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A NEW PHYSIOLOGICAL APPROACH TO CONTROL ESSENTIAL HYPERTENSION

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Abstract : This study was conducted on 20 male patients of Essential Hypertension (EH) in order to explore the possible role of baroreflex mechanism in the etiology of EH and also to find out whether by restoration of baroreflex sensitivity to normal level either by postural tilt stimulus on a tilt table or by the equivalent yogic postural exercise (Yogic asanas), the EH could be cured or controlled. Patients on therapeutic regime were gradually withdrawn from drug therapy, and later divided into two groups of 10 each. Group–I (age 34 ± 1.7 years) was subjected to a 3 week course of 70° head-up tilt for 30 min daily, while in group–II (age 50 ± 3.3 years), specific yogic exercises equivalent to head-up or head-down tilt were administered for the same duration. The progressive autonomic re-adjustments were assessed by a battery of tests including cardiovascular responses to head up tilt, cold pressor response at 4°C water (CPR), alpha index of EEG (AI), level of blood catecholamines (CA) and plasma renin activity (PRA). At the end of 3 weeks, there was a significant reduction ($P < 0.001$) in blood pressure in both the groups. Progressive changes in BP and HR response to tilt during 3 weeks course of tilt and yogic exercise clearly indicated gradual improvement in baroreflex sensitivity. Likewise, changes in other indices like CPR, AI, CA and PRA indicated progressive attenuation of sypatho-adrenal and renin-angiotensin activity. All these changes together with the reduction in BP strongly suggest a close link between the etiology of EH and baroreflexes on the one hand and controlling influence of the latter on sympatho-adrenal and renin-angiotensin systems on the other. It also throws light on the physiological mechanism underlying the effects of selected yogic exercises in the treatment of EH.

Key words : orthostatic stimulus, baroreflex, sympathetics, yogic exercises, catecholamines, renin, electrolytes

INTRODUCTION

Inspite of great efforts spread over several decades, the etiology of Essential Hypertension (EH) continues to be an enigma both to the clinicians and the physiologists alike. Opinions are divided on the issue between the protagonists of an

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unitarian model and those in favour of its multifactorial origin. In a review of the physiological aspects of EH, Folkow has suggested three major, strongly dependent causative elements in EH, viz, a polygenetically transferred predisposition, environmental factors and early structural adaptation of heart and blood vessels. In general, the treatment of EH has primarily been directed towards the effector limb of vasomotor control i.e. the sympatho-adrenal axis, and to a lesser extent on the corticohypothalamo-limbic system, or the removal of etiological factor/factors. Considerable efforts in evaluating the role of baroreflex mechanism in the etiology of EH have established the existence of a diminished baroreflex sensitivity in patients of EH (2, 3, 4). Earlier preliminary studies of Sinha had demonstrated the blood pressure (BP) lowering effect in EH patients (6, 7). However, the mechanisms underlying these findings had not been clearly established and remained speculative. Therefore, in the present study, the emphasis has been on the objective assessment of the status of baroreflex sensitivity in patients of EH, and to find out whether by restoration (if possible to do so) of the sensitivity of baroreflex mechanism using the orthostatic tilt method or by equivalent yogic postural exercise, the BP can be controlled without the aid of drugs.

METHODS

Subjects

Twenty male patients of Indian Army with uncomplicated Essential Hypertension (EH) of atleast two to five years duration, volunteered to be the subjects of the study. All subjects had elevations of systolic blood pressure (BP) to a level higher than 140 mm Hg and diastolic BP above 90 mm Hg. All of them were subjected to a complete clinical and medical screening in order to exclude any known cause of secondary hypertension such as primary aldosteronism, renovascular hypertension, pheochromocytoma or Cushing's disease etc. Clinical laboratory investigations included routine blood and urine analysis and culture, ECG, chest X–ray, 24 hr urinary catecholamines and serum sodium and other electrolytes, rapid sequence of IVP and renal angiogram, when necessary. Patients with complications like congestive heart failure, malignant hypertension and with evidence of primary parenchymal kidney disease were excluded. Only clinically established uncomplicated cases of EH were included in the study.

Protocol

Subjects were divided into two groups of 10 each agewise. The physical characteristics of the subjects are shown in Table I. Informed consent of the subjects was obtained. The younger age group (I) was subjected to a 30 min tilt course at 70° head–up tilt on a tilt table daily for 3 weeks (8) while the older age group (II) was subjected to a 3 week course of certain specific yogic postural exercises (Yoga asanas) which are equivalent to head-up or head-down tilt.

Following is the list of asanas selected for the study: Yoga Mudra, Ardha Halasana, Sarvangasana, Pavanamukhtasana, Bhujangasana, Dhanurasana, Chakrasana

and Savasana (9). These patients were on drug therapy, for a varying period, prior to the commencement of the study: the treatment consisted of alpha methly DOPA (Aldomet) and furosemide (Lasix) either alone or in combination. Before the commencement of study, all the drugs were withdrawn gradually, with an inevitable rise in BP which stabilised at a higher level within two weeks. After the completion of the basal recordings, tilt course and yogic exercises programme commenced. Subjects were kept under the direct supervision of a Medical Specialist in a hospital ward and remained almost sedentary (with only routine physical activity) throughout the period of the study. They were maintained on a constant 100 mEq sodium and 80 mEq potassium daily intake for one week prior to and during the course of the study. They were also briefed about the experimental procedures and their consent was obtained before the commencement of the study, which ensured full cooperation of the subjects.

Several physiological and biochemical parameters were monitored prior to and periodically during the 3 week course in both the groups. Baroreflex sensitivity was indirectly assessed by monitoring heart rate (HR) from ECG in lead II position, blood pressure (BP) using a precalibrated Accosan sphygmomanometer and cardiac output (CO) by the impedance plethysmograph (Bionics) during 30 min of orthostatic tilt at 70° on a tilt table. Audiomonitoring of HR was continuously done on a Grass–model AM 7 audiomonitor to assess the symptoms of syncope, alongwith the periodical monitoring of BP. The status of autonomic balance was measured by a battery of tests consisting of cold pressor response (CPR) at 4°C water (10), alpha index (AI) OF EEG (11), HR, BP, CO and Plasma and urinary catecholamines. Methods employed for the biochemical estimations are described below.

Collection of blood samples

20 ml of blood was collected in supine position in two prechilled dry glass tubes kept in ice, one containing disodium EDTA salt for plasma renin activity (PRA) and the other heparinised tube for the catecholamines and electrolyte estimations, prior to the commencement of the tilt or yoga course on the 11th and 22nd day of the course. Blood was immediately centrifuged in cold, and the plasma was used for biochemical estimations.

Determination of plasma renin activity

Plasma renin activity was measured as the amount of angiotensin–I generated per ml of plasma per hour at physiological temperature (37°C) by the method of Menkard and Catt (12), using the kit supplied by the Bhabha Atomic Research Centre (Bombay).

Estimation of catecholamines and electrolytes

Norepinephrine and Epinephrine in plasma were estimated by fluorometric method of Diamant and Byers (13). Total catecholamine excretion was estimated from 24 hour urine sample preserved with hydrochloric acid by the method of Sobel and Henry (14). Plasma level of sodium and potassium and their 24 hr urinary excretion were estimated by flame photometry.

At the end of the 3 week course, subjective reactions of the patients to the treatment were also assessed by a questionnaire. Statistical analysis of the data was done by paired and unpaired t–test.

RESULTS

Blood pressure

Blood pressure (BP) recorded in supine position after 15 min of complete rest, showed a gradual and significant decline ($P < 0.001$) from the 9th day of the course in tilt group and from 5th day onwards in yoga group (Fig. 1). The drop was observed in both systolic and diastolic BP in both groups. At the end of the course BP returned to near normal level. The decrease in BP showed a significant correlation with the number of days of the course. For example, in tilt group, regression equation for systolic BP was

$y = - 0.9627 x + 147.9948$, $r = - 0.9498$ and for diastolic BP it was

$y = - 0.9577 x + 105.7377$, $r = -0.9462$

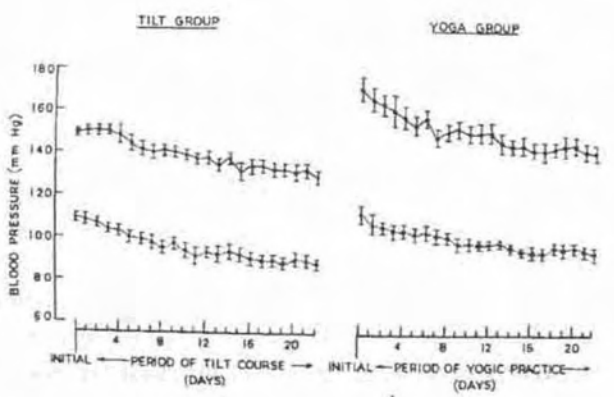

Fig. 1 : Progressive changes in blood pressure during 3 week course of tilt or yoga.

Similar trend was noticed in yoga group also (Fig. 1)

Baroreflex sensitivity

The baroreflex sensitivity was indirectly assessed from the cardiovascular responses to orthostasis on a tilt table. Figure 2 shows the typical pattern of cardioacceleration

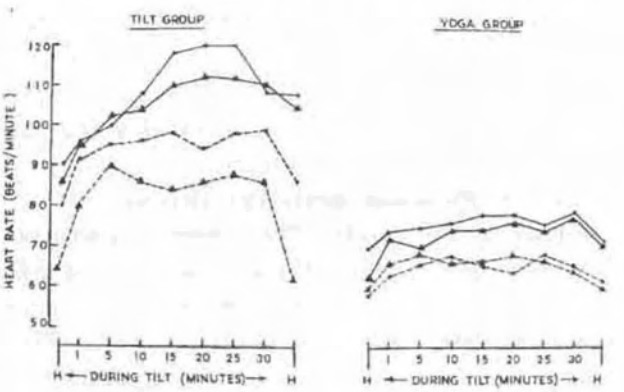

Fig. 2 : Heart Rate response to orthostasis in tilt group and yoga recorded prior to the commencement of the course (●—●), and on 8th day (▲—▲), 15th day (●.....●) and 22nd day (▲.....▲) of the course.

response during 70° head – up tilt observed in two subjects, representing one in each group, at weekly intervals during the course. High resting HR gradually decreased during the progress of the course of treatment. Initially there was a sluggish HR response to orthostasis as observed from the rate and magnitude of cardioacceleration during the first five min of tilt, prior to the commencement of the treatment. At the end of 3 week course, this response was relatively sharper in tilt group. However, in yoga group (older age group of subjects), HR response to tilt showed only a little variation after the course. There was a marked drop in cardiac output (CO) during

30 min of tilt in both the groups, prior to the treatment (Fig. 3). At the end of 3 weeks course, this drop was minimal and relatively higher CO was maintained throughout the tilt as compared to the initial response pattern. The systolic BP variations in the same two subjects were almost similar (Fig. 4). The response pattern observed prior to the treatment in tilt group was a sudden drop which got corrected only by 15th min whereas yoga group took a longer time for restoration of systolic BP to pre tilt values.

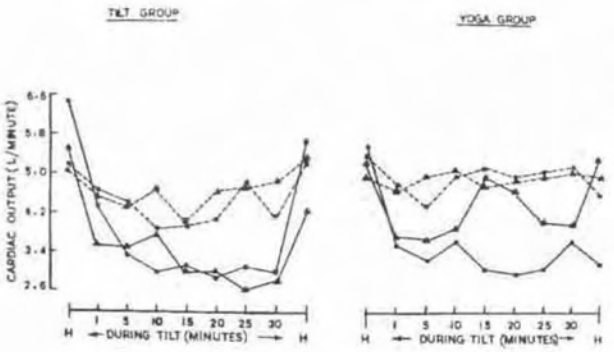

Fig. 3 : Changes in cardiac output response to orthostasis during 3 week course. Initial (●—●) on day 8: (▲—▲) on day 15 (●.....●) and on day 22 (▲.....▲)

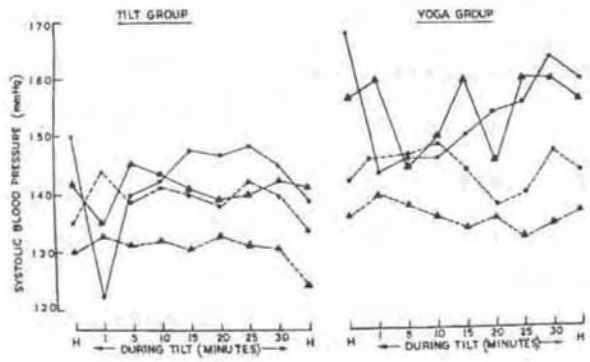

Fig. 4 : Systolic BP during 30 min of orthostasis in both the groups recorded at weekly intervals. Initial (●—●); on day 8 (▲—▲) ; on day 15 (●.....●); and on day 22 (▲.....▲) during the course.

After the three weeks course, the observed initial drop in systolic BP got corrected in both the groups. In other words after 3 weeks course BP was maintained with minor fluctuation at the pre-tilt level during the 30 min of tilt.

Diastolic BP showed some interesting response pattern (Fig. 5). Patients, prior to the course, showed increase in diastolic BP only after 5 min of orthostasis, and there was an exaggerated rise after 15 min of tilt. But at the end of 3 weeks course, both tilt and yoga groups showed optimal increase in diastolic BP within 5 min of orthostasis and this increase was maintained throughout 30 min of tilt without appreciable changes.

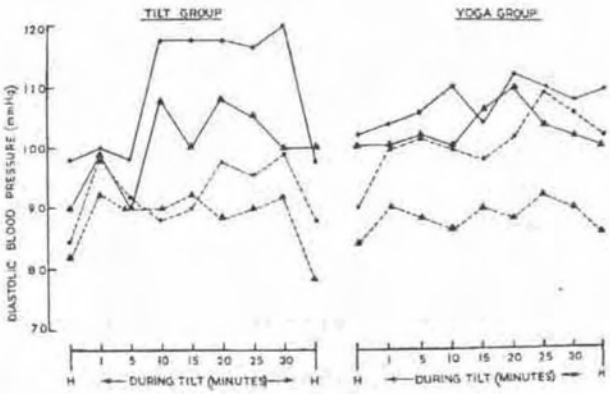

Fig. 5: Diastolic BP response during 30 min of orthostasis in tilt and yoga groups recorded at weekly intervals. Initial (●—●); on day – 8 (▲—▲); on day – 15 (●.....●); and on day –22 (▲.....▲) during the course.

About 70% of the patients showed signs and symptoms of syncope during the later part of 30 min tilt, prior to the commencement of the treatment. These reactions were completely absent after 3 weeks course in both the groups.

TABLE I : Physical characteristics of the subjects.

Group	*Age (yr)*	*BW (kg)*	*HT (cm)*	*BSA (m^2)*
Tilt	33.6 ± 1.7	65.0± 2.9	167.1 ± 2.1	1.73±0.04
Yoga	49.8 ± 3.3	65.1±2.6	167.8 ± 1.7	1.74±0.07

Values are means ± SEM

Autonomic response

Resting HR, CO, BP, cold pressor response (increase in BP during immersion of hand in cold water at 4°C for 2 min) blood norepinephrine and epinephrine showed a significant decrease, while alpha index of

TABLE II : Autonomic responses in tilt and yoga groups before and after 3 weeks course.

Parameters	*Tilt Group*		*Yoga group*	
	Before	*After*	*Before*	*After*
Heart rate (bpm)	75±2.8	66 ± 1.7*	74 ± 3.5	67± 3.4**
Blood pressure (mmHg)				
(Systolic)	149±2.0	128 ± 2.8***	171 ± 6.1	142± 2.5***
(Diastolic)	109±1.5	88 ± 1.8***	112 ± 4.0	95± 2.6***
Cold pressor response (mmHg)				
systolic	35±4.3	23 ± 1.9*	34 ± 3.1	22± 2.0***
Diastolic	28±1.6	20 ± 1.7**	27 ± 1.3	18± 2.2**
Cardiac output (L/Min)	5.78±0.05	5.12 ± 0.27	5.40 ± 0.27	5.29± 0.36
Alpha index (%)	21±2.9	37 ± 4.4***	22 ± 2.5	39± 4.2***

Values are means ± S.E.M. *P < 0.05; **P < 0.01; ***P < 0.00

TABLE III : Changes in biochemical profile in blood and urine.

Parameter	*Tilt group*			*Yoga group*		
	Initial	*Day -11*	*Day -22*	*Initial*	*Day -11*	*Day -22*
Blood Nor-Epinephrine (ng/ml)	1.41 ± 0.11	1.23 ± 0.12**	0.83± 0.08***	1.15 ± 0.06	0.92 ± 0.05***	0.70 ±0.06***
Epinephrine (ng/ml/h)	1.15 ± 0.07	0.72 ± 0.12*	0.48± 0.08***	0.91 ± 0.04	0.63 ± 0.05***	0.45 ±0.07***
Renin activity (ng/ml/h)	5.72 ± 0.50	4.76 ± 0.34**	3.99± 0.28**	5.51 ± 0.44	4.81 ± 0.31**	4.19 ±0.22**
Sodium (mEq/L)	143.5 ± 0.10	142.5 ± 0.10	142.0± 0.09	143.6 ± 0.06	142.0 ± 0.03	140.5 ±0.04*
Potassium (mEq/L)	4.40 ± 0.10	4.32 ± 0.10	4.13± 0.09	4.64 ± 0.06	4.48 ± 0.03	4.38 ±0.04*
Urine Volume (ml/24h)	1652 ± 171.1	1594 ± 196.5	1491± 135.7	2148 ± 123.4	2083 ± 102.9	2079 ±144.3
Catecholamine (mg/24h)	148 ± 35.2	116 ± 12.1	96± 2.9*	130 ± 8.6	116 ± 5.2**	112 ±4.0**
Sodium (mEq/24h)	148 ± 30.0	135 ± 16.0	122± 12.1	138 ± 4.5	126 ± 4.2**	113 ±2.2**
Potassium (mEq/24h)	26.2 ± 1.33	23.4 ± 1.86	22.4± 1.47*	58.9 ± 1.62	49.0 ± 2.44*	46.3 ±3.08**

Values are means ± S.E.M. *P < 0.05; **P <0.01; ***P < 0.001.

EEG ($P_3 - 0_1$) showed an increase after 3 weeks course in both the course (Table II and III).

Biochemical changes : Plasma renin activity (PRA) significantly decreased ($P < 0.01$) in both the groups at the end of the course (Table III). PRA level in the patients of this study were in the normal range but on the higher side, prior to treatment. Plasma sodium and potassium, and their 24 hr urinary excretion did not show any significant difference at the end of the course in tilt group, while in yoga group plasma level of these electrolytes and their urinary excretion were lower.

DISCUSSION

The present study was initiated on the hypothesis that sustained high BP in EH patients is basically due to a sluggish baroreflex mechanism which in turn leads to several physiological and biochemical changes, thus creating a vicious cycle of interrelated chain reactions which finally puts a seal of `permanency`. If the sensitivity of baroreflex mechanism can be restored by some means (if possible to do so), BP can be restored to normalcy. The present study provides evidence in support of this hypothesis.

Patients of EH are reported to possess diminished baroreflex sensitivity (2, 3, 4). Our study lends support to this view, as evidenced from the sluggish cardiovascular responses to orthostasis (Figs. 2–5) prior to the course. BP lowering effect of the tilt course was observed in the earlier study of Sinha (5), however, it had been conducted on a few patients without elucidating the mechanism underlying this effect. The present study confirms his findings and also illustrates the physiological and biochemical responses associated with this responses.

BP gradually started to decline from day–9 onwards from the commencement of the tilt course and reached near normal level at the end of 3 week (Fig. 1). After the termination of the course, BP started rising again after a week. As it is rather difficult to use a tilt table at home, it was thought that some easy to practice specific yogic postural exercises (Yoga asanas) equivalent to head-up or head-down tilt may prove to be a better substitute for tilt table. So a parallel study on both the methods was initiated.

Yoga group had significantly higher ($P < 0.001$) initial BP (prior to treatment) than that of the tilt group. Nevertheless, they showed comparable degree of reduction in BP after 3 weeks course. A significant fall in BP could be observed in yoga group even from 5th day of the course. In this respect, yoga exercises proved to be more effective than tilt table.

It may be noted that in the present study, the elderly group was subjected to yoga course while the younger group to orthostatic stimulus (tilt course) more as a precautionary measure against occurrence of orthostatic syncope more common in elderly people due to diminished baroreflex sensitivity (15, 16). There is a lag in the recovery of HR response during orthostasis even after 3 weeks of yoga course (Fig. 2) however, the cardiac output was maintained at slightly higher level during tilt after 3 week course (Fig. 3) perhaps due

to the starling`s effect. The main reason for choosing the head-up tilt or asanas as a method of treatment is based on the concept that it may be possible to reactivate the sluggish baroreflex mechanism by subjecting it to sudden and sustained (for a brief period) stimuli of higher or lower magnitude than it is normally used to. By repetition of this process, it may be possible to restore the sensitivity of baroreflex and reverse the sequence of chain reaction which ultimately lead to permanency of high BP.

The present study shows that by repetition of such process for 3 weeks it is possible to restore the normal sensitivity of baroreflex mechanism (Figs. 2–5) as seen in both the groups. Once its sensitivity is restored, it does the needful to restore the `health` of the autonomic vasomotor control system. Even some of the anti- hypertensive drugs such as clonidine and propranolol are reported to bring about their anti-hypertensive effects by increasing the sensitivity of baroreflex either centrally or peripherally (16).

The interactions between the baroreceptor mechanism, the sympathetics, vasopressin and renin in the maintenance of BP has recently been demonstrated (17) in normal individuals. Present study also illustrates the close relationship between the baroreceptor mechanism and the other neurohumoral components of BP regulation (18, 19) and suggests an unifying role of baroreceptor mechanism in the etiology of EH. Once the sensitivity of baroreceptor mechanism is restored, it corrects all other neurohumoral malfunctioning, as observed from the reduction in sympathetic activity (Table II), plasma catecholamines, renin activity to optimal level (Table III) after 3 weeks of tilt or yoga course.

There is already an emphatic claim by the protagonists of yoga therapy that some specific yogic exercises could be of therapeutic value in the treatment of hypertension. Some of the scientific studies have offered support to their claim (6, 7, 20) however, the mechanism underlying these beneficial effects have remained rather speculative. Our recent studies on the effects of six months of yogic practice on autonomic responses, show a trend of reduction in sympathetic activity after six months of regular practice even in normal individual (21). In patients of EH, in addition to restoring the normal baroreflex sensitivity, yogic exercises are seen to relieve the stress induced sympathetic hyperactivity thereby restoring the BP to normal level even in elderly patients with long history of EH.

Isometric exercises are reported to elicit certain beneficial effects on carotid baroreflex system in hypertensive patients (22). Yogic exercises are not purely isometric in nature. The asanas selected for the present investigation are mostly postural exercises in which either head-up or head-down tilt are involved. Hence, the involvement of stimulation of vestibular cerebellar system in the BP lowering response of yogic exercise cannot be ruled out as the vestibular cerebellum is known to play an important role in cardiovascular control (23).

The present study demonstrates that the sluggish baroreflex mechanism observed in patients of EH can be reactivated by a 3

week course of orthostatic tilt or selected yogic postural exercises thereby restoring BP to normal level. It also points to a close link between the baroreceptor mechanism, sympathetic activity and renin mechanisms suggesting an unifying role of baroreceptor mechanism in the etilogy of Essential Hypertension.

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