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DIETARY SALT REDUCTION POTENTIATES THE ACTION OF HYPOTENSIVE DRUGS

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ABSTRACT

Hypertension is a common health problem. Hypotensive drugs and low salt diet are used in its treatment. This study was designed to compare the effectiveness of a low-salt diet and drug therapy in the treatment of arterial hypertension. A total of 256 randomly selected patients with essential hypertension consulting the Non-contagious Diseases Clinic in Shahreza, Isfahan, Iran, were included in the study for a period of 28 days. They were divided into four groups. Groups A and B received both methyldopa (250 mg t.i.d.) and hydrochlorothiazide (daily 10 mg), the former consuming a normal and the second a low-salt diet. Groups C and D consumed a low-salt and a salt-free diet, respectively, with no drugs. Both treatments A and B caused statistically significant reductions in blood pressure even after seven days, but treatment B was much more effective. Reductions in blood pressure in Groups C and D were very little, even after 28 days. Using the three-way classification of analysis of variance, it was revealed that interactions existed among the three factors, i.e., age, diet and length of treatment, as regards lowering blood pressure. We conclude, confirming previous reports in the literature, that a low-salt diet potentiates the hypotensive action of antihypertensive drugs.
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INTRODUCTION

Hypertension is a common health problem. There is a large number of antihypertensive drugs with different mechanisms of action which are commonly used to alleviate the condition. In addition to taking drugs, patients are advised in many cases to reduce their dietary salt intake as well, since salt reduction may potentiate the action of anti-hypertensive drugs.[1,2] However, there is some disagreement as to whether or not such salt reduction is effective and should be recommended in all cases. One reason for this is that the direct relationship observed between salt intake and blood pressure is based essentially on results of epidemiological studies,[3] which may not show the complete picture. For example, it is possible that in a particular country or community where hypertension is widespread, factors other than a high salt diet play the major role in the etiology of the disease, such as genetic or ethnic factors, subclinical renal impairment or activity of counter-regulatory mechanism.[4-8]

At any rate, the potential blood pressure lowering of a low-salt diet used as an adjunct to drug therapy has received much attention. The purpose of this study was to compare the effectiveness of diet therapy (reducing dietary salt) and drug therapy with and without salt reduction in the treatment of hypertension.

PATIENTS AND METHODS

Subjects

A total of 256 randomly selected patients with essential hypertension consulting the Non-contagious Diseases Clinic of Sahebazzaman Hospital in Shahreza, Isfahan, Iran, were included in the study. The number

Table I. Treatment groups, diets and drugs

Groups \ Treatments	Diet	Drugs*
A	Normal	Methyldopa + hydrochlorothiazide
B	Low-salt	Methyldopa + hydrochlorothiazide
C	Low-salt	Normal
D	Salt-free	Normal

*Daily doses : Methyldopa, 3 × 250 mg; hydrochlorothiazide, 1× 10 mg.

54 in each of the four treatment groups (A, B, C and D; see Table I) was calculated based on confidence limits of 95%, a precision of 8% and a 10% probability of finding hypertensive patients among those coming to the Clinic. In each group, the 54 patients were divided into two sex subgroups of 27 each, further subdivided into three equal age subgroups of 41-50 years and 61-70 years old.

Treatments

Table I shows the types of diets and drugs used. Before starting the study the patients were interviewed, the purpose of the study explained to them and the dietary and drug instructions given to them. The duration of the study was 28 days. Every day the patients would come to the clinic at 8 A.M., and were allowed to rest for 15-20 minutes and their blood pressure measured by several experienced technicians, using a sphygmomanometer. The mean of three measurements in either of the arms (maximum and minimum B. P.) was recorded. The drugs used were hydrochlorothiazide (a diuretic) and methyldopa, which is an antihypertensive drug acting through α– and β- adrenergic receptors.

Data analysis

Differences between blood pressure on day 1 and day 7,14, 21, or 28 were compared using the student's paired t-test. To find any interactions between any two or all the three factors--age, diet and length of treatment-use was made of the three-way classification analysis of variance.

RESULTS AND DISCUSSION

It is evident from Table II that both treatments A (normal diet + drugs) and B (low-salt diet + drugs) lowered the minimum B.P. significantly after seven days although to different extents. This shows that although drugs alone are effective, if dietary salt is reduced too, the magnitude of the reduction is greatly increased (it almost triples from 4.5% to 12.1%). In both groups A and B, the minimum B.P. continued to decrease after day seven, the decrease being more rapid in the case of group B (see Fig. 1). Erwteman, et al.[2] and Weinberger, et al.[9,10] have also reported that salt reduction potentiates the effect of hypotensive drugs.

The reduction in minimum B.P. brought about by a low-salt diet alone or by a salt-free diet was very little

Table II. Effect of diet with and without drugs on minimum blood pressure (mm Hg)

GROUP*	Day 1 blood pressure			Reduction, compared with Day 1					
	Day 1	Day S**	Day 28	Day S**			Day 28		
	X ± SD	X ± SD	X ± SD	Magnitude	%	P<	Magnitude	%	P<
A	98.8 ± 15.0	94.4 ± 14.6 (Day 7)	90.1 ± 14.4	4.4	4.55	0.005	8.7	8.8	0.005
B	104.6 ± 16.7	91.4 ± 14.1 (Day 7)	79.1 ± 16.4	13.2	12.1	0.005	25.4	24.2	0.005
C	90.6 ± 3.5	88.7 ± 4.0 (Day 28)	88.7 ± 4.0	1.9	2.1	0.005	Day 28 - Day S		-
D	94.5 ± 2.6	93.0 ± 3.8 (Day 28)	93.0 ± 3.8	1.5	1.6	0.005	Day 28 - Day S		-

*Group A: normal diet + drugs; B: low-salt diet + drugs; C: low-salt diet, no drugs; salt-free diet, no drugs.
**When a significant difference, as compared with Day 1, first appeared.

even after 28 days (treatments C and D, Table II). This should not be surprising, since it has been shown by Holden, et al.[11] that salt reduction has no clinically significant effect in people as a whole, although some other workers generally favour such reduction.

It is also possible that the response of the type of hypertension, i.e., whether it is essential or secondary, to the salt level of the diet be different; in the present study all the patients were suffering from the former type. This is an area for further research.

The general picture in the case of maximum B.P. was the same as that for minimum B.P. (Table III): treatment B was much more effective than treatment A. However, while the minimum B.P. reductions were statistically significant even after seven days, significant reductions in maximum B.P. started to appear after a longer lapse of time--on day 21 (treatment A, 4.9%) and on day 14 (treatment B, 9.4%). As in the case of minimum B.P., treatments C and D caused small, although statistically significant, reductions in the maximum B.P., i.e., 2.9% and 4.0%, respectively, after four weeks. Apparently in some hypertensive patients, the blood pressure is "sodium-sensitive" and in others "sodium-non-sensitive".[6] Probably in the present study, at least some of the patients in Groups C and D belonged to the latter category.

Diet type and sex

From Table IV it is seen that as regards diet, the calculated F for the maximum B.P. for men is greater than

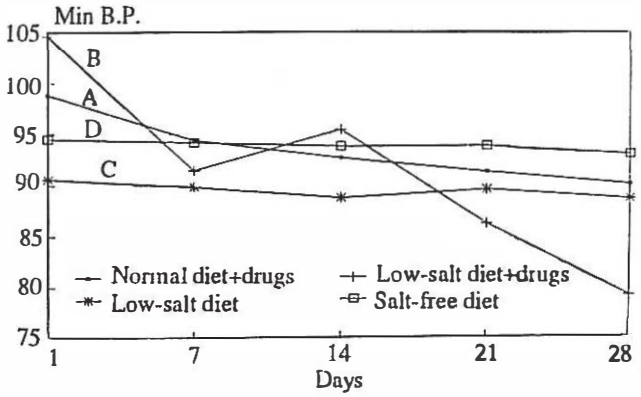

Fig. 1. Effect of different treatments on the minimum blood pressure of the patients.

that for women (270.03 vs 195.72), which indicates that diet is more effective in men than in women. On the other hand, diet can be more effective in reducing the minimum B.P. in women, the calculated F's being 30.02 and 21.45 for women and men, respectively. The reason for this difference is not known; whether it is a real sex difference or it is due to some environmental factor(s), remains to be elucidated.

Combined effects of age, diet and length of treatment

Table IV shows the combined effects of factors influencing blood pressure in men and women, using the

Table III. Effect of diet with and without drugs on maximum blood pressure (mm Hg)

GROUP*	MAXIMUM BLOOD PRESSURE			REDUCTION, COMPARED WITH DAY 1					
	Day 1	Day S**	Day 28	Day S**			Day 28		
	X ± SD	X ± SD	X ± SD	Magnitude	%	P<	Magnitude	%	P<
A	188.2 ± 13.6	178.8 ± 18.8 (Day 21)	175.9 ± 16.8	9.31	4.9	0.005	12.3	6.5	0.005
B	187.6 ± 13.7	169.9 ± 10.8 (Day 14)	154.7 ± 18.2	17.62	9.4	0.005	32.8	17.8	0.005
C	162.7 ± 3.7	161.7 ± 3.9 (Day 14)	159.9 ± 1.7	0.7	4.8	0.05	4.8	2.9	0.005
D	163.7 ± 3.5	162.1 ± 3.4 (Day 14)	157.1 ±	1.6	1.00	0.05	6.6	4.0	0.005

*Group A: normal diet + drugs; B: low-salt diet + drugs; C: low-salt diet, no drugs; D: salt-free diet, no drugs.
**When a significant difference, as compared with Day 1, first appeared.

Table IV. Interaction among factors affecting pressure in men and women (three-way classification analysis of variance)

Parameter / Sex group / Variation			MINIMUM BLOOD PRESSURE				MAXIMUM BLOOD PRESSURE			
			Men		Women		Men		Women	
Source of Varation	df[a,b]	Table F[a]	Calculated F	P<	Calculated F	P<	Calculated F	P<	Calculated F	P<
No. of Days (d)	4	4.62	30.23	0.001	71.27	0.001	49.02	0.001	23.01	0.001
Age in Years (a)	2	6.91	149.66	0.001	7.35	0.001	8.06	0.001	12.54	0.001
Diet (dt)	3	5.42	21.45	0.001	30.02	0.001	270.03	0.001	195.72	0.001
d×a	8	3.27	1.32	NS[c]	0.83	0.05	0.53	NS[c]	0.12	NS[c]
d×dt	12	2.74	18.17	0.001	30.34	0.001	17.56	0.001	12.27	0.001
a×dt	6	3.09	3.09	0.001	12.59	0.001	16.52	0.001	3.90	0.001
d×a×dt	24	2.13	3.85	0.001	4.07	0.001	5.03	0.001	432.31	0.001

a-Since the number of patients was the same in all groups and subgroups, the respective df's and Table F's were the same in all cases
b- Residual = 480; Total = 539 c- Non-significant

three-way classification analysis of variance. While each one of the three factors alone was effective in lowering both the minimum and maximum B.P. in both men and women, there was no interaction between the number of days of treatment and age. There were, however, interactions between the number of days and diet, age and diet, as well as among all the three factors in both sexes.

These findings suggest that when designing a study to study blood pressure changes by diet and /or drugs, all the three factors discussed should be taken into consideration, which will have implications from a clinical point of view as well.

Implications

Reduction of dietary salt potentiates the hypotensive effect of drugs in hypertensive patients. A low-salt or salt-free diet alone has very little effect. In making dietary recommendations, however, one must consider all aspects of the matter. Two points are worth considering: (1) the fact that some investigators have found beneficial effects of reducing dietary salt, and (2) that salt reduction may actually have different effects in normal subjects from those in hypertensive patients. At the present state of knowledge, we favour the recommendation that people should generally reduce their salt intake.

It was also found in this study that several factors may interact in producing reductions in the blood pressure of hypertensive patients being treated by diet and/or drugs; namely age, diet, diet, and length of treatment. This has obvious implications both in designing studies of this type and in clinical and dietetic practice.

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