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Adiponectin in Relation to Glucose and Insulin Resistance in Asthma Patients

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ABSTRACT
Although there is evidence of a positive association between asthma and obesity in adults and children, the specific mechanisms responsible for these observations are not obvious. The purpose of this study was to examine the relation of serum adiponectin with to marker indicators of blood glucose and spirometry indexes in asthma patients.
For this purpose, Forty eight sedentary males with mild to moderate asthma were enrolled to the study by voluntarily. All patients underwent anthropometrical measurements, a resting spirometry testing and fasting blood sampling for measuring serum adiponectin, insulin and glucose. Insulin resistance and Beta cell function were assessed using the homeostasis model assessment for insulin resistance formula derived from fasting insulin and glucose levels. Pearson correlation method used to determine the relationship between adiponectin with the other variables.
A statistically significant inverse correlation was observed between serum adiponectin with insulin, glucose, insulin resistance and marker indicators if asthma diagnosis such as FEV1 ($p < 0.05$). In addition, serum adiponectin level was positive correlated with Beta cell function ($p < 0.05$).
Based on our results, it seems that In addition to spirometry testing, serum adiponectin is a indicator of asthma diagnosis in obese subjects. Also, serum adiponectin is a precise predictor of glucose and its determinatives in asthma patients.
***Keywords**: Asthma, Spirometry, serum adiponectin, insulin resistance*

INTRODUCTION

Increased visceral fat affects insulin sensitivity and energy metabolism by releasing adipokines into the blood circulation. So with the absorption of these cytokines by target tissue, fat and carbohydrate metabolism is affected [1]. Longitudinal studies have shown that obesity is a precursor of the prevalence of asthma and that the relative risk of asthma prevalence escalates by obesity [2, 3]. The developing mechanisms of this relationship can include mechanical effects such as narrowing of respiratory channels smooth by the flat muscles of respiratory routes, adipose tissue immunological effects, unidentified hormonal factors, nutritional factors and sedentary [4]. Serum adiponectin as an anti-inflammatory adipokine decreases in the presence of obesity that is associated with decreased absorption of muscle glucose and fat oxidation [1]. The insulin-like function of this 244-amino-acid peptide hormone [5, 6] has shown that the reduction of its plasma concentration is effective on obesity and its related diseases like diabetes II [1]. Decreased adiponectin concentration in obese individuals compared with people with normal weight as well as insulin resistant populations has been frequently observed [7, 8].

There is also this hypothesis that decreased serum adiponectin concentration in humans due to obesity is effective on the spread of asthma [9]. Since adiponectin receptors exist in smooth muscle cells of the respiratory pathways, this hypothesis has been propounded by some researchers that reduced adiponectin concentration in obese individuals is effective in proliferation of smooth muscle cells of the respiratory pathways in asthma [10]. Moreover scientific sources maintain that adiponectin level also decreases in obese asthmatic patients [11]. These findings also suggest increased insulin resistance and impaired insulin secretion and glucose metabolism in asthmatic patients [12]. Asthma is an inflammatory disease and in recent years obesity has also been listed as an inflammatory disease [13]. This hypothesis is always raised that insulin resistance and impaired glucose uptake are always effective in obesity induced asthma but there is no comprehensive information in this area [13,14]. Some studies have revealed that reduced systemic adiponectin is associated with increased blood glucose concentration [15]. These studies argue increased adiponectin levels due to increased muscle glucose uptake leads to a decrease in blood glucose concentration [1]. On the other hand, in spite of the impact of decreased blood adiponectin levels on muscle glucose uptake in asthmatic patients, the mechanisms responsible for it are not yet known

[16]. It is likely that the impact of adiponectin on muscle glucose uptake and its concentration in blood circulation and other tissues is also associated to some extent with the presence of insulin and its secretion from pancreatic beta cells; because regardless of the numerous findings about increased insulin resistance in asthmatic patients, particularly in obese asthma patients some recent findings have also reported that insulin resistance in these patients would not increase [12]. Certain studies have also suggested there that no significant correlation between plasma or serum adiponectin levels with insulin resistance in asthmatic patients [14].

These findings some how amplify the importance of there being a relationship between adiponectin levels with the amount of insulin or the function of beta cells in secreting insulin on blood glucose concentration. In this regard, a recent review of studies argues that in addition to anti-inflammatory and anti-atherogenic effects adiponectin also seems the increase plasma insulin [17]. Also, some studies also mention the large number of adiponectin receptors in pancreatic beta cell which is the main place of insulin secretion [18] and this somehow supports the possible effect of adiponectin on insulin secretion from beta cells and the functioning of these cells. In this area, studies on other diseases associated with obesity such as type II diabetes have shown that the baseline adiponectin concentration has a positive correlation with insulin sensitivity and insulin secretion by beta cells and by influencing these variables its increase would reduce blood glucose concentration, especially in people hyperglycemia [19].

It has also been established that there is a significant correlation between increase in adiponectin levels and decreased blood glucose concentration caused by exercise [20]. Study on patients with type II diabetes which is another obesity-related chronic disease has indicated that like insulin, as an anti-inflammatory peptide hormone adiponectin reduces hyperglycemia phenomenon these patients by affecting muscle glucose uptake [1]. However, there few studies on the relationship between serum or plasma adiponectin with blood glucose levels and its influencing factors in asthmatic patients and there are very few documented findings available. Hence, this study aims to explore the relationship between serum adiponectin with glucose and other components affecting it such as insulin concentration and beta cell function in adult asthmatic patients.

MATERIALS AND METHODS

The statistical population of this correlation study consists of a group of asthmatic men in Saveh City, Iran. The sample of the study consists of 48 obese or overweight asthmatic man (BMI ≥ 26, age: 38 to 50 year, weight: 78 to 112 Kg) without any type of orthopedic diseases and after assessment of their medical history and determination of the Illness severity level by heart and lung specialist physicians participated in the study by Easy sampling. Intensity Illness Asthma severity was determined by specialist physicians measuring spirometry indices (Minispire model, Made in Italy). History of asthma and medication were recorded by a specialist physician. Participants were included if they had not been involved in regular physical activity/diet in the previous 6 months. Subjects were reported to be non-smokers, not currently taking supplements of any kind, and having no major health problems (i.e., diabetes, cardiovascular disease, etc.). All subjects had a body mass index (BMI) of upper than 26. Written informed consent was obtained from all participants.

At first, each participant underwent a resting spirometry testing for measuring FEV1/FVC, FEV1, FVC, FEF% 25 /% 75, PEF. Also, anthropometric indices of the individuals were measured and recorded. Body composition monitor (BF508-Omron made in Finland) with a precision error of less than 100 g was used to measure weight of the subjects. Subjects' height was carefully measured while standing along the wall without shoes while their shoulders were in normal conditions. Body mass index (BMI) was calculated using weight divided by squared height.

In next stage, after anthropometric measurements, all patients were asked to attend Hematology Lab following 12 hours of overnight fasting, between the hours of 8 to 9 am for blood sampling. The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. Fasting blood samples were collected from brachial vein in sitting position in order to measuring serum adiponectin, glucose and insulin.

Blood samples were centrifuged for 10 Minutes with 2000 rpm to separate serum. Blood glucose concentration was performed by Kobas auto-analyzer by glucose oxidase enzyme method (Pars Azmoon kit, Tehran). Serum adiponectin was determined by ELISA method, using a Biovendor-Laboratorial kit made by Biovendor Company, Czech. The Intra- assay coefficient of variation and

sensitivity of the method were 3.9% and 5-50 ng/mL, respectively. Serum insulin was determined by ELISA method (Demedite, German). The Intra- assay coefficient of variation and sensitivity of the method were 2.6% and 2.88 µg/L, respectively. Beta cell function was calculated using fasting glucose and insulin in the respective formula [21].

Statistical analysis: Data were analyzed by computer using SPSS software version 15.0. Pearson correlations were used to establish the relationship between adiponectin concentration with spirometry and biochemistry markers. A p-value < 0.05 was considered to be statistically significant.

RESULTS

This study was conducted aiming to determine the relationship between serum adiponectin levels and beta cells function and respiratory parameters selected in 45 adult asthmatic men. All numerical information of adiponectin in relation to the other spirometry indices and biochemical parameters are summarized in Table 1. Statistical results showed that serum adiponectin levels would decrease in patients parallel to reduction of each spirometry indices such as FEV1/FVC ،FVC ،FEF%25 / %75 و PEF. Also a significant positive relationship was revealed between adiponectin concentration and asthma severity index (FEV1). Significant correlations were found between in serum adiponectin and beta cell function. Adiponectin showed a significant positive relationship with serum insulin. Also a significant negative correlation was observed between fasting glucose and serum adiponectin concentrations.

Table 1: Association between serum adiponectin and spirometric and biochemical indexes in studied patients

Variable	Mean	Standard deviation	Range	Relation with adiponectin
FEV1 (%)	71.42	7.14	64 - 74	P = 0.0 02 , r = - 0. 69
FVC (%)	79.18	4.28	74 - 82	P = 0.0 36 , r = - 0. 49
FEV1 / FVC (%)	67.11	5.11	62 – 73	P = 0.0 41 , r = - 0. 38
PEF (%)	78.44	10.23	68 – 85	P = 0.0 21 , r = - 0. 58
FEF %25 / %75	59.21	10.14	52 – 68	P = 0.0 31 , r = - 0. 51
glucose(mm/L)	115	23	93 – 125	P = 0.0 32 , r = - 0. 47
Insulin(µIU/ml)	11.65	4.12	6 – 14	P = 0.0 25 , r = - 0. 52
Insulin resistance	2.89	0.58	1.98 – 3.23	P = 0.0 41 , r = - 0. 43
Beta cell function	65.5	18.21	47 – 78	P = 0.0 04 , r = - 0. 52
Adiponectin (µg/ml**)**	5.29	1.68	3.78 – 4.11	----------

FEV1*: forced expiratory volume in 1 s* **, FVC***; forced vital capacity,*
FEV1 / FVC ratio*: forced expiratory volume in 1 s / forced* vital capacity
PEF: Peak Expiratory Flow**, FEF %25 / %75 :** Forced inspiratory flow 25–75%

DISCUSSION

The findings of this study showed that serum adiponectin have an inverse and significant correlation with blood glucose concentration and that it is directly related to beta cells function. Also the findings of this study also indicate a significant inverse relationship between adiponectin and BMI. Human and animal studies support the relationship between asthma and obesity and confirm the potential effect of obesity on inflammation of respiratory pathways [9, 22] bronchospasm of respiratory pathways [23, 24] and respiratory pathways remodeling [25]; although the exact molecular mechanisms that justify this correlation are not yet fully known. However in asthmatic patients decreased FEV1 is known as a sign of intensified disease. The findings of this study showed that the decrease in serum adiponectin levels of the subjects were significantly positive correlated with FEV1 as a marker indicator of asthma severity. In other words, in asthmatic patients the more the disease intensity increases from mild to moderate the more does decrease blood adiponectin concentration. In spite of these findings, serum adiponectin levels had a significant positive correlation with other spirometry indices such as, FEV1/FVC, FVC, PEF and FEF% 25 /% 75 all of which point out that the reduction in systemic adiponectin in these patients is associated with a reduction in spirometry indices. Increased proliferation of smooth muscles of respiratory pathways

in obese individuals is the main narrowing factors of respiratory pathways and adiponectin prevents proliferation of muscles in the respiratory pathways in obese asthmatic mice [9]. Subcutaneous injection of adiponectin in a recent study reduced the inflammation of respiratory pathways in asthmatic mice [9, 10].

Studies in the recent years demonstrate that in addition to having great energy reserve, the fat tissue as an endocrine organ plays an important role in homeostasis and energy metabolism. In addition to production of free fatty acid, fat tissue secrete some cytokines too and these proteins have biological functions like regulation of energy uptake and expenditure, regulation of glucose and lipid metabolism and also inflammatory and inflammatory features [26]. Scientific studies maintain that some of these molecules derived from adipose tissue are involved in the pathophysiology of atherosclerosis, insulin resistance and obesity related chronic diseases like diabetes II and inflammatory diseases such as asthma [27, 28]. Meanwhile, some reports focus on identification of adiponectin and its function in diseases associated with obesity.

Despite numerous studies, effective factors and precursors of insulin sensitivity and function of beta cells in healthy adult populations and the patient are not yet fully known. The effective role of blood insulin concentration, insulin sensitivity and beta cells function has been demonstrated repeatedly in blood glucose concentration. As any change in any of them would somehow influence the blood glucose concentration [29, 30, 31]. Hence, it appears that determining the relationship between adiponectin and these factors that determine blood glucose is of particular importance. In a recent study showed that adiponectin concentration has a positive correlation with each insulin sensitivity index and beta cells function and their increased would prevent the phenomenon of hyperglycemia [19]. Also extensive studies have concentrated the relationship between blood adiponectin and glucose with different types of diseases. The findings of this study on adult asthma patients showed that as a pre-inflammatory cytokine baseline adiponectin probably plays an effective role in the alteration of blood insulin levels. With regard to this, a significant relationship between serum adiponectin and beta cells function was obtained in this study. In such a way that the pattern of direct linear relationship demonstrates that increased systemic adiponectin levels would probably leads to enhanced Beta cells function. These findings were observed while in some recent studies have reported high levels of adiponectin receptors in pancreatic beta cells [18]. However, the findings of this study indicate significant positive correlation between serum adiponectin and insulin. In the study of weyer et al a significant correlation between adiponectin and insulin levels was observed [8]. The boosting effect of adiponectin on systemic insulin has also been reported in the study of Spranger et al [32]. Also considering the pattern of significant negative relationship between adiponectin and fasting glucose in the present study, it appears that the decrease in fasting glucose levels in dependent on the pattern of direct correlation between adiponectin and insulin or beta cells function. In line with these findings, in a recent study, injection of adiponectin significantly decreased blood glucose levels which were accompanied by increase in insulin function [33]. Some scientific studies also notes that the spherical shape of adiponectin increases glucose uptake in muscle cells by GLUT 4 and also slow down glycogen synthesis all which play a significant role in reducing blood glucose concentrations [34].

CONCLUSION

The direct link between adiponectin levels and spirometry indices showed that decreased adiponectin concentration is associated with increased severity of this disease. Also decreased adiponectin levels in asthmatic patient are associated with increased blood glucose concentration. These findings along with other previous human and models animal studies suggest that adiponectin levels in blood circulation due influence on Insulin would affect insulin resistance pancreatic beta cells function, and blood glucose levels. Of course it is likely that the association observed between serum adiponectin concentration and beta cells function is not specific to asthma patients. Hence, it is recommended that similar studies should be conducted on other chronic diseases associated with obesity and with a larger number of samples.

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Conflict of interest

The authors declare that they have no Conflict of Interests