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Original Article

Cardiovascular Autonomic Response During a Cold Pressor Test in Overweight Individuals

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Abstract:

Background: Body mass has been associated with changes in the cardiac autonomic activity and potential risk factor for cardiovascular morbidity and mortality. The cold pressor test considered to be a sympatho-excitatory manoeuver is a simple, non invasive and validated test of sympathetic activation. **Objectives:** The objective of this study was to assess the cardiovascular response to cold pressor test in normal weight and overweight healthy individuals. **Methods**: This cross sectional analytical study was conducted from July 2017 to June 2018 in the Department of Physiology, Rangpur Medical College, Rangpur. After obtaining permission the subjects who would meet the inclusions and exclusions criteria were enrolled in the study after briefing them about objectives. A total number of 80 age, sex matched individuals were selected, among them 40 were apparently healthy normal weight individuals (group A) and 40 were apparently healthy overweight individuals (group B). The blood pressure responses could be used as a tools for cold pressor test which is indicators of sympathetic activation and thus, of cardiac status. The subjects were selected from different areas of Rangpur division. For statistical analysis, unpaired't' test was performed by computer based software SPSS 23.0 version for windows. **Results:** Results showed that in resting condition the mean systolic blood pressure was significantly ($p<0.05$) higher but mean diastolic blood pressure was higher but non significant ($p>0.05$) in overweight individuals than normal weight individuals. After cold pressor test the mean change of both systolic and diastolic blood pressures were significantly lower ($p<0.05$) in overweight individuals as compared to control group. **Conclusion:** The study concluded that the change in systolic and diastolic blood pressures after cold pressor test was decreasing with increase body mass index and thus indicating impaired sympathetic activity in healthy overweight individuals.

Key words: Overweight, Body mass index, Cold pressor test, Sympathetic nervous system

Introduction:

Worldwide the incidence of overweight and obesity is increasing at a faster rate.In Bangladesh, 7% adults were overweight or obese in 1980 but those rates had claimed to 17% in 2013[1]. The imbalance between energy consumption and energy expenditure causes overweight and obesity. When a person's body mass index (BMI) is above the normal range but below the threshold for obesity, he or she termed as overweight. People who are overweight today will become obese if they are not aware of the consequences of inappropriate weight gain. This is mainly due to stress, sedentary life style and increased intake of high calorie food[2].

Mortality rates increase with increasing degrees of overweight[3]. According to World health organization (WHO) the most commonly used indicator of general adiposity is "Body mass index (BMI)" measured in kg/m^2. A BMI of 20-25 kg/m^2 is considered as normal. If it is between 25-29.9kg/m^2 is termed as overweight. If it is more than 30 kg/m^2 then it is referred as obese[4]. The world health organization recommends the cut off values for the definitions of overweight

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and obesity should be lower for Asian populations as follows[5];

Normal weight	Overweight	Obese
BMI 18.5 to 22.9 kg/m^2	BMI 23 to 24.9 kg/m^2	BMI ≥ 25 kg/m^2
WC: Male<90 cm Female<80 cm	WC: Male ≥ 90cm Female<80cm	WC: Male≥ 94 cm Female<88 cm

The autonomic nervous system is the part of the nervous system that is responsible for regulation and integration of internal organs functioning[6]. As energy metabolism as well as regulation of cardiovascular system is influenced by sympathetic nervous system, so overweight and its clinical consequences may be promoted by altered Autonomic nervous system (ANS). Stimuli that raise blood pressure (BP) activate sympathetic outflow and are a reflection of sympathetic activity[7].

Augmented sympathetic reactivity may be one possible mechanism underlying the increased risk of developing hypertension and cardiovascular disease in overweight individuals[8]. So investigations of autonomic nerve functions in overweight individuals, for detection of early autonomic impairment can be potentially important to prevent complications[9]. Several test are used for evaluation of the cardiovascular reflexes triggered by performing specific provocative manoeuvers[6]. A commonly used technique to rapidly elicit a stress reaction is cold Pressor Test (CPT).

Cold pressor response is an indicator of sympathetic activity after cold stress. Cold stress causes massive discharge of the sympathetic nervous system and release of norepinephrine. This sympathetic discharge triggers responses in the cardiovascular (CV) system that includes arteriolar constriction, increased HR, and increased cardiac contractility. These responses combine to increase BP. This is known as the pressor response, and testing a subject with cold stress in this fashion is known as the cold pressor test.

In overweight individuals initially sympathetic stimulation occur to reduce body weight (catabolic effect). That causes an increase in vasomotor tone and cardiac output. So the final result is increase in basal systolic and diastolic blood pressure in overweight adults. But beyond equilibrium, sympathetic nervous system cannot act to reduce body weight. This causes sympathetic insufficiency in overweight adults that makes them pre-hypertensive. Cold pressor test is an indicator of vasomotor tone[3]. The cold pressor test in healthy subjects triggers a vascular sympathetic activation and increase in blood pressure[10]. The lesser increase in systolic and diastolic pressure during cold pressor test from its basal value in overweight group in compare to control group suggest sympathetic insufficiency[3]. This finding strongly indicates that overweight individuals as an at-risk population[11].

As body mass index increases, modifications in autonomic nervous system found, characterized by a reduction in sympathetic activity[3]. These abnormalities in autonomic responses during stress may precede the development of overt clinical disease in overweight individuals[11]. Therefore the CPT may be a reliable, clinically useful adjunct to predict the future risk cardiovascular complications[10].

Methods:

This is cross-sectional analytical study was conducted in the Department of Physiology, Rangpur Medical College, Rangpur from July 2017 to June 2018. A total number of 80 apparently healthy subjects, aged 20-40 years were included in this study from different community of Rangpur division. Before perform the cold pressor tests and collection of sample all the subjects were briefed about the objectives of the study. Informed written consent of the study subjects were taken in easily understandable Bengali phrases. A standard questionnaire was filled up after taking history and thorough clinical examinations.

All the study subjects were divided into two groups on the basis of their body mass index,among them 40 normal weight individuals was denoted as group A and 40 overweight individuals was denoted as group B. They were matched with age, sex and socioeconomic condition.Study was carried out with prior protocol approved by the thesis protocol review committee and ethical committee of Rangpur Medical College. Obese and history of Diabetes mellitus, Chronic renal failure, Hypertension, Cardiac complication, Chronic obstructive lung diseases, Smoking and alcohol abuse,Any Neurological disorder, Psychiatric disorders

(Depression) taking any neurotoxic drug, Endocrine disorders (thyroid, adrenal etc) and Previous history of head injury were taken as exclusion criteria.

For calculation of BMI weight in Kg and height in m^2 of each subjects was taken by medical weighing machine and measuring tape respectively for measuring waist circumference (WC).

From the previous night up to the examination, they should not undergo any physical or mental stress and not to take any sedatives or any drugs affecting central nervous system. Then the autonomic nerve function parameters were assessed by cardiac reflex tests using sphygmomanometer. Cold pressor tests were conducted in a comfortable environment in the departmental physiology laboratory from 9.00am - 2.30pm.

Resting blood pressure[12]:
The subjects were asked to take rest for 10 minutes in supine position. The resting blood pressure (BP) was recorded in supine position using mercury sphygmomanometer and expressed in mmHg. Three readings were taken and the average of the three was taken as the resting blood pressure.

Cold Pressor Test[4,13]:
After recording basal blood pressure, subjects were asked to immerse left hand (up to 2 inches proximal to wrist crease) in the cold water for 2 minutes and temperature was maintained at 4-6^oC throughout the procedure. Blood pressure measurement was made from right arm at pain threshold time, which is defined as time between immersion of hand and subjective feeling of pain. Maximum increase systolic and diastolic pressure was recorded. A rise of diastolic pressure ≥10 mm of Hg and increase in the systolic pressure 10-20 mm of Hg was taken as normal response and less than this considered as abnormal.

All data were recorded systematically in a preformed history sheet and all statistical analysis was done by computer using the software SPSS 23.0 version for windows. Comparison between the experimental groups (overweight) with control group (normal weight) was done by unpaired 't' test. In the interpretation of results, <0.05 level of probability (p) was accepted as significance.

Results:
The mean ± SD of age were 29.1500 ± 6.33489 years in group A and 30.7 ± 7.63 years in group B. The mean ± SD of height was 1.62± 0.12 m in group A & 1.65 ± 0.09 m in group B and the mean ± SD of weight was 56.15 ± 8.53 kg in group A, 63.07 ± 8.08 kg in group B. The mean ± SD of BMI were 21.39 ± 0.95 kg/m^2 in group A, 23.63 ± 0.54 kg/m^2 in group B. The mean ± SD of WC were 71.82 ± 6.55 cm in group A, 86.7 ± 5.22 cm in group B. The age and height were statistically non significant between the groups but weight, BMI and WC were very highly significant in group B than group A (Table I).

Table I: Showing mean ± SD of age, height, weight, WC and BMI of the study subjects in group A and group B.

Parameters	Mean ± SD		't' value	P value
	Group A	Group B		
Age-years	29.15±6.33	30.7±7.63	-989	86^{NS}
Height-m^2	1.61±0.12	1.65±0.09	-1.45	21^{NS}
Weight- kg	56.15±8.53	63.06±8.08	-3.72	.001**
BMI-kg/m^2	21.39±0.95	23.63±0.54	-2.91	.000***
WC-cm	71.82±6.55	86.7± 5.22	-1.23	.000***

The mean ±SD of resting systolic blood pressure were 114.75 ± 10.19mm of Hg in group A and 120.5 ±9.32 mm of Hg in group B.The mean systolic blood pressures were significantly (p <0.05) higher in group B than group A.

The mean ±SD of resting diastolic blood pressure were 72.5 ± 7.84 mm of Hg in group A and 74.38 ±8.41 mm of Hg in group B. The mean diastolic blood pressures were nonsignificantly (p<0.05) higher in group B than group A (Table II).

TableII: Showing mean ± SD of resting systolic and diastolic blood pressure of the study subjects in group A and group B.

Variables	Mean ± SD		't' value	P value
	Group A	Group B		
Resting systolic blood pressure (mm of Hg)	114.75± 10.19	120.5 ± 9.32	-2.63	.027*
Resting diastolic blood pressure (mm of Hg)	72.5 ±7.84	74.38 ± 8.41	-1.03	.560^{NS}

The mean ± SD of systolic blood pressure after cold pressor test were 13.75 ± 3.94 and 10.38 ± 6.48 in group A and B.In systolic blood pressure changes, the mean values were significantly (p <0.05) lower in group B than group A.

The mean ± SD of diastolic blood pressure after cold pressor test were 14.25 ± 7.56 and 9.88 ± 7.29 in group A and B. In diastolic blood pressure changes, the mean values were significantly (p <0.05) lower in group B than group A (Table III).

Table III: Showing mean ± SD of systolic and diastolic blood pressure of the study subjects in group A and group B after cold pressor test.

Variables	Mean ± SD		't' value	P value
	Group A	Group B		
Systolic blood pressure (mm of Hg)	13.750± 3.94	10.38 ± 6.48	2.81	.018*
Diastolic blood pressure (mm of Hg)	14.25 ± 7.56	9.88 ± 7.29	2.63	.027*

Discussion:

The result of the present study shows that, the mean change in systolic blood pressure before and after CPT was statistically significant, and mean change in diastolic blood pressure after CPT was statistically significant in the study group as compared to control group. It indicates as body mass increases, change in the blood pressure response is decreasing, so overweight group is less responsive to blood pressure changes to acute cold stimulus than the normal weight group. The impaired CPT in the overweight group could possibly because of hypofunctional sympathetic nervous system. The results of the study correlate with observations made by other authors[4,9,14-16].

The cold pressor test (CPT) elicits the pressure response to a cold stimulus and is an indicator of vasoconstrictor tone. The response of blood pressure to cold pressor test is characteristics for the individual. With increase in body mass index impairment of autonomic control of heart rate and blood pressure was found, so overweight subjects exhibit lower sympathetic response on exposure to cold[9]. The afferent fiber for this response are the pain fibers which are stimulated by placing the hand in cold water and the efferent fibers are the sympathetic fibers. Hence, a lesser increase in the blood pressure after the cold water immersion points towards sympathetic insufficiency in overweight adults[15].

Sympathetic nervous system is a determinant of energy expenditure[16]. The lower sympathetic activity is related to lower energy expenditure and consequently to a positive energy balance and increase of body weight. Decrease in the sympathetic activity may result in a disordered homeostatic mechanism thus promoting excessive storage of energy[9].

Cold pressor test provokes a remarkable increase in sympathetic reactivity in humans mediated by central command and local metabolites particularly adenosine[12]. The vasopressor response to locally applied cold was due to an increase in the total peripheral resistance as a result of vasoconstriction and that the cardiac output did not change. In normal condition sympathetic activity increases during cold pressor test. This reduced sympathetic reactivity in established overweight may be responsible for the maintenance of overweight state[9].

Therefore, CPT, being a reliable, non-invasive and simple screening tool in early diagnosis of autonomic cardiac dysfunction, may prove an

important aid in identification of those prone to weight gain and are at higher risk of cardiovascular complications. Weight loss following low calorie diet can cause improvement in autonomic function as is demonstrated by a study in which there was improvement in blood pressure to stress test as cold pressor test[17].

Conclusion:

Overweight individuals have altered cardiac autonomic function with reduced sympathetic activity. Autonomic instability enhanced basal vasoconstrictor tone and pressor response to applied acute cold stimulus could make these overweight subjects prone to hypertension and other cardiovascular disorders later in life. Thus CPT could be employed as a mode of screening for those prone to overweight, allowing for early interventional programmes (lifestyle and dietary modifications) in order to prevent the onset of overweight related cardiovascular sequelae in future. However, study with larger sample including both sexes from different rigions of Bangladesh is recommended to extrapolate the results of cardiac autonomic responses in prehypertensives.

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