Medical Memoranda

Comparison of the Effects of Three Rauwolfia Alkaloids in Hypertension

The rauwolfia alkaloid reserpine has been shown to produce a significant fall in blood-pressure in patients with essential hypertension (Cooper and Cranston, 1957). However, reserpine has from time to time produced unpleasant and sometimes severe side-effects, notably depression or frank psychosis (*Brit. med. J.*, 1955). It has been suggested that other rauwolfia alkaloids, such as rescinnamine, have equally satisfactory hypotensive properties, but might not have the side-effects of reserpine (Smirk and McQueen, 1955). For this reason a small controlled trial has been carried out, to compare the hypotensive properties and side-effects of the rauwolfia alkaloids reserpine, rescinnamine, and deserpidine.

METHODS

The series consisted of five men and five women whose ages ranged from 26 to 62, all of whom were thought to have essential hypertension. They all received reserpine, rescinnamine, deserpidine, in doses of 0.5 mg. t.d.s., 0.75 mg. t.d.s., and 1.0 mg. t.d.s., and inert control tablets. The drugs and control tablets were identical, so that neither the patient nor the examiner knew which tablet was being taken, and the drug order was randomized. Each patient was treated for 12 consecutive weeks with each tablet, and attended once weekly, at the same time of day on each occasion. Because the effectiveness of these drugs was uncertain, and because regular attendance over a long period was necessary for the trial, only patients with mild hypertension were included. Blood-pressures were measured by the same person with the same sphygmomanometer each time, in both the lying and the standing position. The readings during the first six weeks of each trial were ignored, so as to exclude errors due to delayed hypotensive action both from overlap from the previous trial and of the drug in use in any one trial period.

None of the patients had any family or personal history of depression, anxiety, or other mental illness, and their nasal airways were not congested at the beginning of the trial. At each attendance they were weighed, and questioned about nasal congestion, tiredness, depression, and appetite. The data for the last six weeks of each period were used for comparison.

RESULTS

Blood-pressure.—For each patient the mean level was calculated with its standard error, for the last six weeks of each period, in the standing and lying positions. The mean levels during the control period and the mean fall in blood-pressure during the second six weeks of treatment with reserpine, rescinnamine, and deserpidine are shown in Table I. Reserpine produced a significant fall in blood-pressure in seven of the patients, and its overall effect was highly significant. The mean fall was $12.08 \pm 2.56/13.33 \pm 2.35$ mm. Hg in the lying, $16.00 \pm 3.34/15.04 \pm 3.43$ mm. Hg in the standing position. Deserpidine produced a significant fall in blood-pressure in five patients. The hypotensive action was less consistent than that of reserpine. The mean fall was $9.59 \pm 5.46/10.93 \pm 3.98$ mm. Hg in the lying, $10.96 \pm 5.93/11.23 \pm 3.10$ mm. Hg in the standing position. The fall in systolic blood-pressure in both positions is not significant. The fall in diastolic pressure is less than that seen with reserpine. Rescinnamine produced a significant fall in blood-pressure in only four patients. The hypotensive action was so marked in these patients that the mean fall for the whole group was $12.73 \pm 4.75/10.27 \pm 2.48$ mm. Hg in the lying, $11.78 \pm 5.50/9.96 \pm 2.53$ mm. Hg in the standing position.

Side-effects.—These were recorded as none, slight, or marked. The only mental changes observed were depression and/or tiredness. The results are summarized in Table II. There is no clear correlation between observed mental changes and nasal congestion. Neither do the side-effects occur only in patients with a significant fall in blood-pressure. The number of patients is small, but it would appear that side-effects occur more often in those treated with reserpine than in those on

TABLE I.—Effect of Three Rauwolfia Alkaloids in Essential Hypertension

No.	Age and Sex	Position	Control	Fall in Blood-pressure		
				Control-Reserpine	Control-Deserpidine	Control-Rescinnamine
5	26 M	Lying	$160.8 \pm 4.73/111.7 \pm 4.01$	$17.3/25.4$	$14.8/19.1$	$5.6/14.0$
		Standing	$165.0 \pm 4.83/115.8 \pm 2.71$	$29.8/26.1$	$25.0/13.8$	$5.3/8.3$
3	57 F	Lying	$151.3 \pm 3.71/83.5 \pm 2.51$	$22.3/10.8$	$7.0/8.0$	$20.6/6.0$
		Standing	$138.5 \pm 3.69/82.7 \pm 1.35$	$6.2/3.6$	$-5.8/+1.4$	$7.6/0$
7	33 M	Lying	$153.8 \pm 7.35/113.3 \pm 4.21$	$23.3/22.2$	$36.3/26.1$	$31.1/18.3$
		Standing	$147.5 \pm 7.16/116.7 \pm 5.1$	$27.3/26.9$	$29.7/28.7$	$22.5/15.0$
6	57 F	Lying	$263.7 \pm 2.74/133.8 \pm 2.46$	$9.7/19.1$	$34.9/21.6$	$44.5/27.1$
		Standing	$249.5 \pm 3.74/130.3 \pm 2.91$	$27.7/28.8$	$46.5/25.0$	$51.2/28.6$
8	62 M	Lying	$188.3 \pm 3.85/102.0 \pm 2.22$	$20.8/13.7$	$0.8/2.5$	$10.3/4.0$
		Standing	$191.5 \pm 7.35/106.0 \pm 3.98$	$21.5/8.2$	$1.5/2.8$	$21.0/9.7$
18	51 M	Lying	$174.8 \pm 3.25/95.4 \pm 5.05$	$3.2/5.4$	$3.6/4.6$	$+0.5/-4.1$
		Standing	$166.0 \pm 5.10/102.4 \pm 2.02$	$4.0/16.4$	$-1.3/+14.2$	$-3.7/+3.2$
13	57 F	Lying	$182.7 \pm 6.49/108.2 \pm 3.75$	$3.9/3.5$	$-5.3/+0.9$	$4.4/5.7$
		Standing	$187.3 \pm 5.55/112.8 \pm 3.35$	$12.3/10.1$	$-2.2/+4.6$	$11.6/5.6$
10	55 F	Lying	$201.8 \pm 5.12/96.0 \pm 2.45$	$10.0/15.7$	$21.3/18.5$	$9.4/10.2$
		Standing	$200.2 \pm 5.89/103.8 \pm 4.20$	$18.0/23.5$	$24.7/15.3$	$6.8/14.4$
12	62 F	Lying	$159.5 \pm 3.97/90.0 \pm 2.56$	$4.0/5.2$	$0.1/3$	$-3.8/+9.0$
		Standing	$156.3 \pm 2.35/86.8 \pm 2.46$	$0/-2.0$	$0.5/3.0$	$-13.5/+5.8$
2	54 M	Lying	$153.0/100.0$	$6.3/12.3$	$-17.5/+6.7$	$4.7/12.5$
		Standing	$154.0/99.0$	$13.2/8.8$	$-9.0/+3.5$	$9.0/9.0$
		Mean lying		$12.08 \pm 2.56/13.33 \pm 2.35$	$9.59 \pm 5.46/10.93 \pm 3.98$	$12.73 \pm 4.75/10.27 \pm 2.48$
		Mean standing		$16.00 \pm 3.34/15.04 \pm 3.43$	$10.96 \pm 5.93/11.23 \pm 3.10$	$11.78 \pm 5.50/9.96 \pm 2.53$

control tablets, and that side-effects occur no more frequently in patients treated with rescinnamine and deserpidine than in those on control tablets.

TABLE II

Drug	Mental Changes, Tiredness, or Depression			Nasal Congestion		
	Marked	Slight	None	Marked	Slight	None
Reserpine ..	2	4	4	3	3	4
Rescinnamine ..	0	1	9	1	3	6
Deserpidine ..	0	4	6	1	3	6
Control ..	1	2	7	1	3	6

TABLE III

Drug	Appetite		Weight		
	Increase	Normal	Increase	Stationary	Loss
Reserpine ..	4	6	3	4	3
Rescinnamine ..	2	8	4	1	5
Deserpidine ..	3	7	3	3	4
Control ..	0	10	4	3	3

Weight and Appetite.—In this series the weight changes were variable, and there was no correlation between the subjective impression of appetite, and weight changes. The results are summarized in Table III. The changes in weight show no striking differences in the four trials, whereas there appears to be a slight subjective feeling of increased appetite when the patients were treated with rauwolfia alkaloids.

COMMENT

The blood-pressure levels were relatively stable in each patient, as shown by the small standard error of the means during each period. Reserpine produced a fall of diastolic blood-pressure in 10 patients in the lying and in nine in the standing position, while it produced a fall in systolic pressure in 10 patients in the lying and in nine in the standing position. Rescinnamine caused a fall in diastolic blood-pressure in nine patients in the lying and in nine in the standing position, while it produced a significant fall in systolic blood-pressure in nine patients in the lying and in seven in the standing position. Deserpidine caused a fall in diastolic blood-pressure in 10 in the lying and in 10 in the standing position, while it produced a fall in systolic pressure in six in the lying and in six in the standing position. This confirms the observation of Cooper and Cranston (1957) that reserpine, in a dose of 0.5 mg. thrice daily, almost invariably, and usually significantly, lowers the blood-pressure. Rescinnamine, in a dose of 0.75 mg. thrice daily, and deserpidine, in a dose of 1 mg. thrice daily, sometimes lower the blood-pressure and on occasion significantly and markedly, but the effect is not predictable.

Though the overall diastolic fall in blood-pressure produced by rescinnamine and deserpidine is very similar and less than that produced by reserpine, the fall in the individual patient varies greatly. The observations on side-effects suggest that they are more likely to occur when the patient is receiving reserpine than when he is being treated with rescinnamine or deserpidine in these doses. In this series none of the three drugs had any consistent effect on the patients' weights.

The conclusion one may draw from the results of this trial is that of the three rauwolfia alkaloids in these doses reserpine is the drug of choice because of its

predictable effect on the blood-pressure. If the side-effects from reserpine are troublesome, it is worth trying the effect of rescinnamine or deserpidine, which may produce a satisfactory fall in blood-pressure even though the effectiveness of the drug in the individual patient cannot be predicted but must be discovered by trial and error.

SUMMARY

The effects on the blood-pressure of the three rauwolfia alkaloids—reserpine, rescinnamine, and deserpidine—have been compared in a small controlled trial of 10 patients with essential hypertension. The side-effects of the three drugs were observed.

Reserpine, in a dose of 0.5 mg. thrice daily, produced a predictable fall of blood-pressure in all the patients. Rescinnamine in a dose of 0.75 mg. thrice daily, and deserpidine in a dose of 1 mg. thrice daily, produced a significant fall of blood-pressure in some patients, but this effect was not predictable. Reserpine appears to produce side-effects more often than rescinnamine and deserpidine.

Of the three alkaloids, reserpine is the drug of choice, but if the side-effects are troublesome it is worth trying rescinnamine or deserpidine, which may produce a substantial but not predictable fall in blood-pressure.

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"[It was at one time the custom in the Western Province of Tanganyika to treat] the young victims of smallpox by hyperextension and traction of both elbows and also sometimes of both ankles until they 'cracked.' The object of this painful procedure was to 'bring out the rash' satisfactorily and so to safeguard the life of the patient. Last year, when visiting one of the mission bedded dispensaries, the nursing sister asked me to see a case of smallpox in a small boy. She was puzzled because the patient, who was by now recovering from the smallpox, had fracture dislocation of both elbows. The parents told me rather shamefacedly that the child's grandparents had taken charge of the patient and had insisted on applying the old treatment. I was reminded again of this barbarous custom a few weeks ago. A very old African woman was admitted with pneumonia, and while feeling for her wrist under the blanket to take her pulse I found she could not extend the arm, which was ankylosed at the elbow at about a right angle. When I asked her the reason for the deformity she whispered 'smallpox'; and her deeply pock-marked face showed that without doubt she had at some time suffered from severe smallpox. The custom of treating smallpox in this way is fortunately disappearing and may not be known to many medical practitioners, but it is recorded as a matter of interest." (Dr. A. J. Keevill in *East African Medical Journal*, October, 1960.)