Sympathetic Activity and Heart Rate Variability in Response to Cold Pressor Test and Hand Grip Test among Obese and Nonobese Adults: An Original Research Study

M.Shareefa¹, RVBS Sarma², Sunil Kumar.A.Rayan³, Syeda Sobia Harmain^{4*}

1.M.Shareefa

Associate Professor, Department of Physiology Kakatiya Medical College Hanumakonda, Telangana, India 2.RVBS Sarma Tutor, Department of Physiology Dr PSIMS &RF_Chinnoutpally, Andhra Pradesh, India 3.Sunil Kumar.A.Rayan Associate Professor, Department of Physiology Government Medical College Suryapet, Telangana, India 4.Syeda Sobia Harmain Assistant Professor, Department of Physiology Kakatiya Medical College Hanumakonda, Telangana, India <u>Name, Address, Email of the Corresponding author</u> Dr. Syeda Sobia Harmain Assistant Professor, Department of Physiology Kakatiya Medical College Hanumakonda, Telangana, India Email:syedasobia721@gmail.com

ABSTRACT

Background: Obesity is a health hazard throughout the world. weight gain and obesity are responsible for a growing threat to health throughout the world objectives: To evaluate and compare the cardiovascular autonomic response to cold pressor test and hand grip test among obese and non-obese adults. Methodology: Cardiovascular sympathetic function tests were carried out in 100 obese adults and 100 non obese adults aged between 28-58 years. Recording of ECG was performed in normal breathing, deep breathing and in condition of cold pressor. Time-domain method was used to record HRV Results: Study demonstrated significant decreased BP(BP)(systolic and diastolic) to cold pressor and to sustained handgrip. Responses in cases were significantly correlated to Body Mass Index. Our findings shows increased sympathetic activity was seen in obese patients and vagal activity was also withdrawn. Conclusion: There is remarkable change observed in the cardiac autonomic dysfunction responses between obese and non-obese subjects. Normal BMI showed a better HRV response to cold pressor test, indicating a better parasympathetic activity as compared to obese subjects. In cold pressor test BP was reduced in obese compared to non-obese individuals suggesting decreased vascular sensitivity to the amplified adrenergic activity in healthy obese individuals(adults).

Key Words: Heart rate variability, Cardiovascular function, Time domain, Body Mass Index, Cold Pressor Test, Hand Grip Test

Introduction:

Obesity is a worldwide health problem and it is an important contributor to morbidity and mortality.^{1,2} Currently obesity is one of the most severe public health problems worldwide, and has seeking the attention of many scientists all over the globe.³

Imbalance of autonomic nervous system associating enhanced adrenergic activity and decreased vagal tone has been markedly implicated in the pathophysiology of cardiac arrhythmias and sudden cardiac death.⁴Among the various available non-invasive techniques for evaluating the autonomic status, heart rate variability (HRV) has appeared as a simple, non-invasive procedure to evaluate the sympatho-vagal balance at the sinoatrial level.⁵ It shows the total amount of variations of both instantaneous heart rate and RR intervals (intervals between QRS complexes of normal sinus depolarizations).⁶ Therefore, HRV evaluates the tonic baseline autonomic function. Changes in heart rate over time or the intervals between succeeding normal cardiac cycles were measured by time domain analysis.⁷

Various medical disorders are associated with obesity with cardiovascular dysfunction. The relation between cardiovascular disorders and obesity is well recognized.⁸ The adrenergic system is an vital system in regulation of the CVS and similarly the CVS and energy expenditure, is extensively plays an significant role in the pathophysiology of obesity.⁹Cold pressor test is considered to be a sympatho-excitatory manoeuvre is a simple, non invasive and authenticated test of adrenergic activation.¹⁰ Western population are remarkably involved in these studies relation to autonomic disturbances in obesity, there is a scarcity of information in the population of India.¹¹

Methodology :

The study population comprised of 100 cases of obese and 100 non obese age matched subjects from. The present study included both males and females who were selected by simple random sampling. This study was carried out at Kakatiya Medical College, Hanumakonda, Telangana, India.

Inclusion Criteria: The present study included obese subjects as those who had a BMI (Body mass index) $> 30 \text{Kg/m}^2$ and not suffering from any alternative disease or clinical manifestations. All the healthy subjects (controls) and obese participants (cases) were aged between 28 to 48 years and were subjected to clinical examination.

Exclusion Criteria: Subjects with earlier history of cardio-pulmonary disorder, epilepsy, immobilization, psychologically challenged, physically challenged, spinal defect, infective disorders and neuro muscular disorders and patients taking drugs that influence cardio vascular system, bronchodilators, H1 receptor antagonists and NSAIDS, smokers and alcoholics were excluded from the study.

The following tests were performed to assess the cardiovascular sympathetic functional status; BP response to cold pressor and BP response to sustained handgrip. We performed all the tests between 9:30 AM - 1:00 PM in the months of February-March to avoid diurnal and seasonal variation.

Sympathetic Cardiovascular Parameters: As per the standard protocol subjects were made to take rest for 10 minutes before measuring their baseline systolic and diastolic BP. Suitable cuff size was used to measure BP. For every subject, two readings of BP were taken from which the average baseline BP(systolic or diastolic) was obtained before each of the following tests.

In the supine posture, after resting period, during normal respiration for a 5 minutes duration, ECG of the individual subjects was recorded. This was followed with a break of 2 minutes. During the period of deep breathing for about a minute recording of next ECG was done. subjects were told to inspire for the first 5 seconds from the count of 1 to 5 and expire the next 5 seconds from the count of 5 to 1. This recording was taken for 6 such cycles, i.e. one minute.

Cold Pressor Test (CPT): The right hand of the subject was immersed up to the wrist in cool water at a 4°C of temperature for 1 minute. BP was recorded at 30 seconds and 1 minute of submersion of the hand. After taking out the hand, BP was recorded after every minute, till it gets back to the baseline. The rise in BP from the baseline value to maximal value, known as the range or response, was obtained. The maximal systolic and diastolic values of BP achieved through out the test, designated as the ceiling values, were also noted.

Hand Grip Test (HGT): Handgrip dynamometer test was performed to produce the sympathetic cardiovascular functions during the isometric exercise. The subjects were informed through self-demonstration by the researchers. The baseline systolic and diastolic BP values were recorded.

By gripping the handgrip dynamometer, subjects were asked to perform Maximal Voluntary Contraction (MVC) as hard as possible for few seconds and the maximum force exerted was noted down. Few minutes after giving rest, subjects were instructed to do isometric exercise to the point of fatigue at 30% of the maximal voluntary contraction. Systolic and diastolic BP readings were taken at intervals of every minute during the entire period of exercise. The mean systolic and diastolic BP, the increase in systolic and diastolic BP during the isometric exercise were calculated and the maximal values of systolic and diastolic BP achieved during exercise were noted down.

The statistical analysis after comparison of parameters will be done by using SPSS 21 software. All data will be reported as mean \pm standard deviation (SD). Paired/unpaired 't' test will be used for comparison of variables between the groups.

Ethics: This study was approved by the Institutional Ethics Committee of Kakatiya Medical College, Hanumakonda, Telangana, India. An informed written consent was taken from all the patients involved in the study after explaining regarding the study.

Results:

The results of the tests were compared between the cases (obese) and healthy age matched controls. Values are expressed as mean \pm SEM in the tables.Sympathetic activity was

recorded with the subjects. Mean BP was measured with a sphygmomanometer. Heart rate was measured by ECG during the daytime measurements.

Status of Obesity	Obese	Non-obese	<i>p</i> -value
	Mean ± SD	Mean ± SD	
Age	36.23 ± 8.23	35.17 ± 6.85	0.3234
SBP	8.31 ± 3 .47	9.81 ± 3.12	0.0015
DBP	7.34 ± 3.149	9.23 ± 4.12	0.0003
BMI	31.65 ± 2.78	24.14 ± 0.81	<0.0001

Table 1 Cold pressor test in obese and non-obese adults

Age difference in obese and non-obese adults. The mean SBP difference for obese is 36.23 and for non-obese is 35.17. *p* value and statistical significance: The two-tailed P value equals 0.3234.

SBP distribution in cold pressor test in obese and non-obese adults. The mean SBP difference for obese is 8.31 and for non-obese is 9.81. p value and statistical significance: The two-tailed p value equals 0.0015.

DBP distribution in cold pressor test in obese and non-obese adults. The mean DBP difference for obese is 7.34 and for non-obese is 9.23. P value and statistical significance: The two-tailed P value equals 0.0003

BMI distribution in obese and non-obese adults. The mean BMI for obese is 31.65 and for non-obese is 24.14 which shows highly significant (p<0.0001) correlation of the BMI with the cardiovascular sympathetic function tests in cases.

Table 2 Hand grip test in obese and non-obese adults.

Status of obesity	Obese	Non-obese	<i>p</i> -value
	Mean ± SD	Mean ± SD	
SBP	6.24 ± 3.15	10.23 ± 4.24	<0.0001
DBP	7.29 ± 4.18	9.92 ± 3.91	<0.0001

SBP distribution in hand grip test in obese and non-obese adults. The mean SBP difference for obese is 6.24 and for non-obese is 10.23. It shows highly significant (p<0.0001) difference in BP response to handgrip between two groups of cases.

DBP distribution in hand grip test in obese and non-obese adults. The mean DBP difference for obese is 7.29 and for non-obese is 9.92. It shows highly significant (p<0.0001) difference in BP response to handgrip between two groups of cases.

Discussion: The cold pressor test stimulates a significant increase in adrenergic activity in humans mediated by central command and local metabolites. Cold pressor test is commonly used to screen the sympathetic influence on circulation in humans. The autonomic nervous system consists of sympathetic and parasympathetic divisions. Intact cardiac autonomic innervations are essential for normal heart rate. The sympathetic nervous system regulates the myocardial contractility and heart rate. Tests of cardiovascular sympathetic function which were used in this study have been widely used by various researchers. They are standard, non-invasive, safe and easily reproducible. In our study no significant rise in both systolic and diastolic BPs were found in obese group when compared to non-obese group. In obese subjects there is no significant rise of BP within 60 seconds and the basal BP was achieved within 2 minutes. An impaired cold pressor response was found in obese subjects.

BP and heart rate in normal subjects are well categorized and diverse responses were observed in a wide variety of individuals. In normal subjects heart rate is expected to increase 7-12 beats/min during the first 1-2 minutes of immersion and may stabilize or decrease with more prolonged immersion. This change was exactly noted in the control group but there was a diminished response in the obese group. The present study showed BMI<25 had a better heart rate variability response to a cold pressor test than those with a BMI >25 demonstrated a poor heart rate variability. Thus it was inferred that a better parasympathetic response was noted in the nonobese rather than in the obese group.

Schobel HP et al,. suggested that during cold pressor test there is impaired raise in BP due to high levels of FFAs, leptin and increased insulin resistance which cause vascular endothelial inflammation, in turn leading to increased vascular resistance to other stimuli.¹² Chronic hyper insulinemia causes vasodilation and decreases the sensitivity of vascular muscle. Cold pressor stimulus causes no significant raise in DBP, due to impaired vascular smooth muscle responses.

Children with obesity were showed an enhancement in the LF/HF ratio and a reduction in the HF index in comparison with eutrophic children. According to Vanderlei LC, et al.,¹³ these differences may be related to the difficulty in controlling variables such as gender, age, family history, other medical conditions, diets, behavioral habits, level of physical activity and emotional stress.

Vijayalakshmi P, et al, study showed Hand grip test is an isometric exercise and produces a significant increase in BP, a response which can be easily elicited by using sustained hand grip. In hand grip test, increase in BP is due to increased sympathetic activity mediated by the alpha adrenergic receptors of the autonomic nervous system.¹⁴ An increase in sympathetic

activity in response to handgrip is due to impulses from the limbic cortex, motor cortex and the proprioceptors within small hand joints acting as afferent inputs into the medullary cardiac centers causing increase in BP, both SBP and DBP. Cornelissen VA, et al, study result correlated with present data, indicating sustained isometric exercise results in a significant decrease in both SBP and DBP.¹⁵ It can be assumed that increased baseline BP in obese group could be due to higher vasoconstrictor tone and increase in the cardiac output due to increased circulatory overload on the heart, as consequence of increase in body mass index. The lower BP response to handgrip test in obese group is more likely be due to either a lower sympathetic activity or to a peripheral vascular resistance in response to a normal or subnormal sympathetic stimulation.

Conclusion: The present study concluded significant differences in the cardiac autonomic dysfunction responses between obese and non-obese subjects. Normal BMI subjects showed a better HRV response to cold pressor test, indicating a better parasympathetic activity as compared to obese subjects. In handgrip test, there are decreased SBP and DBP values in obese subjects when compared to non-obese controls. BP response to cold pressor test was decreased in obese compared to non-obese subjects indicating reduced vascular sensitivity to sympathetic activity in healthy obese adults. The present study shows obese subjects have enhanced sympathetic activity though decreased vascular response and a withdrawal of vagal activity. The responses in obese were significantly correlated to Body Mass Index. BP response to handgrip test was also reduced in obese subjects, likely due to peripheral vascular resistance to sympathetic stimulation.

Conflict of interest: None declared

References:

- 1. Kumanyika S, Jeffery RW, Morabia A, Ritenbaugh C, Antipatis VJ. Obesity prevention: the case for action. International journal of obesity. 2002 Mar;26(3):425.
- 2. Oyeyemi BF, Ologunde CA, Olaoye AB, Alamukii NA. FTO gene associates and interacts with obesity risk, physical activity, energy intake, and time spent sitting: Pilot study in a Nigerian population. Journal of obesity. 2017;2017.
- 3. Caballero B. The global epidemic of obesity: an overview. Epidemiologic reviews. 2007 Jan 1;29(1):1-5.
- 4. Sztajzel J. Heart rate variability: a noninvasive electrocardiographic method to measure the autonomic nervous system. Swiss medical weekly. 2004 Sep 4;134(35-36):514-22.
- 5. Thireau J, Zhang BL, Poisson D, Babuty D. Heart rate variability in mice: a theoretical and practical guide. Experimental physiology. 2008 Jan 1;93(1):83-94.
- 6. Karim N, Hasan JA, Ali SS. Heart rate variability-a review. J. Basic Appl. Sci. 2011;7(1):71-7.
- 7. Von Borell E, Langbein J, Després G, Hansen S, Leterrier C, Marchant-Forde J, Marchant-Forde R, Minero M, Mohr E, Prunier A, Valance D. Heart rate variability as a measure of autonomic regulation of cardiac activity for assessing stress and

welfare in farm animals—a review. Physiology & Behavior. 2007 Oct 22;92(3):293-316.

- Mechanick JI, Youdim A, Jones DB, Garvey WT, Hurley DL, McMahon MM, Heinberg LJ, Kushner R, Adams TD, Shikora S, Dixon JB. American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery. Surgery for Obesity and Related Diseases. 2013 Mar 1;9(2):159-91.
- 9. Achten J, Jeukendrup AE. Heart rate monitoring. Sports medicine. 2003 Jun 1;33(7):517-38.
- 10. Pai SR, Mary A, Kini RD. Effects of cold pressor test on BP and heart rate variability in the wards of hypertensive parents. International Journal of Pharmaceutical, Chemical & Biological Sciences. 2013 Jul 1;3(3).
- Gianaros PJ, Van der Veen FM, Jennings JR. Regional cerebral blood flow correlates with heart period and high-frequency heart period variability during working-memory tasks: Implications for the cortical and subcortical regulation of cardiac autonomic activity. Psychophysiology. 2004 Jul 1;41(4):521-30.
- 12. Schobel HP, Fischer T, Heuszer K, Geiger H, Schmieder RE. Preeclampsia—a state of sympathetic overactivity. New England Journal of Medicine. 1996 Nov 14;335(20):1480-5.
- Vanderlei LC, Pastre CM, FreitasJúnior IF, Godoy MF. Analysis of cardiac autonomic modulation in obese and eutrophic children. Clinics. 2010 Jun;65(8):789-92
- 14. Vijayalakshmi P, Madanmohan BA, Patil A, Babu K. Modulation of stress induced by isometric handgrip test in hypertensive patients following yogic relaxation training. Indian J PhysiolPharmacol. 2004 Jan 24;48(1):59-64.
- 15. Cornelissen VA, Smart NA. Exercise training for BP: a systematic review and metaanalysis. Journal of the American Heart Association. 2013 Feb 22;2(1):e004473.