JK SCIENCE pISSN: 0972-1177

ORIGINAL ARTICLE

Assessment of Autonomic Functions in Obese Adults

Gurmeet Kaur, Sandeep Kaur, Sunil Sachdev

Abstract

Background: Association between obesity and dysregulation of autonomic functions has long been established and is believed to be the cause of increased risk of cardiovascular morbidity and mortality. Furthermore, early detection of impaired autonomic functions and hence timely intervention can prevent many of the obesity-related cardiovascular complications. ***Purpose:*** The present study was carried out with the aim of assessing the relationship between autonomic dysfunction and obesity in adults using autonomic function tests as diagnostic tools. ***Material and Methods:*** This cross-sectional study involved 200 subjects, divided into two groups (n=100 each) on the basis of Body Mass Index (BMI) into control (non-obese) and study (obese) groups. The autonomic functions were assessed by six autonomic function tests: Orthostatic Tolerance Test, Cold Pressor Test, Handgrip Test, Standing to Lying Down Ratio (S/L Ratio), Heart rate response to postural change (30:15 ratio) and Heart rate response to Valsalva manoeuvre. ***Results:*** There was statistically significant decrease in both the sympathetic and parasympathetic activity in the obese adults. ***Conclusion:*** The present study suggests that there is impaired functioning of autonomic nervous system in otherwise healthy obese adults.

Key Words

Obesity, Autonomic function tests, Body mass index, Autonomic Dysfunction

Introduction

Obesity has become a major public health challenge. The worldwide prevalence of obesity has nearly doubled in the past decade and its incidence is still rising rapidly in many countries, leading the World Health Organization to coin the word 'globesity' to describe the worldwide situation (1).

Physiologically, obesity is an excess of body fat resulting in weight gain (2). Body Mass Index (BMI) provides the most useful population level measure of obesity as it is the same for both sexes and for all ages of adults. BMI is calculated as weight (kgms) divided by the square of height in meters. (kg/m^2 - Quetelet's Equation) (3).

Weight of an individual depends on the balance between one's energy intake and energy expenditure. The autonomic nervous system (ANS) plays a major role in the integrated regulation of food intake, involving satiety signals and energy expenditure; thus, ANS dysregulation could be the factor favouring body weight gain. ANS dysfunction has a two-way relationship with obesity; alterations of the ANS might be involved in the pathogenesis of obesity whereas on the other hand the excess weight induces ANS dysfunction (4). The altered function of ANS in obesity consequently leads to cardiovascular disorders. Hence the study of ANS function in obesity is of considerable clinical interest (5).

Obesity and more specifically visceral obesity has been found to be strongly associated with hypertension and

Department of Physiology, Government Medical College, Jammu, Jammu and Kashmir, India

Correspondence to: Dr. Gurmeet Kaur, Assistant Professor, Department of Physiology, Government Medical College, Jammu (J&K)

Manuscript Received: 28 May 2020; **Revision Accepted**: 05 August 2020;

Published Online First: 15 March 2021

Open Access at: https://www.jkscience.org/

Cite this article as: Kaur G, Kaur S, Sachdev S. Assessment of autonomic functions in obese adults. JK Science 2021;23(1):33-37.

increased cardiovascular risk (6). Disturbed sympathetic nerve function may be of significance in obesity (7). SNS is the primary regulator of cardiovascular system activity; obesity might trigger alteration in the sympathetic regulation of cardiovascular function, thus favouring the development of cardiovascular complications and morbidity (3).

The link between obesity and cardiac autonomic dysfunction highlights the significance of adopting lifestyle interventions including diet and physical activity to reverse and prevent the cardiac autonomic neuropathies. Significant improvement has been reported in cardiac autonomic modulation after a weight loss of 10% (8). The present study was carried out with the aim of assessing the association between obesity and autonomic nervous system in our local adult population.

Materials and Methods

This study was carried out in the Department of Physiology, Government Medical College, Jammu. A total of 200 healthy subjects in the age group of 18-40 years of both sexes were selected from different areas of Jammu city. Voluntary participants were preferred for the study. The aim of the study and tests were explained to each subject in detail and informed consent was taken. Approval from Institutional Ethical Committee was obtained.

Detailed medical history and family history was taken. A thorough clinical examination was done to rule out any co-morbidity. All relevant information was recorded in a preformed questionnaire. Height and weight of the subjects was recorded and BMI was calculated according to Quetelet's equation. Autonomic function tests were then conducted in a comfortable environment in the Departmental Physiology Laboratory from September 2018 to November 2018.

Inclusion Criteria: 18-40 years of age group of both sexes, healthy individuals.

Exclusion Criteria: Cardiovascular diseases, any respiratory illness, hypertension, diabetes mellitus, any psychiatric disorder or history of drugs which could alter ANS function.

Total subjects taken 200; were divided into two groups based on their BMI as follows: (9)

BMI 18.5 – 24.9 – Non-Obese / Control Group

BMI ≥ 25 – Obese / Study Group

Blood Pressure recordings were done with the Mercury Sphygmomanometer by auscultatory method. The ECG recordings were taken with simple compact electrocardiograph (CARDIOMIN); it incorporates an electronic 12 lead selector with push switches, which advances and reverses leads in quick succession. All the ECG readings were carried out with Lead –II. The subjects were asked to take rest and relax for ten minutes upon arrival. Following autonomic function tests were done in both the groups (10,11).

Tests to Assess Sympathetic Activity:

1. Orthostatic Tolerance Test (OTT) - Blood Pressure response to standing: After recording BP in the supine position, the subject was made to stand up immediately (within 3 seconds) and remain still. Blood pressure was then recorded after 30 seconds. The change in Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) in response to change in position from supine to standing position was calculated. Normally ≤10mmHg; Borderline: 11-20 mmHg; Abnormal ≥30mmHg.

2. Cold Pressor Test (CPT): The baseline BP was recorded after giving rest to the subject for 10 minutes. Then the dominant hand of subject was immersed in cold water at a temperature of 4-6^{0}C, up to the wrist joint. Blood pressure was recorded in the contralateral arm at pain threshold time (which is defined as a time between immersion of hand and subjective feeling of pain). After taking out the hand, blood pressure was recorded after every one minute, till it returns to the baseline. The maximum increase in SBP and DBP above the base level was taken as a measure of the size of the cold pressor response. A rise of DBP >15mmHg was taken as normal and less than this was considered as abnormal.

3. Hand Grip Dynamometer Test (HGT) - Blood Pressure response to sustained handgrip: After recording the baseline BP, the subject was asked to perform maximum grip of handgrip dynamometer with his/her dominant hand and the maximum capacity was noted down. Then he/she was asked to maintain handgrip with 30% of the maximum capacity for 5 minutes. The BP was recorded just after the release of the grip. Difference in SBP and DBP before and after sustained handgrip was calculated. Normal ≥16mmHg; Borderline: 11-15 mmHg; Abnormal <10mmHg.

Tests to Assess Parasympathetic Activity:

1. Standing to Lying Ratio (S/L Ratio): The subject was asked to stand quietly for two minutes and then lie down. ECG was recorded from 20 beats before to 60 beats after lying down. The point at which subject started

to lie down was marked. S/L ratio was calculated as the ratio of the longest R-R interval during the 5 beats before lying down to the shortest R-R interval during 10 beats after lying down. Normal >1 and <1 is abnormal.

2. Heart Rate Response to Immediate Standing (30:15 Ratio): The subject was given a rest for 15 minutes in the supine position then asked to stand up from the supine position as quickly as possible. The ratio of 30:15 was calculated by taking ratio of the longest R-R interval at beat 30 and the shortest R-R interval at beat 15 after standing up. Normal ≥1.04; Borderline: 1.01 - 1.04; Abnormal ≤1.00.

3. Valsalva Ratio (Heart Rate response to Valsalva manoeuvre): The subject was asked to blow into a mouthpiece attached to a sphygmomanometer against 40mmHg for 15 seconds. ECG was recorded during the manoeuvre (strain period 15 sec) and for 30 seconds more after the manoeuvre. Valsalva ratio was calculated as ratio of longest R-R interval after manoeuvre to shortest R-R interval during strain. Normal: ≥1.21; Abnormal ≤1.20.

Statistical Analysis

Statistical analysis was performed by the SPSS program for Windows, version 17.0. Continuous variables are presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. Normally distributed continuous variables were compared using Student's *t*-test assuming standard assumptions regarding variability. Categorical variables were analyzed using the chi square test. For all statistical tests, a p-value less than 0.05 was taken to indicate a significant difference.

Results

The mean age of the subjects in the two groups was: Control: 27.73 years and Obese: 28.60 years, and the difference in mean age between two groups was statistically insignificant (p = 0.702) (*Table1*). The proportion of males to females in terms of BMI was statistically insignificant between the two groups (p = 0.841) (*Table 2*).

There was statistically high significant difference in the SBP (p = 0.037) and DBP (p = 0.048) between the control group and obese group on OTT (change from lying to erect position) with obese subjects showing significantly more change (fall in blood pressure) in comparison to control subjects (*Table 3).*

There was significant difference in the SBP (p = 0.042) and highly significant difference in DBP (p < 0.001) before and after cold pressor test between the control group and obese group; the obese adults reported less change in mean SBP and DBP values after the CPT. The obese adults reported significant lower change in mean SBP (p = 0.037) and mean DBP (p = 0.049) with HGT as compared to the control group adults. (*Table 3*)

The obese adults reported lower mean Standing to

Table 1: Comparison of Mean Age Between Two Groups: Control (Non-Obese) Vs Obese (Study Group)

	Control	Obese	*p* value
	Mean ± SD	Mean ± SD	
Age	27.73 ± 7.36	28.60 ± 7.41	0.702

Table 2: Comparison of Sex Distribution Between Two Groups in Terms of BMI

Sex	BMI		*p* value
	Control	Obese	
	Frequency (%)	Frequency (%)	
Female	51 (51.0%)	48 (48%)	0.841
Male	49 (49.0%)	52 (52%)	
Total	100 (100%)	100 (100%)	

Table 3: Comparison of Sympathetic Tests Between Two Groups

Variable		BMI		*p* value
		Control	Obese	
	(mm of Hg)	Mean ± SD	Mean ± SD	
OTT	SBP	4.52 ± 10.5	6.86 ± 4.51	0.037
	DBP	3.05 ± 2.76	4 ± 1.97	0.048
CPT	SBP	18.19 ± 7.7	16.36 ± 4.64	0.042
	DBP	13.89 ± 8.99	9.96 ± 4.26	0.001*
HGT	SBP	16.9 ± 4.56	12.92 ± 5.47	0.037
	DBP	11.07 ± 13.6	9.81 ± 6.89	0.049

p value <0.05 is considered Statistically Significant; * Highly Significant. OTT - Orthostatic Tolerance Test; CPT - Cold Pressor Test; HGT - Handgrip Tests; SBP - Systolic Blood Pressure; DBP - Diastolic Blood Pressure

Table 4: Comparison of Parasympathetic Activity Between Two Groups

To Asses Parasympathetic Activity (ECG tests)	BMI		*p* value
	Control	Obese	
	Mean ± SD	Mean ± SD	
S / L Ratio	1.12 ± 0.33	0.98 ± 0.18	0.003
30:15 Ratio	1.06 ± 0.13	1.00 ± 0.09	0.020
Valsalva Ratio	2.55 ± 12.37	1.35 ± 0.28	0.008

Lying (S/L) ratio ($p = 0.003$), lower mean 30:15 ratio ($p = 0.020$), lower mean Valsalva ratio ($p = 0.008$) as compared to control group adults and all the values were significantly lower in obese group (*Table 4*).

Discussion

The results of present study show statistically significant decreased autonomic reactivity in obese i.e., hypofunctioning of both sympathetic and parasympathetic activity. Several studies have reported similar results (12,13). Esler *et al*. (14) implied decreased sympathetic nervous system activity to be a potential cause of weight gain in humans because of its crucial role in energy metabolism. Sympathetic nervous system is involved in virtually all the individual components of daily energy expenditure including resting metabolic rate, energy expenditure related to physical activity, the thermic effect of food and in cold induced thermogenesis. It seems logical to assume that reduced sympathetic nervous activity leads to decreased thermogenesis and consequently to a positive energy balance and obesity (15). Valensi *et al*. (16) proposed that cause of the cardiac parasympathetic dysfunction in obese subjects could be higher carbohydrate intake and lower fat and protein intake. Rissanan *et al*. (17) have reported increase in parasympathetic activity with weight loss.

Other studies have reported different results. Colak *et al*. (18) and Pal *et al*. (19) reported hypoactivity of sympathetic nervous system and normal parasympathetic system activity in obese individuals. Shetty *et al*. (20) and Yakinci *et al*. (21) found decreased parasympathetic activity but no significant difference in sympathetic activity in overweight individuals. Lower sympathetic and parasympathetic activity in obese children and adolescents was reported by Nagai *et al*. (15). These conflicting results could be because of the fact that different age groups were recruited in the study and there was difficulty in controlling variables such as family history, diet, level of physical activity and stress (4). The physical activity profile of the subject affects the cardiorespiratory fitness and hence parasympathetic nervous activity.

Another reason for varying results could be duration of obesity and the fact that autonomic alterations may be more related to body fat percentage rather than BMI which does not differentiate between fat weight and fat free weight (22). Also, different guidelines are taken for classification of obesity by different authors. Recent comparative studies have shown that Indians have a higher percentage of body fat for a given BMI compared with white Caucasians and African-American but lower muscle mass (23). In a review study, William *et al*. (24) reported evidence of association between central obesity (increased waist to hip ratio) and dysregulation in cardiac autonomic functions, consequently leading to cardiovascular autonomic neuropathy (CAN). Similar observations were reported by Oliveira *et al*. (25) in their study. The authors of these studies emphasize upon the screening and diagnosis of autonomic dysfunction at an earlier stage when risk factors modification and reversibility is possible.

Preliminary clinical trials exploring autonomic modulation as a treatment for obesity have yielded contrasting results. Yet many studies support this therapeutic intervention as an appealing and promising approach for obesity treatment (1).

Limitations

In our study the classification of obesity done was based on BMI, which is a crude indicator and does not differentiate the type of obesity (central or peripheral) which is known to influence the results. Also, confounding factors such as duration of obesity and levels of physical activity were not taken into consideration into present study. These also may affect the outcome of the study.

Conclusion

Obese adults have decreased sympathetic and parasympathetic activity. Early detection of altered ANS functioning by simple, easy-to-do, autonomic function tests may help in early intervention and subsequent decrease in morbidity and mortality related to ANS dysfunction.

Acknowledgement

We thank the participants of the study and the research personnel who assisted us.

Financial Support and Sponsorship

Nil.

Conflicts of Interest

There are no conflicts of interest.

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