

Leptin Effect in the Development of Obesity –Related Hypertension in Postmenopausal Women

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ABSTRACT:

BACKGROUND:

Obesity in humans causes hypertension, myocardial hypertrophy and coronary atherosclerosis, and increased cardiovascular morbidity and mortality that is thought to be related to sympathetic overactivity. Leptin is an adipocyte-derived hormone that acts in the hypothalamus to regulate appetite, energy expenditure and sympathetic nervous system outflow. One of the major mechanisms leading to the development of obesity-induced hypertension appears to be leptin-mediated sympatho-activation.

OBJECTIVE:

This study is done to evaluate the contribution of leptin in the development of obesity related hypertension in post menopausal women.

SUBJECTS AND METHODS:

A total number of 64 subjects (post menopausal women) included in the study were divided into obese hypertensive group (n= 38)and non obese non hypertensive group (n=26) , age(57±4.5year) and (56±2.7year) respectively(mean±SD).

Obese hypertensive group defined as (BMI ≥ 30 kg/m² and blood pressure ≥ 140/90 mmHg with or without history of taking anti hypertensive medications)and Non-obese non hypertensive group defined as (BMI < 30 kg/m²- blood pressure < 140/90 mmHg).In the present study leptin had been measured.

RESULTS:

Leptin level is higher in obese hypertensive group than in non obese non hypertensive group and it was 29.2±4 and 15.2±2.1(mean±SD) respectively and this difference is statistically significant with p value < 0.001.

CONCLUSION :

leptin may play a role in the development of obesity- related hypertension and may be an independent predictor of hypertension.

KEYWORDS: leptin , obesity , hypertension.

INTRODUCTION:

Hypertension – a very important cardiovascular risk factor – has been observed in roughly 50% of obese individuals, which has led researchers to consider obesity as one of the most common causes of hypertension. Hence, hypertension in obesity has become a topic of extensive ongoing research. Now, several mechanisms have been implicated in the association between obesity and hypertension, including activation of sympathetic nervous system, abnormal renal sodium handling, insulin resistance, and physical compression of the kidney⁽¹⁾.

In this respect, sympathetic activation appears to mediate at least part of the obesity-induced hypertension, and leptin, the adipocyte-derived hormone, has recently been postulated as one of the possible causes of this sympathetic activation in obesity.

Leptin is a 167 amino acid hormone. The major site of action of this peptide located in the hypothalamus, it causes inhibition of appetite and stimulation of metabolism⁽²⁾.

Obesity is strongly associated with hypertension and cardiovascular disease. Several central and peripheral abnormalities that can explain the development or maintenance of high arterial pressure in obesity have been identified. These include activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system. Obesity is also associated with endothelial dysfunction and renal functional abnormalities that may play a role in the development of hypertension⁽³⁾.

SUBJECTS AND METHODS:

Sample subjects were randomly selected from the patients' relatives attending the external lab department at Al-Zahra' teaching hospital during the period from December 2006 through March 2007.

A total number of 64 subjects (post menopausal women) included in the study were divided into

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obese hypertensive group (n= 38)and non obese non hypertensive group (n=26) , age(57±4.5year) and (56±2.7year) respectively(mean±SD).

Obese hypertensive group defined as (BMI ≥ 30 kg/m² and blood pressure ≥ 140/90 mmHg with or without history of taking anti hypertensive medications)and Non-obese non hypertensive group defined as (BMI < 30 kg/m²- blood pressure < 140/90 mmHg).

Leptin is measured in serum using the leptin (sandwich) Enzyme Immunoassay kit(Monobind Inc., Lake Forest, CA 92630,USA). This assay is intended for in vitro diagnostic use only. It is a solid phase enzyme linked immunosorbent assay (ELISA) based on the sandwich principle.

Statistical analysis

To compare the significance of the difference in the mean values in comparison groups, student t-test was applied; p < 0.05 was considered

statistically significant. The correlation coefficient [r] test is used to describe the association between the different studied parameters; p < 0.05 was considered statistically significant.

RESULTS:

As shown in table 1

There is no statistically significant difference in mean age between obese hypertensive and non obese non hypertensive groups P value >0.05.

Leptin level is significantly higher in obese hypertensive group than in non obese non hypertensive group p value < 0.001.

Mean BMI was significantly higher in obese hypertensive group than in non obese non hypertensive group p value < 0.001.

Mean waist circumference was significantly higher in obese hypertensive group than in non obese non hypertensive P value < 0.001.

Table 1: (Mean ± SD) of studied parameters in obese hypertensive and non obese non hypertensive groups.

Characteristics	Non-obese Non -hypertensive	Obese hypertensive	P value
Number	26	38	-
Age(years)	56.4±2.7	57.1±4.5	>0.05
Leptin(ng/ml)	15.2±2.1	29.2±4	<0.001
Body Mass Index (kg/m ²)	25.3±2.8	33±2.3	<0.001
Waist circumference	85.7±14	108.7±8	<0.001

DISCUSSION:

Leptin is a key neuroendocrine hormone regulating food intake, metabolism, and fat accumulation, and it may also affect blood pressure and contribute to hypertension through sympathetic activation in the vasculature or at the renal level. Although previous studies have shown that the distribution of leptin is significantly different between males and females, as is the risk of hypertension between males and females, results regarding the role of leptin in the gender-specific regulation of blood pressure are controversial. This study was done on post menopausal women and had shown that there is a high concentration of leptin in the obese hypertensive group than in the non obese non hypertensive group and this indicates that there is a role of leptin in hypertension in post menopausal women and this is consistent with the study done by (Duanduan et al 2008) ⁽⁴⁾ who found that there is a significant association between leptin and blood pressure and hypertension in post menopausal women.

The high significant level of serum leptin(29.2±4ng/ml) in obese hypertensive group indicates that leptin play a role in obesity related hypertension and this may be due to increased sympathetic nervous system activity by leptin

effect. Leptin-dependent sympathetic activation to brown adipose tissue(BAT) appears to be mediated by corticotrophin-releasing factor (CRF) because the sympatho-excitatory effect of leptin to this tissue is substantially inhibited by a CRF receptor antagonist ⁽⁵⁾. These findings support the concept that leptin controls sympathetic nerve activity in a tissue-specific manner through different pathways.

A number of studies have found leptin to be positively correlated with systolic and diastolic blood pressure in both obese^(6,7,8) and non-obese individuals ^(9,10,11). Al-Hazimi and Syiamic (2004) ⁽⁶⁾, for example, found that serum leptin and angiotensin II levels were strong predictors of elevated blood pressure in obese women. Likewise, other investigators ^(12,13,9) reported higher leptin levels in obese hypertensives compared with obese normotensive individuals, even after controlling for confounders such as age and body mass index (BMI). In another study leptin correlated stronger with systolic and diastolic blood pressure than did with BMI (or waist circumference) in untreated male adults (Barba et al 2003) ⁽¹⁰⁾. Moreover, one study found that after a 3-month weight reduction program, leptin continued to correlate positively with mean arterial blood pressure in the

hypertensive, but not in the normotensive obese group (Itoh et al 2002) ⁽¹⁴⁾. In disagreement to some of these data, one study found that leptin levels were higher in hypertensives than in normotensive African Americans, but once these individuals were adjusted for obesity, no significant relationship was further observed between leptin and blood pressure (El-Gharbawy et al 2002) ⁽¹⁵⁾.

CONCLUSION :

Leptin may play a role in obesity-related hypertension and may be an independent predictor of hypertension.

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