Leptin and Related Biochemical Parameters in Obese Osteoarthritis

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Received : 17/03/2011    Accepted : 29/05/2011

الخلاصة
الفصال العظمي: هو علة تسبب المفاصل و يتميز بحالة تدهور تدريجي و مستمر للغضاريف المتصلة; و تعتبر السمنة واحدة من العوامل المتعددة التي تساهم في حدوث الفصال العظمي. إن غالبية الأشخاص الذين يعانون من السمنة يكون لديهم مستوى اللبيتين عالي و هذا يشير إلى (Leptin Resistance) كآلة لحدوث السمنة في هذه الحالة.

تم جمع عينات من (80) مريضاً تتراوح اعمارهم بين (45-55) سنة و معدل أعمارهم (52.34±12.12) سنة و تم تقسيمهم إلى أربع مجاميع تتألف كل مجموعة من (20) مريضاً كالتالي:

المجموعة (أ): المرضى يعانون من السمنة و الفصال العظمي.
المجموعة (ب): المرضى يعانون من السمنة فقط.
المجموعة (ج): المرضى يعانون من الفصال العظمي فقط.
المجموعة (د): المرضى الاصحة (مجموعة الـ control).

هناك متغيرات كيميائية حيائية بالإضافة إلى اللبيتين تلعب دور مهم في حدوث السمنة و بالتالي الفصال العظمي منها: الكوليسترول الكلي و الدهون البروتينية مثل: (البروتين الدهني عالي الكثافة و البروتين الدهني واطئ الكثافة).

بينت هذه الدراسة وجود ارتفاع في مستوى اللبيتين و البروتينات الدهنية الواقعة الكثافة في أمصال الأشخاص الذين عانوا من السمنة و الفصال العظمي الذين كان مؤشر البدانة لديهم أكثر من 30 كغم².
ABSTRACT

Osteoarthritis (OA) is a joint disorder characterized by progressive deterioration of articular cartilage. Obesity (OB) is one of many factors that participate in developing OA. Most obese (ob) subjects have high leptin (L) level suggesting “leptin resistance” as a mechanism of OB in this condition. Other biochemical parameter in addition to L are lipid profile (LP) including cholesterol (C), triglycerides(TG), lipoprotein(Lp) such as high & low density lipoproteins (HDL, LDL) that play an important role in OB.

In this study eighty individuals were selected, divided into four groups twenty in each group. The age ranged from (45 to 55) years with mean value ± standard mean of error (52.34±2.12).

Group (A): OB+ OA.
Group (B): OB.
Group (C): OA.
Group (D): Neither OB nor OA as control (c).

This study shows an elevation in L, LP except HDL serum level in obese osteoarthritis (OOA) whose their body mass index (BMI) more than (30) measured by weight in kilograms per height square meters (Kg/m²).

INTRODUCTION

Obesity is a growing health problem regarded as a pandemic with potentially disastrous consequences for human. In 2006 about one quarter in UK were obese; their body mass index > 30 Kg/m2 compared with 7% in 1980 & 16% in 1995 (1)

Obesity is a state of excess adipose tissue mass & white adipose tissue, has been viewed as a passive depository of energy and as a protective mechanism for heat loss (2).

Adipocytes are able to produce & secrete a wide number of molecules including classical cytokines such as interleukin-one & six (IL-1 & IL-6), tumor necrosis factor – alpha (TNF-α ) in addition to noval factors adiponectin, resistin, visfatin, vaspin & Leptin, all called adipokins(3,4,5). Leptin is a peptide in nature, its molecular weight 16 KDa encoded by obese
gene & mainly produced by adipocytes and to a lesser extent other organs (6,7). Leptin expression is prevalently regulated by food intake, hormones and cytokines (8), also its level is directly correlated with insulin and negatively with glucocorticoides (9–10).

The effect of Leptin on body weight are mediated through hypothalamic center that control feeding behavior and hunger, body temperature and energy expenditure (8) In essence Leptin provides the body with an index of nutritional status (11): Cholesterol(C), triglycerides(TG) blood levels are correlated positively with obesity(12) although obesity represents a strongest modifiable risk factor for osteoarthritis. Osteoarthritis (OA) is a condition characterized by a series of inflammatory processes start as synovitis which is common as an early and late face (8, 10).

Clinically OA is a disorder of diarthroidal joints leads to pain and functional limitation (8). Radiography shows the presence of osteophytes and joint space narrowing, while histopathologic feature shows alteration in cartilage integrity, progressive loss of articular cartilage(10).

The aim of this study was to find out if there is any relation between Leptin and some Biomedical parameteres in the blood of Obese patients and the effect of the changes in the levels of these parameters on the joints which may lead to the development of osteoarthritis and to find out if the Leptin is the link between Obesity and Osteoarthritis.

**MATERIALS AND METHODS**

In this study eighty individuals were selected, divided into four groups twenty in each one (25%). The age ranged from (45 to 55) years with mean value ± standard mean of error(52.34±2.12).

**Group (A): OB+ OA.**

**Group (B): OB.**

**Group (C): OA.**

**Group (D): Neither OB nor OA as control (c).**

Osteoarthritis is diagnosed by Dr. Mohammed Al-Osami a Rheumatologist in Medical City, Baghdad Teaching Hospital according to the American College of Rheumatology(ACR) (13).
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Blood samples assessed in Central Public Health Laboratory in Immunological & Clinical Biochemistry Departments by using kits from SPINREACT - CC to determine TG, C, HDL & LDL calorimetrically while Leptin was analyzed by Enzyme Linked Immune Sorbent Assay (ELISA). Body Mass Index represents the ratio of the weight of individual in Kilogram (Kg) to the height in square meters (m²) (14).

Statistical Analysis
The data was analysed on computer statistical program SPSS version 10. The mean + SD was also computed for comparison of the results. The comparsion of mean between the groups was tested by student’s t test. Results were considered statistically significant if P value is less than 0.05, 0.02, 0.01.

RESULTS AND DISCUSSION
After collection and categorization of data taken for 60 patients who were divided into 3 groups as mentioned above and 20 control persons who mentioned as group D. Statistical analysis was done to find out the relation of Leptin with BMI and other blood parameters (TG, Cholesterol, HDL, LDL) for each group, the results revealed the following:

1- Regarding Leptin with BMI:
- There is a significant positive correlation between Leptin and BMI in group A, when mean level of Leptin (20.12±1.45) µg/ml, BMI (37.89±2.34) and P<0.05
- There is a significant negative correlation in group B, between Leptin and BMI when mean of Leptin levels (12.14±1.26) µg/ml, BMI (22.72±1.02) and P<0.05.
- There is no significant correlation in group C and D between the Leptin and BMI when means of Leptin level {((15.72±1.89), (6.44±098)) µg/ml and BMI (34.66±1.75), (22.84±2.31) }.

2- Regarding Leptin with TG:
- There is no significant correlation in group A, B, and D between Leptin and TG, Leptin Level means{((20.12±1.45), (12.14±1.26), (6.44±098)) µg/ml and TG {((150.28±4.22), (133.05±6.19), (120.1±3.25)) mg/dl.}
• There is positive significant correlation in group C between Leptin and TG, Leptin level means \((15.72 \pm 1.89)\) µg/ml, TG \((148.21 \pm 7.25)\)mg/dl and \(P<0.1\).

3- Regarding Leptin with Cholesterol:
• There is positive significant correlation in group A, B, between Leptin and C when Leptin Level means \{(20.12 \pm 1.45), (12.14 \pm 1.26)\} µg/ml, C \{(218.93 \pm 9.22), (196.4 \pm 5.29)\} mg/dl and \(P<0.1\).
• There is no significant correlation in group C and D between the two mentioned parameters Leptin level mean \{(15.72 \pm 1.89), (6.44 \pm 0.98)\} µg/ml, C levels mean\{(201.12 \pm 8.97), (183.02 \pm 7.16)\}mg/dl.

4- Regarding Leptin with HDL:
• There is no significant correlation in group A, and D between Leptin and HDL, when mean level of Leptin \{(20.12 \pm 1.45), (6.44 \pm 0.98)\} µg/ml and mean of HDL level \{(32.78 \pm 1.59), (48.98 \pm 3.53)\}mg/dl.
• There is a significant positive correlation in group B Leptin level mean \(12.14 \pm 1.26\) µg/ml and HDL level mean \(41.19 \pm 2.88\)mg/dl and, \(P<0.001\).
• There is a significant negative correlation in group C between Leptin \(15.72 \pm 1.89\) µg/ml, \(P<0.0\) and HDL mean \(36.55 \pm 2.11\)mg/dl.

5- Regarding Leptin with LDL:
• There is a significant positive correlation between Leptin and LDL in group A, mean of Leptin \(20.12 \pm 1.45\) µg/ml, LDL mean level \(150.78 \pm 7.11\)mg/dl, and \(P<0.05\), and group B when mean Leptin \(12.14 \pm 1.26\) µg/ml, LDL \(125.27 \pm 8.91\)mg/dl and \(P<0.02\).
• There is no significant correlation between Leptin and LDL in group C Leptin mean level \(15.72 \pm 1.89\) µg/ml and LDL\(149.72 \pm 6.08\)mg/dl and group D when mean level of Leptin \(6.44 \pm 0.98\) µg/ml and LDL \(110.21 \pm 7.58\)mg/dl.

Table -1 showed the level of mean ±SD for each parameter in each studied groups.
Table -1: Levels of Mean +SD for each parameter in the four studied groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A (OB+OA)</th>
<th>Group B (OB)</th>
<th>Group C (OA)</th>
<th>Group D (Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI Kg/m²</td>
<td>37.89±2.34</td>
<td>22.72±1.02</td>
<td>34.66±1.75</td>
<td>22.84±2.31</td>
</tr>
<tr>
<td>L µg/ml</td>
<td>20.12±1.45</td>
<td>12.14±1.26</td>
<td>15.72±1.89</td>
<td>6.44±0.98</td>
</tr>
<tr>
<td>TG mg/dl</td>
<td>150.28±4.22</td>
<td>133.05±6.19</td>
<td>148.21±7.25</td>
<td>120.1±3.25</td>
</tr>
<tr>
<td>C mg/dl</td>
<td>218.93±9.22</td>
<td>196.4±5.29</td>
<td>201.12±8.97</td>
<td>183.02±7.16</td>
</tr>
<tr>
<td>HDL mg/dl</td>
<td>32.78±1.59</td>
<td>41.19±2.88</td>
<td>36.55±2.11</td>
<td>48.98±3.53</td>
</tr>
<tr>
<td>LDL mg/dl</td>
<td>150.78±7.11</td>
<td>125.27±8.91</td>
<td>149.72±6.08</td>
<td>110.21±7.58</td>
</tr>
</tbody>
</table>

The figures below show the correlations:

**Fig -1: Leptin with BMI in group A**

**Fig -2: Leptin with BMI in group B**

**Fig -3: Leptin with BMI in group C**

**Fig -4: Leptin with BMI in group D**
Fig-5: Leptin with TG in group A

Fig-6: Leptin with TG in group B

Fig-7: Leptin with TG in group C

Fig-8: Leptin with TG in group D

Fig -9: Leptin with Cholesterol in group A

Fig-10: Leptin with Cholesterol in group B
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Fig-11: Leptin with Cholesterol in group C

Fig-12: Leptin with Cholesterol in group D

Fig-13: Leptin with HDL in group A

Fig-14: Leptin with HDL in group B

Fig-15: Leptin with HDL in group C

Fig-16: Leptin with HDL in group D
These results are due to: obesity as well as related metabolic diseases are the most common and detrimental illness associated with chronic inflammatory response which characterized by abnormal cytokines production, increase synthesis of acute phase reactant and activation of inflammatory signaling pathway (15). The high Leptin level explained “Leptin resistance” mechanism during OB in many subject(16,17). Previous studies showed that numerous inflammation stimuli modulate both Leptin gene expression and circulating Leptin level (18, 19, 20), although Leptin suppresses expression of hypothalamus neuropeptide Y, a potent appetite stimulating factor leading to increase the expression of melanocyte stimulating hormone(MSH) that act through melanocortin-4 receptor(MC-4R) to decrease appetite(21), thus Leptin activate series of downstream neural pathway that alter food seeking behavior and metabolism(22). Modulation of Leptin level during acute inflammatory stimuli suggest that this adipokine is participating in the development of inflammatory processes such as OA(23,24). Leptin as well as other adipokins is likely involved in the development of articular cartilage.
degenerative inflammatory diseases (histopathology of OA) by inducing interferon – gamma, interleukin – one level and nitric oxide production via nitric oxide synthase type II in chondrocyte(25,26). Normal chondrocyte synthesized Leptin in amount less than osteoarthritic one, Leptin expression is increased in articular rat joint injected exogenous Leptin which implies a positive feedback regulation (27). Charles EB in 2004 correlates between OB as risk factor for OA through studying mechanical processes versus metabolic one (28).

The decrement of HDL blood level in concomitant with increment of TG is due to the metabolic interaction between these two lipids (29), as well as the activation of TG synthesis rich Lp in liver latterly increase TG in lipid particle alters their metabolism and as result the hydrolysis of TG rich HDL particle enhanced leading to decline HDL level (30) on other hand the LDL level is increased. The relationship between OA, OB and BMI was determined by others (31). From previous explanations that mentioned above show an agreement with the results that obtained from this study.

So, we can conclude that obesity is considered to be one of the greatest risk factors for osteoarthritis, a progressive musculoskeletal disorder that is characterized by loss of joint cartilage. Leptin is a protein hormone that is produced by fat cells and responsible for regulating appetite and metabolism. The amount of Leptin in the body increases as body fat increases with obese people having high concentrations of the hormone circulating in their bodies. The results indicate that Leptin may play an important role in pathophysiology of OA and that Leptin and BMI were independently associated with lipid and lipoprotein profiles.

REFERENCES

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