Coronary heart disease (CHD) is the prominent cause of death worldwide and the main reason for coronary artery disease, cardiovascular diseases, and stroke is hypercholesterolemia (1). Statins are the most broadly utilized cholesterol-lowering agents. They reduce lipid levels in patients with dyslipidemia, cardiovascular disease and atherosclerosis, furthermore decrease morbidity and mortality (2, 3). Over the previous few years’ lipid-independent actions are attributed to this class of drugs progressing their anti-atherosclerotic role further than lipid lowering i.e., pleiotropic mechanisms (4). The question is whether or not the pleiotropic anti-inflammatory effects of statins are due to the modification of serum adipokines or not. In this perspective, contradictory results have been shown by previous studies that tested the effects of statins on adipokines (5). Visfatin is an adipokine which mostly found in visceral adipose tissue (6). Visfatin, has role in plaque destabilization, the promotion of angiogenesis, and glucose homeostasis, so it may have a role in atherosclerosis and coronary artery disease (7, 8). Visfatin seems to be a direct contributor to vascular inflammation and a distinctive attribute of atherothrombotic diseases linked to metabolic disorders (7). Vaspin is another member of adipokines which eventually identified in visceral white adipose tissue (9). It has anti-inflammatory and anti-apoptotic effects on vascular cells as well as improving insulin resistance. Vaspin could impede inflammatory factor secretion from vascular smooth muscle cells and counteract endothelial cell apoptosis induced by free fatty acid (10). Rosuvastatin is a commonly used HMG-CoA reductase inhibitor (statin) and is used to improve lipid profiles in patients with coronary artery diseases (11).

RESEARCH METHODOLOGY

Patient population and study design

A non-randomized controlled, prospective study conducted on 80 Patients (Figure 1), who underwent coronary angiography due to symptoms of stable angina at Cardiology department, Faculty of Medicine, Tanta University Hospital from January 2017 to January 2018. Stable angina defined as the presence of chest pain that did not change its pattern during the preceding 2 months.

AIM OF THE STUDY: Investigate the effect of Rosuvastatin on serum levels of Vaspin and Visfatin in patients with CAD and determine the association between those adipokines and the severity of CAD.

BACKGROUND: Statin treatment is considered one of the most effective strategies for the stabilization of atherosclerotic plaques and is related with enhancements in result in patients with coronary course diseases (CAD). Vaspin and Visfatin are adipokines involved in atherosclerosis progression. Objective: assess the impact of Rosuvastatin on serum level of Vaspin and Visfatin in patients with CAD and the relationship of those adipokines with seriousness of CAD.

METHODS: 80 patients who underwent coronary angiography due to symptoms of stable angina were enrolled in the study. 40 patients received Rosuvastatin 20 mg/day was compared to another 40 patients, as a control group, who refused statin treatment and preferred lifestyle modifications intervention. Main outcome measure: Clinical parameters, lipid profile, troponin I, high-sensitivity C-reactive protein (hs-CRP), Vaspin and Visfatin levels were assayed at the beginning and after 3 months. CAD severity was assessed by the Gensini score.

RESULTS: Rosuvastatin administration considerably ameliorated most lipid parameters. Moreover, a significant increase of Vaspin and decrease of Visfatin concentrations (p<0.001) after Rosuvastatin treatment were observed (from 2.81 ± 0.74 ng/ml to 4.26 ± 0.76 ng/ml, from 4.62 ± 0.76 to 3.13 ± 0.98 respectively). There was a negative correlation between Vaspin and the Gensini score and positive correlation between Visfatin and Gensini score (r=0.18 and r=0.19, p<0.05, respectively).

CONCLUSION: Rosuvastatin treatment reduces serum visfatin and increase serum vaspin levels in CAD patients. Those effects of Rosuvastatin are of clinical importance.

Key Words: Vaspin; Visfatin; Rosuvastatin; Gensini score; Coronary Artery Disease

Coronary Artery Disease (CAD) is a chronic disease characterized by the accumulation and growth of atherosclerotic plaques in the coronary arteries. It is the leading cause of death in the United States, accounting for more than 600,000 deaths each year (1). CAD is often asymptomatic in its early stages, and symptoms may not appear until the disease is advanced. Some common symptoms include chest pain or discomfort, shortness of breath, and pain or discomfort in other parts of the body. Early diagnosis and treatment are crucial to prevent complications such as heart attack or stroke.

METHODS

Aims and Objectives

The primary aims of the study were to investigate the effects of Rosuvastatin on serum levels of vaspin and visfatin in patients with CAD and to determine the association between these adipokines and the severity of CAD.

Study Design

This was a non-randomized, controlled, prospective study conducted at a single center. A total of 80 patients were enrolled in the study. The patients were divided into two groups: a treatment group (40 patients) and a control group (40 patients). The treatment group received Rosuvastatin (20 mg/day) for three months, while the control group followed lifestyle modifications and received placebo.

Outcomes

The main outcome measure was the change in serum levels of vaspin and visfatin at the end of the study compared to the baseline levels. Secondary outcomes included changes in clinical parameters, lipid profile, troponin I, high-sensitivity C-reactive protein (hs-CRP), and the Gensini score to assess the severity of CAD.

Data Analysis

Statistical analysis was performed using SPSS software. Descriptive statistics were used to summarize the baseline characteristics of the study population. Differences in mean serum levels of vaspin and visfatin between the treatment and control groups were analyzed using the Student’s t-test. The association between these adipokines and the severity of CAD was assessed using the Pearson correlation coefficient.

RESULTS

The results showed a significant increase in the serum levels of vaspin and a significant decrease in the serum levels of visfatin in the treatment group compared to the control group. Additionally, a negative correlation was found between vaspin and the Gensini score, while a positive correlation was observed between visfatin and the Gensini score.

CONCLUSION

Our study provides evidence that Rosuvastatin treatment increases serum levels of vaspin and decreases serum levels of visfatin in patients with CAD. These changes may be attributed to the pleiotropic effects of statins beyond their lipid-lowering properties. The findings also indicate that vaspin and visfatin may be potential biomarkers for assessing the severity of CAD.

Key Words: Vaspin; Visfatin; Rosuvastatin; Gensini score; Coronary Artery Disease

Figure 1: Study flow chart for patients in control and Rosuvastatin groups

For all patients, cardiovascular history was taken, complete physical examination was performed. Electrocardiogram and echocardiography were done then any abnormalities were recorded. Patients with a history of acute coronary syndrome within the past 6 months, severe chronic heart failure, NYHA class III–IV, cardiomyopathy, diabetes mellitus, morbid obesity or surgery, renal insufficiency (creatinine >2 mg/dl), liver impairment (ALT >2 times upper normal limit), acute or chronic infectious disease, or any kind of immune-mediated disease were excluded from the study. According to the study design 61 patients completed the study. 31 patients received Rosuvastatin 20 mg/day for three months were compared to 30 patients who refused statin treatment and preferred lifestyle modifications intervention.
refused to take statin medications, and preferred lifestyle modifications intervention (i.e., adherence to a heart-healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight). Both patient groups were homogeneous and followed up for three months.

Blood assays
After an overnight fasting, 10 ml venous blood samples were withdrawn from the antecubital vein under complete aseptic condition before coronary angiography. The collected blood samples were centrifuged then the separated sera were stored at -80°C until measurement of biochemical parameters. Serum Vasin and Visfatin were measured by an ELISA kit for quantitative determination (GLORY Science, USA). Total cholesterol, triglyceride, high density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured by the enzymatic colorimetric method using Roche/Hitachi/911 automated Clinical Chemistry Analyzer. The Kit manufactured by Roche Diagnostics gmbh, D-68298 Mannheim, USA. The serum Troponin-I was assayed using ELISA kit (Biocheck, Inc-Foster City, California). Highly Sensitive-C-Reactive Protein was determined by the ELISA method [Labor Diagnostika Nord-Nordhorn-Germany] kits. Routine determination of random blood glucose and creatinine level was performed.

Coronary angiography
Diagnostic coronary angiography was done to all patients through either femoral or radial approach. Gensini score was used to assess the severity of CAD by an experienced cardiologist, unaware of the biochemical results of the patients. Gensini score was calculated through multiplication of score used for grading the luminal narrowing of the main coronary artery by a factor which was take into account the site and importance of the lesion. The score of luminal narrowing was 1 for ≤ 25% stenosis, 2 for 26-50% stenosis, 4 for 51-75% stenosis, and 8 for 76-90% stenosis, 16 for 91-99% stenosis and 32 for total occlusion. The factor of location was 5 for left main, 2.5 for the proximal lesion of either LAD (left anterior descending) or LCX (left circus anterior) coronary artery. Then the sum of scores of all coronary arteries was used to express the total Gensini score (12).

### STATISTICAL ANALYSIS

Variables were presented as mean ± SD. Comparisons between two groups were carried out using an independent sample t-test. Correlation analysis using the Pearson coefficient of correlation was performed. p-value<0.05 will consider significant. SPSS for windows software was used for statistical analysis (Version 22, SPSS Inc., Chicago, IL, USA).
**DISCUSSION**

The present study showed that treatment with Rosuvastatin increased Vaspin serum levels in patients compared to control groups. In agreement with a recent study stated that Rosuvastatin significantly increases vaspin serum levels in acute coronary syndrome (13). On the other hand, a reduced Visfatin serum levels were observed in patients treated with Rosuvastatin compared to control groups. Consistence with a meta-analysis found that visfatin levels slightly reduced after statin therapy (14).

Furthermore, the present results showed a negative correlation of Vaspin with severity of CAD which assessed using Gensini score. In agreement with the present results, Kadoglou et al. (15) revealed a decreased Vaspin serum levels in asymptomatic patients with CAD compared with healthy control subjects. Moreover, they observed that low circulating vaspin concentrations were significantly correlated with CAD severity. In addition, Kobat et al. (16) found that, serum Vaspin levels significantly lower in patients with CAD consistently with our result. So, it may be used as a prognosticator of this disease However, they did not define the correlation of Vaspin and its relation to the severity of CAD. Moreover, Li et al. (17) studied the association of Vaspin gene polymorphisms with CAD in Chinese population. Their results showed that the serum Vaspin levels and risk for CAD. On the other hand, AUST et al. (18) could not found any relation between serum Vaspin levels and severity of atherosclerosis but they demonstrated that lower Vaspin serum levels had correlation with recent ischemic events in patients with carotid artery stenosis. Accordingly, they assumed that this biomarker may have a protecting role in patients with CAD. On the other hand, our results revealed a significant positive correlation between Visfatin serum levels with severity of CAD which assessed using Gensini score. In agreement with our result, Fu et al. (19) found a significant positive correlation between plasma Visfatin level and coronary lesion severity score. They concluded that there is a link between Visfatin level and the pathogenesis of CAD, so the detection of this adipokine might be useful for early diagnosis of CAD. In addition, Liu et al. (20) found that, plasma Visfatin levels were significantly higher in chronic CAD and acute coronary syndromes compared with control patients. The present study also found a significance decrease in total cholesterol and triglyceride LDL-cholesterol levels in patients received Rosuvastatin for three months compared to control group. In agreement with a recent study stated that treatment with Rosuvastatin displays a high efficacy in the improvement of lipid profile, and its pleiotropic effects (anti-inflammatory, antioxidant and antiatherogenic), represents a fundamental role for cardiovascular primary and secondary prevention (21).

The present study revealed that Rosuvastatin therapy significantly decrease the serum level of hs-CRP level compared with control. This effect could be associated with the ability of statins to block pro-inflammatory transduction pathways (22). Pervious study assessed the effect of statin on inflammatory markers in chronic heart failure patients demonstrated that significant decrease in hs-CRP level was associated with statin therapy (13,23). The present study found a significant negative correlation between hs-CRP serum levels with Vaspin serum levels. Consistently, Seeger et al. (24) found a negative relationship between Vaspin and CRP in patients on chronic hemodialysis and Kadoglou et al. (15) found an independent association of reduced Vaspin with increased hs-CRP and Visfatin levels suggesting a protective mechanism. Previous studies also, have indicated that CRP is an independent risk factor for atherosclerotic cardiovascular disease (25).

The present study also revealed that serum Troponin I levels, as indicator of myocyte injury, were decreased after Rosuvastatin treatment but insignificant difference was found when compared Rosuvastatin group with control group (p=0.07). Consistently, Everett et al., found no difference in high-sensitivity cardiac troponin I concentrations after Rosuvastatin 20 mg/d or control (26). Conversely, with the present results a recent study conducted on rats by Zhou et al. (27) showed that Rosuvastatin (5 mg/kg) significantly reduced the increased serum content of cardiac troponin I. The present study showed that Rosuvastatin treatment reduce serum Visfatin levels and increase serum Vaspin level, that may represent an antiatherogenic property of the drug, which is independent of its lipid-lowering capability.

**CONCLUSION**

Rosuvastatin treatment rather than lifestyle modification reduce serum visfatin and increase serum vaspin levels in CAD patients. Those pleiotropic-associated effects of Rosuvastatin are of clinical importance. Moreover, low vaspin and high visfatin levels were significantly correlated with CAD severity suggesting a relation between atherosclerosis and adiposity.

**CONFLICTS OF INTEREST**

The authors declare no conflicts of interest.

**ETHICS APPROVAL**

The study was approved by the ethical committee of Tanta University. All patients were informed about the study, and their written consent forms were obtained.

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**REFERENCES**


