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ANALYSIS OF ROLE OF GHRELIN IN OBESITY AND HYPERTENSIVE PATIENTS IN PAKISTAN

Dr. Hazim Afzal[1], Dr. Sidra Rehman[2], Dr. Tabassum Bashir[3], Zoha Rafaqat[4]

[1]MO at BHU Nathu Sevia District Gujranwala.

[2]WMO at DHQ Hospital Lodhran

[3]Assistant Professor, Department of Paediatrics Nawaz Sharif medical college, Gujrat

[4]Foundation University Medical College, Islamabad.

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Abstract:

Introduction: *Ghrelin is also called orexigenic and it is a peptide hormone released from the P/D1 cells in fundus in upper part of stomach and in the pancreas. Ghrelin secreting cells are also called epsilon cells. It is released when stomach is empty and its release is inhibited when stomach is stretched. It's a potent appetite stimulant.* ***Objectives of the study:*** *The main objective of the study is to analyze the role of Ghrelin in obesity and hypertensive patients in Pakistani environment where obesity is the common issue now a days.* ***Methodology of the study:*** *This study was conducted at Gujranwala and DHQ hospital Lodhran during April to July 2018. This study was done with the permission of ethical committee of hospital. This was basically a cross sectional study. For this purpose we collected the data of 113 patients of both genders.* ***Results:*** *Total 113 obese patients were selected for this study, of which 57 hypertensive and 57 were normotensive. Minimum age was age was 10 years and maximum age was 25 years with mean age 39.35 ± 10.086 years. Mean age of hypertensive obese was 43.42 ± 10.466 years and mean age of normotensive was 35.28 ± 7.876 years.* ***Conclusion:*** *It is concluded that Ghrelin was positively associated with hypertension in obese patients and this association was inversely influenced by the increase of BMI.*

Corresponding author:

Dr. Hazim Afzal,

MO at BHU Nathu Sevia District Gujranwala, Pakistan.

Contact: *0092-322-4849448.*

E-mail: *hazimafzal08@gmail.com*

QR code

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INTRODUCTION:

Ghrelin is also called orexigenic and it is a peptide hormone released from the P/D1 cells in fundus in upper part of stomach and in the pancreas. Ghrelin secreting cells are also called epsilon cells. It is released when stomach is empty and its release is inhibited when stomach is stretched. It's a potent appetite stimulant. Ghrelin effects on GIT and its motility, bone formation, cardiovascular cells and insulin as well[1]. Previous studies show that its levels are low in obesity and also in hypertension; however ghrelin has important vascular and metabolic effects. It increases the gastric secretion and gut motility as well. Ghrelinergic cells are located in stomach, jejunum, lungs; islets of Lange hen's, adrenal cortex, placenta, and kidney and according to recent studies in brain as well. Ghrelin-O-acyl transferase (GOAT) is an enzyme which modifies the 3serine by n-octanoic acid to increase ghrelin activity and this enzyme. It was discovered by Yang, (2008), and is present in GIT and testis. Its optimum temp is 37-50 °C and pH between 7-8. Growth hormone, the receptors for Ghrelin are called growth hormone secretogogous receptor 1. Its mRNA is present in arcuate (ARC), ventromedial nuclei (VMN) of hypothalamus and in hippocampus [2]. It is a heterotrimeric G protein-coupled receptor (GPCR) containing 366 amino acids with the typical seven transmembrane domain [3].

Ghrelin receptor (GHSR1) is involved in biological effect of ghrelin including growth hormone release, increase in hunger lipid and glucose metabolism, increased regulation of motility and secretion of GIT, and protection of nervous and cardiovascular cells. It also plays a role in cell signaling mechanism [4].

Hypertension and obesity

Obesity is a common disease in our population and has adverse effects on health. Subjects having BMI ≥ 30 kg/m² considered to be obese. Excessive food intake, lack of physical activity and genetic susceptibility are contributing factors for obesity. Obesity causes various types of diseases, especially heart diseases, Type 2 diabetes and certain types of cancers and osteoarthritis. Obesity has become an important public –health challenge worldwide. Similarly hypertension is the main cause for cardiovascular disease morbidity and mortality. According to American association 140mmHg is systolic and 90mmHg is diastolic. There are general risk factors for hypertension including age, sex, size, race, life style and obesity. Some risk factors are specific for causing hypertension such as tumor, kidney failure, diabetes, hyperthyroidism, menopause, pregnancy and Cushing syndrome[5].

Although relationship between obesity and hypertension is well known there is scope for further exploration. Activation of sympathetic nervous system is the major pathogenesis of obesity induced hypertension. Plasma rennin activity, angiotensinogen, Angiotensin ĮI and aldosterone considerably increases in obesity. The arterial pressure control by natriuretic and diuresis. Reason behind this retention of sodium and water in extracellular fluid increases blood pressure which lead to obesity induced hypertension [6].

Significance of the problem

Obesity related hypertension is a very common problem in our population. Ghrelin has enhanced the perception of feeding regulation, dietetic hemostasis and metabolic process. There are evidences that in future ghrelin and obestatin will most likely generate new pharmacological advancement to establish and treat different diseases including those correlates to the obesity and metabolism. It will improve the endothelial function by increasing nitric oxide availability and lowering peripheral resistance improving contractility and cardiac output. Aim of current study is to evaluate ghrelin and obestatin levels in obesity hypertension [7].

Objectives of the study

The main objective of the study is to analyze the role of Ghrelin in obesity and hypertensive patients in Pakistani environment where obesity is the common issue now a day.

Methodology of the study

This study was conducted at Gujranwala and DHQ hospital Lodhran during April to July 2018. This study was done with the permission of ethical committee of hospital. This was basically a cross sectional study. For this purpose we collected the data of 113 patients of both genders.

Inclusion criteria

1. 10 years to 25 years subject of both sexes will be included
2. Diagnosed hypertensive subjects at or above 150/90mmHg
3. Diagnosed Obese with BMI ≥30

Exclusion criteria

Subjects with known history of Diabetes mellitus, malignancy and major abdominal surgery and on any major Drug e.g metocloperamide will be excluded from participating in the study

Informed consent

Written Informed consent will be obtained. A detailed history will be taken from the subjects to fulfill the inclusion and exclusion criteria. There will be questions regarding dietary habits, duration of

disease and anti-hypertensive drugs, any past medical and surgical history.

Sampling

A fasting venous blood sample with a total volume of 4 ml will be collected from each study participant. One ml of this will be used in for routine testing FBS and 1 ml for fasting lipid profile.

The remaining 2ml of blood sample will be collected in potassium/ethylene diamine tetracetic acid coated tubes containing 500 KIU aprotinin for the measurement of plasma levels of total ghrelin. Sample will be centrifuged at 2000g for 10 min. Plasma will be kept at -40 C until analyzed. Ghrelin levels will be determined using ELISA kit. Sensitivity of assay would be 8pg/ml for ghrelin.

Statistical analysis

Statistical analysis will be done on SPPS 20 software. Mean ± SD will be given for quantitative variables. Comparisons between the groups will be done using t test. Level of significance will be taken as $p \leq 0.05$.

RESULTS AND DISCUSSION:

Total 113 obese patients were selected for this study, of which 57 hypertensive and 57 were normotensive. Minimum age was age was 10 years and maximum age was 25 years with mean age 39.35 ± 10.086 years. Mean age of hypertensive obese was 43.42 ± 10.466 years and mean age of normotensive was 35.28 ± 7.876 years.

Table 01: Comparison of mean fasting ghrelin levels between hypertensive and normotensive obese

Group	n	Mean	Std. Deviation	P Value
Hypertensive obese	57	0.572	0.514	0.013
Normotensive obese	57	0.387	0.202	

Mean ghrelin levels in hypertensive obese were 0.572±0.514 and mean ghrelin levels in normotensive obese was 0.387 ± 0.202. Statistically significant difference of mean fasting ghrelin levels between hypertensive obese and normotensive obese was noted with p value 0.013.

Table 02: Comparison of mean fasting ghrelin levels for age group 10-25 years between hypertensive and normotensive obese

Group	n	Mean	Std. Deviation	P Value
Hypertensive obese	36	0.676	0.610	0.001
Normotensive obese	53	0.386	0.205	

Mean fasting ghrelin levels in hypertensive obese was 0.676 ± 0.610 and in normotensive obese was 0.386 ± 0.205 in age group 10-25 years. Statistically significant difference of mean fasting ghrelin levels between hypertensive obese and normotensive obese was detected with p value 0.001.

Obesity is known to be strongly associated with hypertension and other arteriosclerotic disease, but the pathogenic mechanisms linking hypertension and obesity have not been fully determined. The possible roles of obestatin and ghrelin in obesity and metabolic syndrome have been studied. Changes in the concentrations of these hormones, and in the ghrelin/obestatin ratio, may be risk factors for obesity and hypertension [8].

Ghrelin is a peptide hormone secreted primarily from the stomach and duodenum; it is a stimulant of appetite and increases adiposity in rodents. However, many studies have shown that obesity is associated with a decrease in circulating ghrelin. Ghrelin has also been reported to have potent anti-inflammatory actions, including inhibition of pro inflammatory cytokine production and mononuclear cell binding in vascular endothelial cells. Ghrelin may therefore have a protective effect on endothelial function and has been shown to lower blood pressure levels. Low plasma ghrelin has been reported to be associated with insulin resistance, hypertension and type 2 diabetes [9].

Obestatin is a 23-amino acid amidated peptide encoded by the ghrelin gene that is also released from the stomach. It has been shown to interact with the orphan receptor G-protein-coupled receptor 39, and to oppose the stimulatory effect of ghrelin on food intake and gastrointestinal function. Studies in humans have shown that blood obestatin levels are significantly lower in obese subjects and correlate negatively with body mass index, insulin, glucose and the homeostasis model assessment of insulin resistance (HOMA-IR), indicating an important role for obestatin in body weight regulation. In addition, obestatin has been shown to be positively correlated

with ghrelin [10]. This suggests that levels of both obestatin and ghrelin may be altered in obesity and insulin resistance. Obestatin has been reported to decrease vascular cell adhesion molecule-1 expression in endothelial cells when stimulated with tumor necrosis factor-a, and to increase oxidized low-density lipoprotein binding to macrophages. Therefore, it may also have a potential function in the regulation of blood pressure [11].

CONCLUSION:

It is concluded that Ghrelin was positively associated with hypertension in obese patients and this association was inversely influenced by the increase of BMI.

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