ORIGINAL ARTICLE

SERUM VISFATIN IN NON-OBESE MALE NORMAL AND CORONARY ARTERY DISEASE PATIENTS

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Background: Mechanism of direct cardioprotective action of visfatin is still unclear. The aim of this study was to detect the serum visfatin concentration in healthy males and compare it with non-obese male patients of coronary artery disease to access the cardioprotective role of visfatin. **Methodology:** It was a cross-sectional, comparative study. Data was collected from July to December 2018 after obtaining informed consent of the subjects. The participants included 20 non-obese healthy males, and non-obese males angiographically confirmed having coronary artery disease. All participants were non-smoker, non-diabetic, and age matched from 35–55 years. Serum visfatin was analyzed using ELISA. Anthropometric measurements including waist circumference, hip circumference, and body mass index was evaluated and correlated with serum visfatin. Statistical analysis was done using SPSS-20. The values were considered significant at $p<0.05$. **Results:** Serum visfatin levels were significantly lower (3.90 ng/ml) in non-obese coronary artery disease group as compared to healthy males (4.85 ng/ml). No significant correlation was found with anthropometric measurements. **Conclusion:** Significant lower level of serum visfatin in non-obese male coronary artery disease patients depicts its probable cardioprotective role that is independent of anthropometric measurements.

Keywords: Visfatin, waist circumference, hip circumference, body mass index

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INTRODUCTION

The adipocytokine visfatin that simulates the glucose decreasing effect like insulin, and initiates phosphatidylinositol-3-OH kinase (PI3K) pro-survival kinases-protein kinase B and mitogen-activated protein kinase 1 and 2 (MEK1/2)-extracellular signal-regulated kinase 1 and 2 (Erk 1/2)[1] may have an anti-apoptotic effects[2]. Inhibition of mitochondrial permeability transfer pore (mPTP), activation of these kinases reverses cardioprotection. Mechanism of direct cardioprotective action of visfatin is still unclear. Visfatin can minimize myocardial damage within murine heart and insulated murine cardiomyocytes when directed during myocardial recovery. The mechanism has a tendency to cover MEK1/2, the PI3K pathways and mPTP.[3] This may be due to the lack of serum visfatin in male patients with non-obese coronary artery disease. Initiation of the above-mentioned kinases maintains powerful cardioprotection at the time of myocardial reperfusion[4,5], and that inhibition of the mitochondrial permeability transition pore (mPTP)[6] is the second consequence. mPTP is a non-specific mitochondrial channel whose initiation of myocardial reperfusion in the first few minutes is a major contributing factor to cardiomyocyte death.[7]

The visfatin gene is impaired by hypoxia-inducible factor[8,9] increasing the likelihood of up-regulation of visfatin in response to myocardial ischemia. Visfatin was previously known as a pre-B cell colony enhancing factor (PBEF)[10], a growth factor associated with a number of cellular processes for early B cells, with studies showing that PBEF acts as a biomarker of acute pulmonary injury[11,12] up-regulated in infected foetal membranes[13], neutrophil apoptosis is prevented by laboratory inflammation and clinical sepsis[2] and is involved in the growth of vascular smooth muscle cells through a mechanism based on nicotinamide adenine dinucleotide (NAD)[14]. The enzyme nicotinamide phosphoribosyltransferase (Nampt), the rate-limiting enzyme in NAD biosynthesis that mediates the conversion of nicotinamide into nicotinamide mononucleotide[15], was also known as PBEF/visfatin. It is uncertain if visfatin contributes in clinical setting to cardioprotection. Recent studies have related visfatin to MAPK-mediated angiogenesis[16] and to a possible pro-inflammatory facilitator in atherosclerotic plaques, indicating that endogenous visfatin may have a negative effect on coronary artery disease.[17]

Visfatin plasma concentrations have no significant variations in visfatin *m*RNA expression between human visceral and subcutaneous adipose tissue.[18] The levels of circulating visfatin were decreased in morbidly obese men after gastric banding.[19] In acute and chronic cases, these effects of visfatin vary. The aim of this study was to detect the serum visfatin concentration in healthy males and compare it with non-obese male patients of coronary artery disease to access possible cardioprotective role of visfatin.

METHODOLOGY

This was a cross-sectional study including 20 non-obese healthy males without coronary artery disease and 20 non-obese male patients with angigraphically confirmed coronary artery disease. The sample size was calculated to be 20 in each group.

Waist and hip circumferences were recorded (Cm). Waist to hip ratio was calculated. Height (m) and weight (Kg) in all subjects were recorded wearing usual clothes, without shoes. Body mass index (BMI) was calculated as:

BMI=Weight in Kg/(Height in m)²

Subjects were categorized as normal, BMI=18.0–22.9, over weight, BMI=23.0–24.9, and obese, BMI≥25 (Table-1).

Serum visfatin levels were determined by Nampt/PBEF, Human ELISA kit manufactured by Enzo Life Sciences (ELS) AG Switzerland, with an analyzer STAT FAX 303 Reader. The intensity of the colour reaction was measured at 450 nm after acidification and was directly proportional to the concentration of Nampt in the samples. Statistical analysis was done using SPSS-20, and $p<0.05$ was taken as significant.

RESULTS

There was no significant difference between BMI, Waist circumference, and Waist-Hip ratio in group A and group B (p=0.979, 0.126, and 0.978 respectively). The difference between group A and group B was significant (p=0.048) in hip circumference (Table-1).

Median (IQR) of group A was 4.85 ng/ml (3.55–8.60), group B was 3.90 ng/ml (2.70–5.0) compared using Mann-Whitney U test as data was not normally distributed (Table-2).

Statistically non-significant negative correlation was observed with serum visfatin and BMI. (r= -0.19, p=0.419) in group A. No significant correlation was observed between serum visfatin and BMI in group B; waist circumference, hip circumference, and waist-hip ratio in group A and B (Table-3).

Table-1: Comparison of anthropometric measurements between groups A and B

Anthropometric Parameters	Group A Healthy (n=20)	Group B CAD (n=20)	*p*
BMI (Kg/m²)	22.00±0.73	22.07±0.89	0.979
Waist Circumference (Cm)	77.85±5.71	80.75±3.24	0.126
Hip Circumference (Cm)	89.00±6.37	92.85±3.66	0.048*
Waist-Hip Ratio	0.87±0.01	0.87±0.02	0.978

Mean±SD, *Statistically significant

Table-2: Comparison of serum visfatin between group A and group B using Mann-Whitney U test

Biochemical Parameter	Group A (n=20)	Group B (n=20)	*p*
Serum Visfatin (ng/ml)	4.85 (3.55–8.60)	3.90 (2.7–5.0)	0.046*

Values are given as Median (IQR), *Statistically significant

Table-3: Correlation of serum visfatin with anthropometric measurements

Serum visfatin & anthropometric measurements	Group A (n=20)		Group B (n=20)	
	r	*p*	*r*	*p*
BMI	-0.19	0.419	0.37	0.113
WC	0.13	0.591	0.40	0.083
HC	0.11	0.644	0.22	0.346
WHR	0.35	0.132	0.19	0.428

DISCUSSION

Serum visfatin concentrations are significantly lower in male subjects with coronary artery disease as compared to healthy non-obese male patients in our study. Serum visfatin shows no significant correlation with waist circumference, hip circumference, and body mass index.

Recent evidence indicates that visfatin can be responsible, depending on the cell type and length of treatment, for a variety of cardiovascular effects, one of which involves the ability to shield the myocardium from adverse effects of acute ischemia-reperfusion injury.[19] As such, visfatin may not only provide a potential new cardioprotection target but may also serve as an anti-diabetic agent with an exclusive mechanism of action to provide diabetic patients of an episode of acute myocardial ischemia-reperfusion injury with a potential new drug target. This is also confirmed by Lovren *et al*[20] who stated that visfatin-containing plasmid injection in a unilateral limb ischemia mouse model resulted in improved limb perfusion compared with untreated animals.

Results are contradictory on the relationship between anthropometric parameters and levels of visfatin. Some researchers found associations between visfatin and BMI, others showed no correlation[21] or even negative correlation[22]. There were no changes in the BMI or waist circumference between the patients and the controls in our study. The findings showed that visfatin and BMI levels were not significantly associated with coronary artery disease in non-obese male patients.

BMI plays a major role in the development of cardiovascular diseases and is shown in Table-3 in the current study. In healthy groups, there is a negative but not significant association. With respect to cardiovascular disease[20], visfatin has been reported to have many different effects. These involve endothelial dysfunction, angiogenesis, instability of the atherosclerotic plaque, and cardioprotection. The interesting finding is that visfatin can directly protect the myocardium at the cardiomyocyte level against the symptoms of acute ischemia-reperfusion injury.[23] The function of visfatin levels that are lowered in non-obese male patients with coronary artery disease is difficult to determine as being cardioprotective. Reduced levels of visfatin in non-obese male CAD patients may play a protective role in the heart. Visfatin's vascular function in chronic and acute cases is different.

High visfatin concentrations stimulate endothelial dysfunction, atherosclerotic plaque unstabilization, angiogenesis, such as in obesity and type 2 diabetes mellitus when exposed for longer time. Immediate visfatin administration stimulates endothelial nitrous oxide synthase expression and activity in endothelial cells and directly protects cardiomyocytes from the adverse effects of acute ischemia-reperfusion injury.[24] The role of visfatin as a cardioprotective agent may be observed in large-scale studies.

CONCLUSION

Significant lower levels of serum visfatin in non-obese male patients with coronary artery disease represent most likely its cardioprotective role and are independent of anthropometric measurements. Further studies on a larger scale are recommended including females subjects.

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