The correlation between nesfatin-1 and blood pressure in healthy normal weight and obese adults

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ABSTRACT: Nesfatin-1 is an anorexigenic peptide with 82 aminoacides expresses in hypothalamic cells, adipose tissue, gastric mucous and pancreatic β-cells. Its precursor protein is named nucleobindin-2 (NUCB2). Recently it is suggested that nesfatin-1 may influence blood pressure both via direct effect on vessels and by affecting central nervous system. This is the first study to investigate the association between blood pressure and nesfatin-1 serum level in normal weight and obese subjects considering the nesfatin-1 as an adipokine. The study population consists of 40 obese and 40 normal weight individuals who did not have any significant disease in their medical history. Despite the significant difference in blood pressure in both groups (systolic and diastolic blood pressure in the normal group were respectively 106.50±11.88 and 73.75±11.91 mmHg and in the obese group were respectively 115.25±12.75 and 80.50±9.59 mmHg) no significant correlation was observed between nesfatin-1 serum level and blood pressure (P<0.05). Despite the previous observations indicating nesfatin-1 role in regulating blood pressure our results did not show any correlation between nesfatin-1 serum level and blood pressure in obese and normal weight group. It is speculated that the obesity related resistance in transferring nesfatin-1 to the CNS may cause the lack of association between nesfatin-1 and blood pressure.

Keywords: Nesfatin-1, Blood pressure, Obesity, Iran

INTRODUCTION

The prevalence of obesity is increasing in the worldwide. Obese individuals are at higher risk for obesity related diseases such as type 2 diabetes, hypertension, other cardiovascular diseases and renal failure. A strong correlation between nesfatin-1 and hypertension exists (Rahmouni et al. 2005). More than 40% of obese people are suffering from hypertension. Hypertension can elevate the risk for cardiovascular diseases and death (Dorresteijn et al. 2011). It is estimated that 60-70% of hypertensions in adults can be attributed to obesity. Several central and peripheral causes have been identified for obesity related hypertension. Evidence-based data suggest that sympathetic activity of kidney and skeletal muscle is raised due to obesity. The cause for the obesity related stimulation is yet to be identified. The possible mechanisms include renin-angiotensinogen, adipokines and insulin. Another mechanism is increased absorption of sodium in renal tubes (Kotchen et al. 2010).

Since leptin discovery adipose tissue is no longer regarded as an elite place for lipid accumulation. Adipose tissue secretes various cytokines with different activities named as adipocytokines. Studies suggest that adipocytokines are able to affect the contractile reactivity of blood vessels (Xi et al. 2010). Leptin and blood pressure are correlated in normotensive and hypertensive individuals regardless of the fat mass. It is demonstrated that chronic systemic and intracerebral administration of leptin increases blood pressure in rats (Correia et al. 2004). Transgenic overexpression of leptin in rat cased hypertension despite weight loss. Blood pressure was not enhanced in obese leptin deficient mice and human (Ozata et al. 1999). Leptin activates sympathetic nervous system both peripherally and centrally (Mark et al. 2009).

Nesfatin-1 is a peptide with 82 aminoacides which is derived from its precursor protein named Nucleobindin-2 (NUCB2) (Oh et al. 2006). It was firstly discovered in hypothalamus as an anorexigenic hormone...
acting via leptin-independent, melanocortin dependent pathway. Later nesfatin-1 was identified in human and mouse adipose tissue. It was revealed that the nesfatin-1 expression in adipose tissue is reduced under food deprivation but significantly increased in high fat fed mice (Ramanjaneya et al. 2010). It is shown that an increase in mean arterial blood pressure happens in rats due to an intracerebroventricular injection of nesfatin-1. It is presumed that nesfatin-1 centrally affect blood pressure via the activation of sympathetic nerves through melanocortin-3/4 receptors (Yosten et al. 2009). In 2012 it was revealed that nesfatin-1 directly inhibits peripheral arterial blood vessels smooth muscle relation via impairing the cGMP relation (Yamawaki et al. 2012).

METHODS AND SUBJECTS

Totally 40 obese and 40 normal weight adults were recruited in this study. Participants were between 20 to 0 years olds normal weight and ones individuals without any significant medical complication history. Those with significant weight changes during recent 4 weeks, those who follow a specific diet, who attend vigorous physical activity were not included in the study. He anthropometric measurements were done by a trained nutritionist. Systolic and diastolic blood pressures were measured using a standard sphygmomanometer. The measurements were repeated 2 times during a 30 minute interval. The nesfatin-1 serum levels were assessed using Enzyme-linked immunosorbent assay (ELISA) method with the kits purchased from Cusabio (Hebei, China). Blood samples were taken between 8-9 am after a night fasting and before any significant physical activity. Data are expressed as Mean±SE and analyzed by SPSS version11.

RESULTS

Mean systolic and diastolic blood pressure in the normal weight group were 106.50±11.88 and 73.75±11.91 respectively. In the obese subjects both mean systolic and diastolic blood pressure were significantly higher (115.25±12.75 and 80.50±9.59 respectively P<0.002, P< 0.007). No significant correlation was observed between nesfatin-1 serum level with blood pressure neither in the groups nor in the pooled subjects (table1).

Table 1. The linear regression between nesfatin-1 and blood pressure in normal weight and obese subjects

<table>
<thead>
<tr>
<th>Factors</th>
<th>Nesfatin-1 Obese group</th>
<th>Normal weight group</th>
<th>Pooled subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=40</td>
<td>n=40</td>
<td>n=80</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>r</td>
<td>r</td>
</tr>
<tr>
<td>Systolic blood</td>
<td>0.138</td>
<td>0.239</td>
<td>0.170</td>
</tr>
<tr>
<td>pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood</td>
<td>0.554</td>
<td>0.097</td>
<td>0.653</td>
</tr>
<tr>
<td>pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

r: Pearson Correlation Coefficient

DISCUSSION

Using in situ hybridization and immunohistochemistry procedures the distribution of nesfatin-1 mRNA and protein was mapped in rat CNS. Nesfatin-1 like immunoreactivity was detected in the neurons producing vasopressin, corticotropin releasing hormone, POMC, Oxytocin, melanin concentrating hormone and many other areas. These findings indicate the possibility that nesfatin-1 involves in the other functions such as cardiovascular regulation (Foo et al. 2008). A relation between nesfatin-1 and blood pressure was suggested since many of the peptides that affect food intake are also able to influence cardiovascular function. A significant increase in mean arterial blood pressure (MAP) was detected when nesfatin-1 was administered centrally in rats. The raise in the MAP was inhibited when the subjects were pretreated with the melanocortin3/4 receptor antagonist that indicates the involvement of central melanocortin pathway to enhance sympathetic nerve activity (Yosten et al. 2009). Based on previous studies an intravenous administration of nesfatin-1 elevated blood pressure moreover it impaired the sodium nitroprusside induced relaxation of the smooth muscle cells (Yamawaki et al. 2012). This is the first study which assessed the relation between nesfatin-1 and the blood pressure in obese and normal weight subjects. In our results no correlation was observed between nesfatin-1 and the blood pressure neither in the normal weight nor in the obese group. Peripheral Nesfatin-1 has to pass the blood brain barrier (BBB) in order to play its role as a blood pressure elevating hormone (Pan et al. 2007) (Price et al. 2007). Previously nesfatin-1 existence was detected in the cerebrospinal fluid (CSF). It was shown that the CSF/plasma nesfatin-1 ratio decreased with increasing BMI that may suggest a saturated transportation for nesfatin-1 (Tan et al. 2011). Here we suggest that the lack of association between nesftin-1 and the blood pressure is possibly due to the decreased nesfatin-1.
transportation to hypothalamus. A new study which compares the nasfatin-1 serum level in the recently diagnosed hypertensive patients and the healthy adults will be helpful to clarify the aforementioned relation.

CONCLUSION

In conclusion despite the previous evidences indicating nesfatin-1 role in regulating blood pressure in non-human subjects, our results did not show any correlation between nesfatin-1 serum level and blood pressure in obese and normal weight group. It is speculated that the obesity related resistance in transferring nesfatin-1 to the CNS may cause the lack of association between nesfatin-1 and blood pressure.

ACKNOWLEDGMENT

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REFERENCES


