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AUTONOMIC FUNCTIONS IN BUERGER'S DISEASE

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Abstract : One of the pathophysiological features in Buerger's disease, i.e. thromboangitis obliterans (TAO), is vasospastic phenomena. So autonomic reactivity was evaluated in 12 patients of Buerger's disease (1–6 years duration) and compared to age and sex matched controls (nonsmokers). Basal heart rate was significantly (P<0.001) higher without any variation in blood pressure in TAO group compared to controls. Valsalva ratio (P<0.01) and 30:15 ratio (P<0.001) were increased without any effect on E:I ratio in TAO group versus controls. On head up tilt (HUT), there was significant (P<0.001) fall in blood pressure in TAO group compared to controls. On cold pressure test (CPT), systolic blood pressure was reduced significantly (P<0.01) in TAO group than that of controls, however, diastolic blood pressure showed no change in two groups. Responses indicate towards lower sympathetic reactivity in Buerger's patients.

Key words : thromboangitis obliterans cold pressure test vasospasm head up tilt valsalva

INTRODUCTION

The etiology of Buerger's disease, i.e. thromboangitis obliterans (TAO), is yet unknown except that smoking has a close relation with exacerbation and remission of the disease. One of the pathophysiologic features in this disease is vasospasm (1). Vasospastic features in Buerger's disease lead to Raynaud's phenomenon (2). In these vasospastic phenomenon, a high sympathetic response is assumed to contribute (3). Sympathectomy for the treatment of Buerger's disease is clinically effective for skin symptoms e.g. coldness, rest pain and ischaemic ulcer. But the role of sympathetic nervous system remains unclear (4).

So the purpose of the present study was to evaluate autonomic reactivity in patients of Buerger's disease.

METHODS

The present study was carried out in 12 patients having 1–6 years history of Buerger's disease with mean age of

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32.16 ± 6.84 years. These patients (Thromboangitis obliterans-TAO group) has following criteria i.e. smokers, symptoms occurring before the age of 40 years, Phlebitis migrans and absence of arteriosclerotic risk factors (Table I). No patient underwent lumbar sympathectomy. None of the patients had history suggestive of diabetes, atherosclerosis, hypercholesterolemia. Femoral arteriogram was recorded for evaluation of condition of vessels. Patient's symptoms were gangrene of toes in 7 cases, rest pain in toes in 2 cases, coldness and pallor of toes in 3 cases. Results were compared with 12 male controls with a mean age of 33.28 ± 2.87 years.

Both the groups (TAO group and control group) underwent a battery of following tests :–

(i) *Breathing test*: Subjects were instructed to take deep breath, each of 10 sec (5). The expiration: inspiration ratio (E:I ratio) and difference in heart rate during inspiration and expiration were calculated.

$$\text{E:I ratio} = \frac{\text{Maximum R – R interval during expiration}}{\text{Minimum R – R interval during inspiration}}$$

(ii) *Vaslsalva monoeuvre:* Valsalva manoeuvre was carried out in the subjects by expiring forcefully in a closed tube to raise and maintain a pressure of 40 mmHg for 15 seconds. Due care was taken to prevent deep breathing before and after the release of strain (6). Valsalva ratio (7) was calculated using the following formula :–

$$\text{Valsalva ratio} = \frac{\text{Longest R – R interval after manoeuvre (phase IV)}}{\text{Shortest R – R interval during manoeuvre (phase II)}}$$

(iii) *Heart rate response to standing (30:15 ratio)*: Ratio of longest R-R interval about 30th beat after standing from supine position to shortest R-R interval about 15th beat after standing.

(iv) *Head up tilt test (HUT 70°)*: Subjects were made to lie down on tilt table. From lying position (0°) subjects were tilted to 70° head up tilt position. The speed of tilting was 5°/sec. Blood pressure and heart rate were recorded in lying position and immediately on HUT.

(v) *Hand Grip Test (Isometric exercise)*: This is a sympathetic test. The patients were asked to grip the dynamometer with their dominant hand at 30% of their maximum voluntary capacity. The blood pressure and heart rate were taken just before the release of hand grip.

(vi) *Cold Pressure Test (CPT)*: CPT was evaluated by immersion of subject's left hand (upto wrist) in cold water at 8°C for 2 min. in recumbent state. Blood pressure and heart rate were measured 1 min. after immersion of hand and on removal of hand.

A continuous recording of electrocardiogram (EKG) (Lead II) was taken on polyrite (INCO) and measurements were performed manually to calculate heart rate. Blood pressure was recorded by auscultation and standard sphygmomanometer. Tests were performed

in same order with sufficient rest between tests to allow heart rate and blood pressure to return to stable base line. Statistical analysis was done using unpaired 't' test.

RESULT

Basal heart rate was significantly higher (P<0.001) without any variation in blood pressure in TAO group compared to controls. There was significant increase in parasympathetic tests i.e. in valsalva ratio (P<0.01) and 30:15 ratio (P<0.001) without any variation in E:I ratio TAO group versus controls. Tests reflecting sympathic activity i.e. diastolic blood pressure response to hand grip showed insignificant change between two groups. On HUT, there was significant (P<0.001) fall in blood pressure (systolic/diastolic) in TAO group versus controls. On CPT, systolic blood pressure was decreased significantly (P<0.01) in TAO group compared to controls, without any effect on diastolic blood pressure in two groups. Although, blood pressure (both systolic/diastolic) raised from basal level in both the groups, more so, in control group (systolic 12.10%/diastolic 16.25% in controls and systolic 9.25%/diastolic 12.68% in TAO group). On removal of hand from cold water, blood pressure decreased immediately in TAO from cold water, blood pressures decreased immediately in TAO group (Table II).

TABLE I: Anthropometric data of TAO group and control group.

	Age	*Sex*	*Smoking*	*Height*	*Weight*	*Duration of disease*
Control group	33.28±2.87 years	M	–	5.5±.14"	47.33±3.29kg	–
TAO group	32.16±6.84 years	M	+	5.59±.12"	48.10±2.31kg	1–6 years

Case no. (TAO group)	*Smoking*	*Phlebitis migrans*	*Involvement of upper extremity*	*Presence of pulse in lower limbs*			*Leg involved*
				Fm	*P*	*DP*	
1	+	+	+	+	–	–	Right
2	+	–	–	+	+	–	Left
3	+	–	–	+	+	–	Right
4	+	+	–	+	+	F	Right
5	+	–	–	+	+	F	Left
6	+	–	–	+	+	F	Right
7	+	+	–	+	–	–	Right
8	+	–	–	+	–	–	Left
9.	+	–	–	+	–	–	Right
10	+	–	–	+	+	F	Left
11	+	–	–	+	+	F	Left
12	+	–	–	+	–	–	Right

Fm = Femoral; P = popliteal; DP = Dorsalis Pedis
F = Feeble

TABLE II: Parameters recorded in TAO group and control group (mean ± SD).

Parameter	*Control group*	*TAO group*	*p value*
1. Basal HR (beats/min)	78.73±13.88	95.74±5.48	<0.001
2. Blood pressure			
Systolic (mmHg)	115.63±12.17	107.77±9.71	p<0.05
Diastolic (mmHg)	71.72±6.78	74.44±11.30	NS
3. E:I ratio	1.33±0.04	1.36±0.03	NS
4. Valsalva ratio	1.61±0.66	2.01±0.39	<0.01
5. 30:15 ratio	1.8±0.34	1.24±0.14	<0.001
6. BP response to hand grip:			
Systolic (mmHg)	108±9.64	110.86±13.72	NS
Diastolic (mmHg)	71±6.84	71.95±10.60	NS
7. HUT (70°): BP			
Systolic (mmHg)	104.25±17.17	88.51±10.65	<0.001
Diastolic (mmHg)	66.60±10.04	58.08±8.07	<0.001
8. CPT:			
On immersion of hand in cold water (8°c)			
Systolic BP (mmHg)	129.63±8.17	118.17±7.72	<0.01
Diastolic BP (mmHg)	84.54±7.95	83.88±11.99	NS
On removal of hand from cold water			
Systolic BP (mmHg)	122.72±11.09	95.83±20.30	<0.001
Diastolic BP (mmHg)	80.72±7.44	71.57±10.44	<0.001

HR: Heart rate; BP: Blood pressure, CPT: Cold pressure test
HUT: Head up tilt, P<0.001–highly significant,
P<0.01–Significant, NS–Non significant

DISCUSSION

Unknown etiology of Buerger's disease is associated with vasopastic phenomenon. Measurement of valsalva ratio and 30:15 ratio showed, involvement of parasympathetic system. The blood pressure response to HUT and CPT reflects lower sympathetic reactivity. Orban et al (8) gave a hypothesis of adenosympathetic over activity and attempted adrenalectomy. Some authors have reported increased level of urinary catecholamines in patients of Buerger's disease (9). However Kulin et al (10) and Tokats (11) revealed that adrenalectomy and sympathectomy did not alter the course of Buerger's disease. So adrenosympathetic overactivity does not seem to be an etiologic factor (11). Sympathetic nervous system 'hypoactivity' is reported earlier in patients of Raynaud's phenomenon (12). Yamamoto et al (13) demonstrated lowered level of muscle sympathetic activity in patient of Buerger's disease, which he suggested could be the reason, to maintain blood flow in muscles of ischaemic limb. He also demonstrated that there was no significant difference in blood pressure elevation to local cold application in patients of Buerger's disease

compared to controls (13). Similarly in the present study, blood pressure response to CPT and HUT have also confirmed the same. Still exact role of sympathetic nervous system remains unclear (4). Recently, altered adrenoreceptor activity (14), an elevation of alpha$_2$ receptor sites, receptor hypersensitivity theories have been forwarded as possible mechanism of Raynaud's syndrome (15). To clarify this contradication, a further study on large number of patients of Buerger's disease is necessary.

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