

HYPERTENSION

Plasma Leptin Level and Plasma Renin Activity in Lean Non-Diabetic Patients

with Essential Hypertension

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The aim of the present study is to examine the relationship between blood pressure, leptin and plasma renin activity in normotensive healthy volunteers and in lean non diabetic patients with essential hypertension. Our work was carried out on subjects classified into 2 groups. Group I included 50 lean non diabetic patients with mild to moderate essential hypertension (age: 38.5 ± 1.8 years, BMI: 21.7 ± 2.5 kg/m², male/female : 25/25). Group II included 30 lean normotensive healthy subjects (age: 39.4 ± 2.2 years, BMI: 21.9 ± 2.5 kg/m², male/female : 15/15). Both groups were properly matched for age, sex and BMI. After the blood pressure measurements, blood samples were collected for the assessment of plasma glucose, creatinine, leptin and renin activity. No significant differences in age, BMI, plasma glucose and creatinine were detected between group I and group II subjects. However, blood pressure (systolic and diastolic),

Introduction and Aim of the Work

Leptin, the 16 KD protein produced by the obese gene, is known to regulate body weight and adipose tissue mass through a feedback mechanism (1). Plasma leptin levels have been found to be elevated in patients with essential hypertension and have been suggested to be a component of metabolic syndrome (2). Although in the short term, leptin may function as a potassium sparing diuretic factor, in the long term, it increases norepinephrine turnover and sympathetic nerve activity. This results in increased blood pressure in rodents but a potential role of hypertension in humans remains to be conclusively demonstrated(3).

plasma leptin levels and plasma renin activity (PRA) were significantly higher in group I patients than in group II subjects ($p < 0.05$).

Blood pressure, age, BMI, plasma creatinine and PRA did not differ significantly between males and females whether normo or hypertensive. However, plasma leptin levels were significantly higher in normotensive and hypertensive females than in normotensive and hypertensive males. Plasma leptin levels were significantly correlated with blood pressure, BMI and PRA in both groups and in both sexes. Furthermore PRA was significantly correlated with BMI in both groups and in both sexes.

These findings support the notion that plasma leptin levels and PRA are related to the adipose mass in normotensive and hypertensive lean subjects. Also, we can conclude that leptin may be involved in blood pressure regulation in both normotensive and hypertensive subjects, and this regulation is possibly mediated via the significant positive correlation between plasma leptin levels and PRA.

Key words : Plasma leptin level, Plasma renin activity, Essential hypertension.

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It has become evident that adipose tissue is a source of metabolically active molecules, including free fatty acids, leptin and angiotensinogen. The latter finding has prompted speculation on the possible role of adipose derived angiotensinogen in the relationship between body weight and blood pressure (4). Uckaya et al (5) demonstrated elevated plasma renin activity in essential hypertension. The present study was undertaken to elucidate the relationship between blood pressure and both plasma leptin levels and plasma renin activity in normotensive healthy volunteers and in lean non diabetic patients with essential hypertension.

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Subjects and Methods

*Subjects

This study was carried out on 80 subjects recruited from Benha University hospital. They were classified into 2 groups.

Group I: This group included fifty patients (25 males and 25 females) with mild to moderate essential hypertension. Their ages ranged from 34-40 years (38.5 ± 1.8).

All patients were selected to be lean (body mass index ranges from 20-24 Kg/m² with a mean of 21.7 ± 2.5 Kg/m²). Patients with diabetes mellitus, chronic debilitating diseases, acute intercurrent infection, catabolic state, renal and liver diseases, heart failure or those taking drugs that elevate blood pressure or PRA were excluded from the study.

Group II: This group included 30 (15 males and 15 females) appropriately age, sex and BMI - matched normotensive healthy subjects. Their ages ranged between 34-40 years (39.4 ± 2.2). Their body mass index ranged between 20-24 kg/m² with a mean of 21.9 ± 2.5 Kg/m².

The following laboratory investigations were formed to every subject:

- Fasting and 2 hours P.P. plasma glucose.
- Plasma creatinine.
- Plasma renin activity.
- Plasma leptin level.
- Urine analysis.

* Sampling :

5 ml venous blood were withdrawn from each subject after an over night fast and in a fixed time in the morning (from 8 a.m to 10 a.m), while the subject in the recumbent position. Each sample was added in an EDTA tube, after centrifugation in a cooling centrifuge, rapid separation of plasma was done for estimation of fasting plasma glucose and creatinine, the remaining plasma was stored at -20 °C till the time of assay of plasma leptin and plasma renin activity. Two h. post prandial plasma glucose sample was collected from each subject.

Methodology

* **Estimation of plasma glucose :** The glucose method is an adaptation of hexokinase glucose 6 phosphate dehydrogenase method presented by Kunst et al (6).

* **Estimation of plasma creatinine :** This was done by colorimetric method (7) based on Jaffe reaction.

* **Estimation of plasma renin activity :** By Radioimmunoassay Kit based on competitive binding principles of RIA in which the antibody is immobilized onto the inner lower wall of the gamma coat tubes (the kit supplied from INCSTAR cooperation USA). The determination involves an initial incubation of plasma to generate angiotensin I, followed by quantitation of angiotensin I by the aid of a standard curve and PRA is expressed as ng/ml/hr of generated angiotensin I.

* **Estimation of plasma leptin :** It was done using the Medizym ELISA Kit manufactured by Medipan diagnostica Germany, it was a sandwich immunoassay, in which samples were incubated in microtitration wells which have been coated with anti-human leptin antibody, after incubation and washing, the wells were treated with another anti-leptin antibody labeled with the enzyme horse-radish peroxidase. After a second incubation and washing, a substrate tetramethylbenzidine was added.

Results

Our results show that plasma leptin level and blood pressure (systolic and diastolic) are significantly high in both hypertensive males and females when compared to normotensive males and females, however no significant difference is elicited between hypertensive and normoten-

sive subjects of both sexes regarding other parameters (age, BMI, plasma glucose and plasma renin activity) (tables 1 and 2).

Plasma leptin level is significantly elevated in females (normotensive and hypertensive) in comparison with males (normotensive and hypertensive). On the other hand, no significant difference is found between both sexes whether normo or hypertensive regarding other parameters (tables 3,4).

Tables 5 and 6 illustrate that plasma leptin level in normo and hypertensive subjects of both sexes shows positive significant correlation with both blood pressure (systolic and diastolic) and plasma renin activity. Other parameters have no significant correlation with plasma leptin level (tables 5 and 6).

Plasma renin activity has positive significant correlation with BMI in patients with essential hypertension and in normotensive subjects of both sexes (tables 7 and 8).

Table 1. Comparison between hypertensive and normotensive males regarding different clinical and laboratory parameters.

Group	Hypertensive males(n=25)	Normotensive males (n=15)	P.value
Parameter	Mean± S.D	Mean± S.D	
- Systolic B P	163.5±4.2	127.5±3.7	<0.05
- Diastolic B P	107.4±2.7	85±1.5	<0.05
- Age (years).	38.2±1.5	39.1±1.9	>0.05
- BMI (kg / m2).	21.4±2.2	21.8±2.4	>0.05
- Fasting plasma glucose (mg /dl).	85.6±4.2	87.2±3.9	>0.05
- Postprandial plasma glucose (mg/dl).	115.3±5.7	114.9±4.8	>0.05
- Serum creatinine (mg / dl).	0.93±0.1	0.92±0.16	>0.05
- Plasma renin activity (ng / ml / hr)	1.6±0.8	1.5±0.6	>0.05
- Plasma leptin level (ng / ml)	6.54±0.2	3.81±0.12	<0.05

P < 0.05: Significant

P > 0.05: Non Significant

Table 2. Comparison between hypertensive and normotensive females regarding different clinical and laboratory parameters.

Group	Hypertensive Females(n=25)	Normotensive females (n=15)	p. value
Parameter	Mean± S.D	Mean± S.D	
- Systolic BP	161.8±6.3	125.9±4.1	<0.05
- Diastolic BP	109.3±3.2	88.2±1.9	<0.05
- Age (years)	38.8±1.7	39.7±2.1	>0.05
- BMI (kg / m2)	22.1±2.7	22.4±2.1	>0.05
- Fasting plasma glucose (mg/ dl)	87±3.8	86.3±4	>0.05
- Postprandial plasma glucose (mg/dl)	117±4.5	118.7±3.7	>0.05
- Serum creatinine (mg/dl)	0.87±0.18	0.95±0.13	>0.05
- Plasma renin activity (mg / ml /h)	1.73±0.9	1.47±0.8	>0.05
- Plasma leptin level (mg / ml)	13.7±0.42	8.59±0.13	<0.05

Table 3. Comparison between normotensive males and normotensive females regarding different clinical and laboratory parameters.

Parameter	Group	Normotensive males (n=15)	Normotensive females (n=15)	p. value
		Mean± S.D	Mean± S.D	
• Systolic BP		127.5±3.7	125.9±4.1	>0.05
• Diastolic BP		85±1.5	88.2±1.9	>0.05
• Age (years)		39.1±1.9	39.7±2.1	>0.05
• BMI (kg / m2)		21.8±2.4	22.4±2.1	
• Fasting plasma glucose (mg/ dl)		87.2±3.9	86.3±4	>0.05
• Postprandial plasma glucose (mg/dl)		114.9±4.8	118.7±3.7	>0.05
• Serum creatinine (mg/dl)		0.92±0.16	0.95±0.13	>0.05
• Plasma renin activity (mg / ml /hr)		1.5±0.6	1.47±0.8	>0.05
• Plasma leptin level (mg / ml)		3.81±0.12	8.59±0.13	<0.05

Table 4. Comparison between hypertensive males and hypertensive females regarding different clinical and laboratory parameters.

Parameter	Group	Hypertensive Males (n=25)	Hypertensive females (n=25)	p. value
		Mean± S.D	Mean± S.D	
• Systolic BP		163.5±4.2	161.8±6.3	>0.05
• Diastolic BP		107.4±2.7	109.3±3.2	>0.05
• Age (years)		38.2±1.5	38.8±1.7	>0.05
• BMI (kg / m2)		21.4±2.2	22.1±2.7	
• Fasting plasma glucose (mg/ dl)		85.6±4.2	87±3.8	>0.05
• Postprandial plasma glucose (mg/dl)		115.3±5.7	117±4.5	>0.05
• Serum creatinine (mg/dl)		0.93±0.1	0.87±0.18	>0.05
• Plasma renin activity (mg / ml /hr)		1.6±0.8	1.73±0.9	>0.05
• Plasma leptin level (mg / ml)		6.54±0.25	13.7±0.42	<0.05

Table 5. Correlation coefficient and probability value between plasma leptin level and other variables in hypertensive patients.

Variable	Plasma leptin level			
	Males		Females	
	r	p	r	p
• Systolic BP	+ 0.47	<0.05	+ 0.492	<0.05
• Diastolic BP	+ 0.452	<0.05	+ 0.510	<0.05
• Age	+ 0.124	> 0.05	+ 0.143	> 0.05
• BMI	+ 0.575	<0.05	+ 0.627	<0.05
• Fasting plasma glucose	+ 0.152	>0.05	+ 0.137	> 0.05
• Post prandial plasma glucose	+ 0.147	> 0.05	+ 0.182	>0.05
• Serum creatinine	+ 0.133	>0.05	+ 0.145	>0.05
• Plasma renin activity	+ 0.587	<0.05	+ 0.567	<0.05

Table 6. Correlation coefficient and probability value between plasma leptin level and other variables in normotensive subjects.

Variable	Plasma leptin level			
	Males		Females	
	r	p	r	p
• Systolic BP	+ 0.392	<0.05	+ 0.41	<0.05
• Diastolic BP	+ 0.37	<0.05	+ 0.38	<0.05
• Age	+ 0.123	>0.05	+ 0.110	>0.05
• BMI	+ 0.356	<0.05	+ 0.385	<0.05
• Fasting plasma glucose	+ 0.192	>0.05	+ 0.178	>0.05
• Post prandial plasma glucose	+ 0.173	>0.05	+ 0.182	>0.05
• Serum creatinine	+ 0.156	>0.05	+ 0.17	>0.05
• Plasma renin activity	+ 0.47	<0.05	+ 0.43	<0.05

Table 7. Correlation coefficient and probability value between plasma renin activity and BMI in hypertensive patients.

Variable	Plasma renin activity			
	Males		Females	
	r	p	r	p
BMI	+ 0.313	<0.05	+ 0.295	< 0.05

Table 8. Correlation coefficient and probability value between plasma renin activity and BMI in normotensive subjects.

Variable	Plasma renin activity			
	Males		Females	
	r	p	r	p
BMI	+ 0.293	<0.05	+ 0.280	< 0.05

Discussion

Our results show that plasma leptin levels are significantly elevated in both normotensive and hypertensive subjects in comparison with both normotensive and hypertensive males. However, body mass index (BMI) doesn't differ significantly between both sexes (tables 3 and 4).

Level et al.(8) stated that circulating leptin levels are higher in females than males even after controlling for body mass index. This difference does not appear to result from the continuous presence of oestrogen, since levels are comparable between pre- and post- menopausal women. However, Sheu et al. (9) confirmed a sex difference in leptin levels both in hypertensive and

normotensive subjects. They demonstrated a higher plasma leptin concentrations in hypertensive men but not in hypertensive women when compared with normotensive control individuals.

The age doesn't significantly influence plasma leptin levels in our subjects of both sexes, whether normo- or hypertensive (tables 5 and 6). The same result was obtained by Howard et al. (10) who stated that in their study no correlation was found between serum leptin level and age within the groups when they analysed individually after adjustment for body fat content.

In our work, no significant correlation is found between plasma leptin levels and serum creatinine in all