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Study of Serum Adiponectin level in Obese and Non-obese Asthmatic Patients

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Abstract

Background : Asthma is a worldwide problem, with an estimated 300 million affected individuals. Although central (visceral) adipocytes are the most important source of adiponectin (APN), there is a tendency for reduced serum adiponectin concentration among obese subjects suggesting that decreased APN levels may contribute to the increased inflammatory state as in asthma.

Aim of the work: The aim of this work was to determine whether serum concentration of adiponectin changed in asthmatic patients during acute attack and in remission or not.

Subjects and Methods: Fifty five subjects were included in this study from Chest department, Benha university hospital .40 patients with bronchial asthma(20 obese and 20 nonobese) and 15 age related healthy subject(7 obese and 8 nonobese**)** as a control. All asthmatic patients and control group were divided into non-obese and obese according to their body mass index(BMI) Those with BMI < 25& >18.5 were considered non-obese, Those with BMI> 30 were considered obese .Those with BMI . 25 and. 30 were considered overweight and were not included in this study (NIH/NHLBI, 1998). All subjects were submitted to the following, Full history taking ,Complete physical examination(General & Local),Plain x-ray chest P-A & left lateral views ,Complete blood count , Erythrocyte sedimentation rate, Liver and kidney function tests, Fasting and post prandial blood sugar, Ventilatory function tests , Venous blood samples were taken for Adiponectin level measurement.

Results : Serum adiponectin(µg/ml) in obese control subjects (3.25 ± 0.65 µg/ml) was highly significant lower than that in nonobese control subjects(10.51 ± 1.55µg/ml), (P-value < 0.001). Also serum adiponectin revealed highly significant decrease in obese asthmatics during attack (1.58 ± 0.724 µg /ml) than in obese asthmatics during remission (2.08 ± 0.74 µg /ml) and that in obese control subjects (3.25 ± 0.65 µg /ml), (P-value < 0.001).Serum adiponectin(µg/ml) was significantly higher in nonobese asthmatics during remission (9.49 ± 2.49 µg /ml) than in nonobese asthmatics during attack (7.89 ± 2.7 µg /ml) and both was lower than that in nonobese control subjects , (p-value < 0.05).Serum adiponectin (µg /ml) was highly significant lower in obese asthmatics during attack (1.58 ±0.72 µg/ml) than in obese asthmatics during remission(2.08 ± 0.74 µg /ml), (P-value < 0.001) and highly significant higher in nonobese asthmatics during

attack (7.89 ± 2.7 ìg/ml) than in nonobese asthmatics during remission (9.49 ± 2.49 µg /ml), (P-value < 0.001).

Conclusion: Serum adiponectin was significantly decreased in asthmatic patients (obese and nonobese) than control subjects also serum adiponectin level was significantly lower during attack than in remission.

Key words: obesity, serum adiponectin level , body mass index, asthma exacerbation & remission.

Introduction

Asthma is a worldwide problem, with an estimated 300 million affected individuals **(Beasley, 2004).**The global prevalence of asthma ranges from 1% to18% of the population in different countries **(Masaki et al., 2004)**.Annual worldwide deaths from asthma have been estimated at 250,000 and mortality does not appear to correlate well with prevalence **(Beasley, 2004).**Worldwide, the economic costs associated with asthma are estimated to exceed those of tuberculosis and HIV/AIDS combined **(WHO, 2004).** Asthma and obesity have an enormous impact on public health. It has been estimated that up to 65% of the adult population of the United States is obese or overweight **(Hedley et al., 2004)** whilst in Spain about 15% of the population is obese and 39% is overweight, and these figures have increased progressively in recent years. Although bronchial asthma affects a smaller percentage of people, its prevalence has also increased since the 1960 according to the Centers for Disease Control and Prevention **(Health united states, 2005).** Although central (visceral) adipocytes are the most important source of adiponectin (**Steffes et al., 2004**), there is a tendency for reduced serum adiponectin concentration among obese subjects, suggesting that decreased APN levels may contribute to the increased inflammatory state as in asthma (**Arita et al., 1999**). Paradoxically, adipose tissue-expressed adiponectin levels are inversely related to the degree of adiposity. A reduction in adiponectin serum levels is accompanied by insulin resistance states, such as obesity and type II diabetes mellitus. Adiponectin has been shown to increase insulin sensitivity and decrease plasma glucose by increasing tissue fat oxidation. It inhibits the inflammatory processes of atherosclerosis suppressing the expression of adhesion and cytokine molecules in vascular endothelial cells and macrophages, respectively (**Okamoto et al., 2006**).

Aim of the work

This work aimed to determine whether serum concentration of adiponectin changed in asthmatic patients during acute attack and in remission.

Subjects and methods

Fifty five cases were included in this study from Chest department, Benha university hospital .40 patients with bronchial asthma and 15 age related healthy subject as a control. All asthmatic patients and control group were divided into non-obese and obese according to their body mass index(BMI) Those with BMI < 25& >18.5 were considered non-obese, Those with BMI> 30 were considered obese .Those with BMI . 25 and. 30 were considered overweight and were not included in this study **(NIH/NHLBI, 1998).**All asthmatic patients met the criteria of GINA guidelines for the diagnosis of asthma **(GINA,2010).**All were in acute attack then in remission ,All subjects were submitted to the following :Full history taking ,Complete physical examination(General & Local), Plain x-ray chest P-A & left lateral views, Complete blood count, Erythrocyte sedimentation rate, Liver and kidney function tests,Fasting and post prandial blood sugar.

-Ventilatory function tests (spirometry) before and after bronchodilatation by using Sensor-medics V max series, 2130 spirometer, V6200 Autobox, 6200DL. All results were calculated as percent of predicted except for FEV1/FVC.

- Venous blood samples were taken for Adiponectin level measurement.

Samples collection and storage

Venous blood samples were obtained at the period from july,2010 till july, 2011 between 8:00 am and 9:00 am after an overnight fast. After clotting at 48◦C, the serum was separated by centrifugation at 1000g for 5 minutes at room temperature and stored at -70◦C until analysis. The serum levels of adiponectin was quantified using a sandwich enzyme–linked immunosorbent assay kit according to the manufacturer's protocol .

Principle of the assay

Adiponectin, also referred to as Acrp30, AdipoQ and GBP-28, is an 244 aminoacid protein, which is physiologically active, specifically and highly expressed in adipose cells (adipokine). Adiponectin forms homotrimers, which are the building blocks for higher order complexes found circulating in serum. This Enzyme Linked ImmunoSorbent Assay (ELISA) is based on the competition between free adiponectin and coated adiponectin, in presence of a known quantity of HRP labeled adiponectin antibody (tracer).

Measurement of serum adiponectin

The serum adiponectin concentration measured by the double antibody sandwich ELISA method with an antibody specific for human adiponectin (Linco Research Missouri, USA.).

Exclusion criteria: all subjects with history of smoking, history of abnormal chest x-ray,

history of diabetes mellitus, cardiovascular disease, liver or kidney affection, history of use of statins, leukotriene receptor antagonists in the last one month, history of other comorbidities that may rise adiponectin as anorexia nervosa (**Pannacciulli et al., 2003**).

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, linear correlation coefficient, analysis of variance [ANOVA] test and chi-square test by SPSSV **(Yadolah 2003).**

Results

The demographic data of the studied subjects included in this study are illustrated in

table (1).The range of body mass index (kg/ m^2) in obese control subjects was from 31.7 to 35.8(kg/ m^2) with the mean body mass index 34 ± 1.4(kg/ m^2).while in nonobese control subjects from 22.6 to 24.9(kg/ m^2) with the mean body mass index 23.7 ±1(kg/ m^2). In obese asthmatics the range was from 30.1to 35.8 (kg/ m^2) with the mean body mass index 32.8±1.6(k/ m^2), while in nonobese asthmatics the range was from 19.1 to 24.9(kg/ m^2) with the mean body mass index 22 ± 1.7(kg/m2).The range of age in obese control subjects was from 29 to 39 years with the mean age 34.5 ± 4.4 years while in nonobese control subjects from 33 to 50 years with the mean age 42.4 ± 7.35 years. In obese asthmatics the range was from 29 to 52 years with the mean age 39.5 ± 6.95 years while in nonobese asthmatics the range was from 25 to 51 years with the mean age 35.5 ± 7.2 years.

The results also showed the sex distribution among the studied groups.25 males included in this study,3 obese control subjects ,4 nonobese control subjects, 8 obese asthmatics and 10 nonobese asthmatics.30 females included in this study, 4 obese control subjects ,4 nonobese control subjects,12 obese asthmatics and 10 nonobese asthmatics. This study showed that serum adiponectin(µg/ml) is highly significant lower in obese asthmatics during attack(1.58 ±0.724 µg/ml) than that in obese asthmatics during remission(2.08 ±0.74 µg/ml) and that in obese control subjects (3.25 ±0.65 µg/ml), (P value < 0.001) (Table 2).

The present study also revealed, serum adiponectin(µg/ml) was significantly higher in nonobese asthmatics during remission (9.49±2.49 µg/ml) than that in nonobese asthmatics during attack (7.89 ± 2.7 µg/ml) and both are lower than that in nonobese control subjects , (P value < 0.05) (Table 3).

This study showed that serum adiponectin (µg/ml) was highly significant lower in obese asthmatics (1.58 ±0.72 µg/ml) than that in nonobese asthmatics (7.89 ±2.7 µg/ml) during attack ,(P < 0.001) and highly significant lower in obese asthmatics(2.08

±0.74 µg/ml) than that in nonobese asthmatics (9.49 ±2.49 µg/ml) during remission, (P<0.001) Table (4)&(5).

Discussion

Asthma is a common chronic disease in people of all ages, affecting daily activities in many patients. It is a major public health problem with a great influence on the health-economic costs for medical services, dependent on disease severity (**Jansson et al., 2007)**. The prevalence of obesity and asthma is increasing concomitantly **(Ford,2005).**Obesity is associated with asthma in both adults and children, as shown by an increasingly large number of cross sectional, case-control, longitudinal, and weight intervention studies **(Jartti et al., 2009).** Most of the prospective studies have demonstrated that obesity antecedes the development of asthma (**Ford, 2005**).Adiponectin is a predominantly anti-inflammatory adipokine. Adiponectin inhibits proinflammatory cytokines, such asTNF-α, IL-6, and nuclear factor k B**(Masaki et al., 2004**), as well as induces anti-inflammatory cytokines, such as IL-10 and IL-1receptor antagonist (**Kumada et al., 2004**).

This work aimed to determine whether serum concentration of adiponectin changed in obese & non obese asthmatic patients during acute attack and in remission or not .This study showed that serum adiponectin(µg/ml) was highly significant lower in obese asthmatics during attack than in obese asthmatics during remission and that in obese control subjects**.** The present study also revealed, serum adiponectin(µg/ml) was significantly higher in nonobese asthmatics during remission than that in nonobese asthmatics during attack and both was lower than that in nonobese control subjects .

Similar results were obtained by **Ding et al. (2012)** who studied 120 patients diagnosed as bronchial asthma ranging in age from 18 to 72 years(average=53.5±6.9) of which 62 were males and 58 were females ,36 out of 120 patients encountered with acute asthma exacerbation and the rest 84 patients were at remission stage , A total of 120 healthy adults ranging in age from 20 to 70 years(average=50.2±5.8) were recruited as controls, of which 60 were males and 60were females and showed that plasma adiponectin was significantly reduced in acute exacerbation (11.7±6.2 µg/ml) in comparison to control group (24.6 ± 8.9 µg/ml)(P<0.01).The level of adiponectin in remission patients(19.3 ± 7.5 µg/ml) was significantly higher than in patients at acute stage (P-value < 0.01) but still lower than that in the controls (P-value < 0.05).The serum adiponectin concentration is characterized by a nocturnal decline in the early morning and a subsequent peak in the late morning. After peak levels are reached, there is minimum daytime variation

suggesting the role of adiponectin in pathogenesis of asthma attack which increase during nocturnal period and early morning(**Gavrila et al., 2003**).

This study showed that serum adiponectin (µg/ml) was highly significant lower in obese asthmatics than in nonobese asthmatics during attack , and highly significant lower in obese asthmatics than in nonobese asthmatics during remission .This is in accordance with the study done by **Lessard et al.(2011)** on 44 obese with mean age (40±14years) of which 7 were males , 37 were females and 44 nonobese asthmatics with mean age (38±13 years) of which 7 were males , 37 were females. Their study showed that serum adiponectin level was lower in obese (12 ± 6.1 µg/ml) than in nonobese asthmatics (17.5 ± 8.5µg/ml),(P=0.0002).Serum adiponectin levels were increased in subjects on inhaled corticosteroids(ICS) ,suggesting an effect of ICS it-self on adiponectin level. This might be explained by the effect of obesity on the level of serum adiponectin (**Nagel et al., 2009**).

Conclusion :The serum adiponectin was significantly decreased in asthmatic patients (obese and nonobese) than control subjects also serum adiponectin level was significantly lower during attack than in remission.

Tables

Table(1): Demographic data of studied subjects as regards, number, sex, age, & body mass index:

		Obese	Non Obese	t-test	p-value
Control					
No.		7 (100 %)	8 (100 %)	3.4	>0.05
Sex	male	3 (43%)	4 (50%)	3.24	>0.05
	female	4 (57%)	4 (50%)	2.7	>0.05
Age/years		34.5±4.44 R:29-39	42.4±7.35 R:33-50	3.6	>0.05
BMI (Kg/m^2)		34±1.4 R:31.7-35.8	23.7±1 R:22.6-24.9	12.6	< 0.005
Asthmatic					
No.		20 (100%)	20(100%)	3.8	>0.05
Sex	Male	8 (40%)	10(50%)	2.95	>0.05
	female	12(60%)	10(50%)	2.8	>0.05
Age/year		39.5±6.95 R:29-52	35.5±7.2 R:25-51	4.1	>0.05
BMI (Kg/m^2)		32.8±1.6 R:30.1-35.8	22±1.7 R:19.1-24.9	11.9	< 0.005

Table(2): Statistical comparison of serum adiponectin (µg/ml) in obese control subjects and obese asthmatic patients during attack and remission.

	obese control	obese asthmatic during attack	obese asthmatic during remission
Number	7	20	20
Mean	3.25	1.58	2.08
SD±	0.655	0.724	0.747
F-value	15.223		
p-value	< 0.001		

Table(3): Statistical comparison of serum adiponectin(µg/ml) in non obese control subjects and non obese asthmatic patients during attack and remission.

	Non obese control	Non obese asthmatic during attack	Non obese asthmatic during remission
Number	8	20	20
Mean	10.51	7.89	9.49
SD±	1.55	2.7	2.49
F-value	3.66		
p-value	<0.05		

Table(4): Statistical comparison of serum adiponectin(µg/ml) in obese and non obese asthmatics during attack.

	obese asthmatics	Non obese asthmatic
Number	20	20
Mean	1.58	7.89
SD±	0.72	2.7
t-value	9.76	
p-value	0.001	

Table(5): Statistical comparison of serum adiponectin (µg/ml) in obese and non obese asthmatics during remission.

	obese asthmatics	Non obese asthmatic
Number	20	20
Mean	2.08	9.49
SD±	0.74	2.49
t-value	12.44	
p-value	< 0.001	

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دراسة مستوى الاديبونيكتين في مصل المرضى البدناء والمرضى غير البدناء المصابين بالربو

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مقدمة: الربو هو مشكلة عالمية، يوجد 300 مليون شخص مصاب على مستوى العالم . وعلى الرغم من أن الخلايا الشحمية هي أهم مصدر للاديبونيكتين ، فان هناك ميل لانخفاض تركيز الاديبونيكتين فى مصل المرضى البدناء مما يشير إلى أن انخفاض مستوي الأديبونيكتن يمكن أن يسهم في زيادة التهابات كما هو الحال في الربو

الهدف من العمل: الهدف من هذا العمل هو تحديد ما إذا كان تركيز مصل الاديبونيكتين يتغير في مرضى الربو أثناء النوبة الحادة عن حالة الاستقرار أم لا.

المواضيع والأساليب: تم تضمين الدراسه خمسة مجموعات من قسم الصدر، بمستشفى بنها الجامعى 40 من المرضى الذين يعانون من الربو (20 يعانون من السمنة المفرطة و 20غير بدناء) و 15 كمجموعه مقارنه من الاصحاء (7 يعانون من السمنة المفرطة و8 غير بدناء). تم تقسيم جميع مرضى الربو والمجموعة المقارنه في غير البدناء والبدناء وفقا لمؤشر كتلة أجسامهم (BMI) ,اعتبرت أولئك الذين لديهم مؤشر كتلة الجسم<25 و> 18.5 غير البدناء، واعتبرت أولئك الذين لديهم مؤشر كتلة الجسم > 30 يعانون من السمنة المفرطة. زيادة الوزن من 25 الى 30 لم تدرج في هذه الدراسة . خضع الجميع للفحص البدني الكامل، وعمل الأشعة السينية على الصدر ، عد الدم الكامل وكرات الدم الحمراءوقياس معدل سرعة الترسيب والكبد وعمل اختبارات وظائف الكلى، ونسبة السكر الصائم في الدم، واختبارات وظائف التنفس الصناعي وتم حفظ عينات الدم لقياس مستوى الأديبونكتين.

النتائج:وجد ان مستوى الاديبونيكتين (ميكروغرام / مل) في المجموعه المقارنه البدينة (3.25 ± 0.65 ميكروغرام / مل) كان كبيرا للغاية لكن أقل من مجموعة المقارنه لغير البدناء (1.55µg/ml ± 0.51، قيمة p <0.001). كما كشفت الدراسة ان مستوى الاديبونيكتين انخفض كثيرا جدا في المصابين بالربو الذين يعانون من السمنة المفرطة أثناء النوبة الحادة (1.58 ± 0.724 ميكروغرام / مل) عن المصابين بالربو الذين يعانون من السمنة المفرطة في حالة الاستقرار (2.08 ± 0.74 ميكروغرام / مل) وكذلك في المجموعه المقارنه البدينة (3.25 ± 0.65 ميكروغرام / مل)، (P-قيمة <0.001) فى حين كان الاديبونيكتين أعلى بكثير في مجموعة الغير بدناء المصابين بالربو خلال حالة الاستقرار (9.49 ± 2.49 ميكروغرام / مل) عن المصابين بالربو في مجموعة الغير بدناء أثناء النوبه الحادة (7.89 ± 2.7 مكغ / مل) وكلاهما أقل من ذلك في المجموعه المقارنه الغير بدناء ، (قيمة p <0.05). كان مستوى الاديبونيكتين (ميكروغرام / مل) أقل فى المصابين بالربو الذين يعانون من السمنة المفرطة اثناء النوبه الحادة (1.58 ± 0.72 ميكروغرام / مل) عن المصابين بالربو الذين يعانون من السمنة المفرطة في خلال حالة لاستقرار (2.08 ± 0.74 ميكروغرام / مل)، (قيمة P <0.001) وأعلى فى المصابين بالربو الغير بدناء خلال الحالة الحادة (7.89 ± 2.7 ميكروغرام / مل) عن المصابين بالربو في الغير بدناء خلال حالة الاستقرار (9.49 ± 2.49 ميكروغرام / مل)، (-قيمة P < 0.001).

الخلاصة:وجد أن مستوى الاديبونيكتين منخفض بشكل ملحوظ في مصل مرضى الربو البدناء والغير بدناء عن المجموعه المقارنه أيضا مستوى الاديبونيكتين كان أقل بكثير مما كان عليه في الحالة الحادة عن حالة الاستقرار.