3.00	21 ± 2.86
Haemoglobin (g%)	11.70 ± 0.34	12.40 ± 0.33	13.00 ± 0.35	13.00 ± 0.32
WBC (cells/HPF)	6995 ± 473.00	7424 ± 451.00	7518 ± 385.00	6791 ± 336.00

DISCUSSION

In recent times, there has been a renewed interest in herbal remedies and studies have been carried out to establish the clinical efficacy of compound preparations⁶. Abana, as mentioned earlier, is a herbomineral compound preparation⁷. Its property of down-regulation of beta-receptors can protect the heart against sympathetic outbursts^{3,8}. Some of the earlier studies have indicated its efficacy and safety in angina pectoris, sinus tachycardia and ischaemic heart diseases^{7,9}. This trial report highlights the antihypertensive effect of Abana, in comparison with an established and widely used older drug, M-DOPA. Treatment with Abana produced an early, sustained and significant fall, both in systolic and diastolic blood pressure, whereas in patients treated with M-DOPA, fall in blood pressure was seen only at the end of 2 weeks. It was observed that out of 21 patients, only 4 did not

respond to therapy with Abana. Thus, the response rate was 80% as against 50% in M-DOPA-treated patients. In addition, the fall in diastolic blood pressure calculated as area under the curve (AUC 0-4 weeks) was significantly greater in Abana-treated patients and there was no evidence of rebound hypertension on its withdrawal. It is well known that with advancing age, responses to beta-receptors decrease¹⁰. This may cause disturbing features like tachycardia and angina. Abana, by down-regulation of beta-receptors, might be bringing about beneficial effects in a more physiological way.

In conclusion, the results of the present study using Abana in a total dose of 2,400 mg per day and M-DOPA 750 mg/day indicated that the antihypertensive effect of the former agent was better than that of M-DOPA. The patient compliance was good for both agents and there were no appreciable side effects. Abana proved to be an effective and safe drug for the therapy of hypertension in our patients.

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