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Evaluation of Apelin, and Tartrate-Resistant Acid Phosphatase-5b in Ankylosing Spondylitis Male Patients With and Without Osteoporosis

Israa Abdelmalik Salem[1*], Adnan F. Al-Najar[1*], Abbas Toma Joda[2*]
[1]Department of Chemistry and Biochemistry, College of Medicine, Al-Mustansiriyah University, Baghdad, Iraq
[2]Department of Medicine, College of Medicine, Al-Mustansiriyah University, Baghdad, Iraq

Abstract

Osteoporosis is a common complication of ankylosing spondylitis (AS), and it is related to the high levels of biochemical markers such as tartrate-resistant acid phosphates (TRACP)-5b and other proinflammatory cytokines. In early AS, osteoporosis may appear due to the action proinflammatory cytokines, however spinal osteoporosis commonly observed in those patients with severe AS of long duration but it can occur as a result of ankylosis and lack of movement. Apelin is a new adipokine that has a negative impact on bone formation and can act as an anti-anabolic agent. The aim of this study is to evaluate serum (apelin and TRACP-5b) levels in ankylosing spondylitis (AS) male patients with and without osteoporosis and look for the relation between osteoporosis and the studied parameters. About fifty-eight male AS patients were included in this study. Serum (apelin and tartrate-resistant acid phosphates (TRACP)-5b) were measured using commercial enzyme-linked immunosorbent assay (ELISA) kits. Bone mineral density (BMD)(Z-score)of Lumbar spine was determined using dual-energy X-ray absorptiometry (DXA).This study shows that AS male patients with osteoporosis had significantly high serum TRACP-5b level (P-value <0.001) while no significant differences of serum apelin level (P-value=0.06) between AS male patients with and without osteoporosis. A significant correlation has been found between BMD (Z-score) and serum TRACP-5b level while no correlation has been found between BMD (Z-score) and serum apelin level. The results of this study suggest that serum TRACP-5b is could be used in detection of AS disease with osteoporosis, while serum Apelin level is would not be effected.

Keywords: ankylosing spondylitis, Apelin, TRACP-5b, osteoporosis, DXA, BMD.

تقييم الابلين و الفوسفاتيز الحمضي المقاوم للترتاريت–5 باء في المرضى الذكورالمصابين بالتهاب الفقار القسطي مع وبدون هشاشة العظام

اسراء عبد المالك[1]،عدنان النجار[1]،عباس طعمة[2]
[1]قسم الكيمياء والكيمياء الحياتية، كلية الطب ، الجامعة المستنصرية، بغداد، العراق
[2]قسم الباطنيه ، كلية الطب، الجامعة المستنصرية، بغداد، العراق

الخلاصة

ترقق العظام هو أحد المضاعفات الشائعة للالتهاب الفقار اللاصق والذي يرتبط بمستويات عالية من العلامات البيوكيميائية مثل الفوسفاتيز الحمضي المقاوم للترتاريت –5 باء وغيرها من السيتوكينات المسببة للالتهاب و قد تظهر العظام في وقت مبكر ترقق كنتيجه لارتفاع هذه السايتوكينات، ومع ذلك فان ترقق العظام للعمود الفقري شائع لدى مرضى التهاب الفقار القسطي الابلين هو اديبوكين جديد له تأثير سلبي على تكوين

*Email: esraaha2000@gmail.com

العظام ويمكن أن يعمل كعامل مضاد للبناء.تهدف الدراسة الحالية الى تقييم مستويات المصل الابلين و الفوسفاتيز الحمضي المقاوم للترتاريت–5 باء في المرضى الذكور المصابين بالتهاب الفقار القسطي مع أو بدون هشاشة العظام والبحث عن العلاقة بين مرض هشاشة العظام والمتغيرات والدوال قيد هذه الدراسة. شملت الدراسة 58 من المرضى الذكور المصابين بالتهاب الفقار القسطي حيث قياس مصل الابلين و الفوسفاتيزالحمضي المقاوم للترتاريت –5 باء باستخدام الاليزا و تم تحديد الكثافة المعدنية للعظم للعمود الفقري للفقرات القطنية باستخدام جهاز امتصاص الأشعة السينية المزدوجة الطاقة. اظهرت هذه الدراسة ان المرضى الذكور المصابين بهشاشة العظام لديهم مستوى عالٍ من الفوسفاتيزالحمضي المقاوم للترتاريت –5 باء في المصل، في حين لا توجد فروق ذات دلالة إحصائية في مستوى الابلين في المصل بين المرضى مع وبدون هشاشة العظام. ولقد تم العثور على ارتباط معنوي بين كثافة العظم ومستوى الفوسفاتيز الحمضي المقاوم للترتاريت–خمسة باء في المصل في حين لم يتم العثور على ارتباط بين كثافة العظم ومستوى الابلين في المصل.تشير نتائج هذه الدراسة الى ان مستوى الفوسفاتيز الحمضي المقاوم للترتاريت– 5 باء يزداد لدى المرضى الذين يعانون من هشاشة العظام في حين ان مستوى الابلين لايتاثر بالتغير في كثافة العظم.

Introduction

Ankylosing spondylitis (AS) is a chronic systemic rheumatic disease with long-term inflammation that affects mostly the joints of axial skeleton (sacroiliac and other joints in the spine (vertebra) and less commonly peripheral joints)[1]. AS influence the quality of life, the newly formed bones (at vertebral sides) is the main factor to determine the disease's outcome[2].

The exact cause of ankylosing spondylitis is still uncertain[3]. There is a combination of genetic and nongenetic factors leads to clinical disease[4]. Ankylosing spondylitis is mostly affected young people usually through the 3rd decade of the life[5]. AS is seen in male more than female, the ratio of 2:1, and the familial occurrence is common[6]. The inflammation is a common feature in AS that leads to bone erosion and destruction[7]. Destruction of bone leads to osteoporosis that commonly appears at the spine in which the trabecular bone in central parts of vertebral bodies is involved [8]. The impairment of movement that occurred during the course of the disease also contributes to the development of osteoporosis[9].

Osteoporosis (OP) is defined as a general skeletal sickness that characterized by the reduction in the mass of the bone and micro-architectural injure of bone tissue, that causes an increase in bone weakness and sensitivity to fracture[10]. Dual-energy X-ray absorptiometry (DXA) of the spine and hip is the gold standard for defining osteoporosis[11], it occurs when bone resorption exceeds bone formation, and it can be predicted by measuring bone turnover markers (BTMs) and bone mineral density (BMD) because the increase in BTMs associated with the reduction in BMD[12], [13]. OP is a common complication of AS and is related to the high levels of biochemical markers such as TRACP-5b and proinflammatory cytokines[14].

In early AS, osteoporosis may appear due to the action proinflammatory cytokines, however spinal osteoporosis commonly observed in those patients with severe AS of long duration but it can occur in apart because of ankylosis and lack of mobility[15], [16].

Apelin is one of adipokines, and it is secreted as a pre-pro-peptide consisting of 77 amino acids which undergo cleavage to produce several active forms containing 13, 17 or 36 amino acids. All of which hold C-terminus of the pre-pro-protein which contains the section of the molecule that responsible for apelin binding to it is receptor [17], [18]. Apelin was found to be expressed by adipocytes and osteoblasts[19]. Also apelin was found to be increased in obesity[20]. The relationship between apelin and bone mineral density has not been well understood[21]. Apelin enhances the proliferation of osteoblast (mitogenic agent) and protect it from apoptosis, in another word it suppresses apoptosis while it has no important effect on bone mineralization, since it does not affect on osteoblast differentiation[21],[22]. In addition to osteoblasts, apelin and apelin receptor also expressed by mature osteoclast, and the effect of Apelin on bone cells did not well explain. It has been suggested that apelin affects on bone in a complex way but generally it has a negative outcome on bone formation in another word it has anti-anabolic effect on bone[22]. Tartrate-resistant acid phosphatase (TRACP)-5b is specifically from osteoclast thus it is considered as a new, sensitive important biomarker of bone resorption, and data show that it is the only marker reflecting osteoclasts

number and metabolic activity of osteoclast[23].. The aim of this study is to evaluate serum apelin and TRACP-5b levels in AS male patients with and without osteoporosis and to look for the correlation between osteoporosis and the studied parameters.

Materials and methods

Fifty-eight male patients with AS whom attending Al-Yarmouk Teaching Hospital outpatient clinics between (November 2017 to March 2018). The age of patients involved in this study were in the range of (20-49) years old. Patients with diseases that may affect the studied parameters (such as hypertension, diabetes mellitus, Asthma, thyroid dysfunction, renal dysfunction, liver disease, pulmonary diseases, prostatic diseases, and malignancy) have been excluded from the study.

Bone mineral density (BMD) of the lumbar spine was measured by using dual-energy x-ray absorptiometry (DXA) for patients in which when Z-score ≤ -2.0 SD, the patient was considered to be osteoporotic. Blood samples were taken from patients in fasting condition to determine serum (Apelin, and TRACP-5b) levels using commercial ELISA Kits and according to the manufacturer's instructions (the kits were manufactured by My Bio Source Inc. USA). Statistical analysis was done using SPSS version 23 computer software and the data were expressed as (Mean ±SD).

RESULTS

According to this study and according to Table-1 there is no statistically significant (NS) difference in serum Apelin level was found when comparing serum Apelin level in AS male patients without osteoporosis (2438.1±393.8 pg/ml) to AS male patients with osteoporosis (2639.1±371.8pg/ml),(P-value=0.06) , while a significant elevation in serum TRACP-5b level was found in AS male patients with osteoporosis (8.2 ± 1.2 mlU/ml), when compared to AS male patients without osteoporosis (5.2 ± 1.6 mlU/ml), (P-value <0. 001). Table-2 shows a strong negative correlation between BMD (Z-score) and serum TRACP-5b (r=-0.611, P-value<0.001) (Figure-1), while there was no significant correlation between BMD and serum Apelin.

Discussion

Bone mineral density (BMD) in AS patient is altered with increasing of the disease duration that reduced the spine BMD (osteopenia or osteoporosis) is usually seen in the early course of the disease and it associated with the activity of the disease (moderate and high) while rise in spine BMD is seen in advance AS (as the length of disease increase)[24-26]. This study shows that serum Apelin is not affected by the changing of BMD that seen among AS male patients, while serum TRACP-5b level shows a significant elevation in of AS male patients with osteoporosis as shown in Table-1. The reason behind this elevation according to (C.H Im et al 2009) is possiply due to the significant elevation of osteoclast number and activity which occurs during the disease process[27], and the fact that the elevation of serum TRACP-5b level reflects the osteoclastic activity. This gives an idea about the role of osteoclast in the pathogenesis of AS which leads to bone resorption and finally osteoporosis[28], [29]. (JM Halleen et al 2002) have revealed that serum TRACP-5b activity was significantly elevated in osteoporotic patients and negatively correlated with BMD[30].

It worth to mention that the present study shows no correlation found between serum apelin and BMD. The present study shows a significant inverse correlation between serum TRACP-5b and BMD as shown in Table-2, and Figure-1 which agrees with previous study by (M. Park et al 2008) who reported that a significant an inverse correlation between bone turnover markers and BMD due to the alteration in inflammatory process which causes change in bone metabolism and leads to osteoporosis[31].

Conclusion

Serum apelin was found and did not affect on AS male patients BMD (DXA Z-score) while serum TRACP-5b was found significantly affected in patients BMD. There is a strong negative correlation between BMD and serum TRACP-5b while BMD did not find and did not correlate to serum apelin.

Table 1 -The comparison of the studied parameters according to bone mineral density (BMD) (DXA Z-score) in ankylosing spondylitis (AS) male patients.

Parameter	Bone Mineral Density (BMD) (DXA Z score)		P-value
	without osteoporosis > -2 No=34	With osteoporosis = < -2 No=24	
Serum apelin (pg/ml) Mean ±SD	2438.1 ± 393.8	2639.1± 371.8	0.06 [NS]
Serum tartrate-resistant acid phosphatase (TRACP 5b mlU/ml) Mean ±SD	5.2 ±1.6	8.2 ± 1.2	< 0.001 [S]

[NS] =no significant differences between two independent means using student-t-test at 0.05 level.
[S]= significant differences between two independent means using student-t-test at 0.05 level

Table 2-The correlation coefficient (r) and the significance between BMD (DXA Z-score) and the studied parameters in ankylosing spondylitis (AS) male patients

	BMD (DXA Z-score)
Serum apelin (pg/ml)	**r=-0.237 P=0.07[NS]**
Serum tartrate-resistant acid phosphatase (TRACP 5b mlU/ml)	**r=-0.611 ** P<0.001**

** Correlation is significant at the level 0.01.
[NS]= no significance.

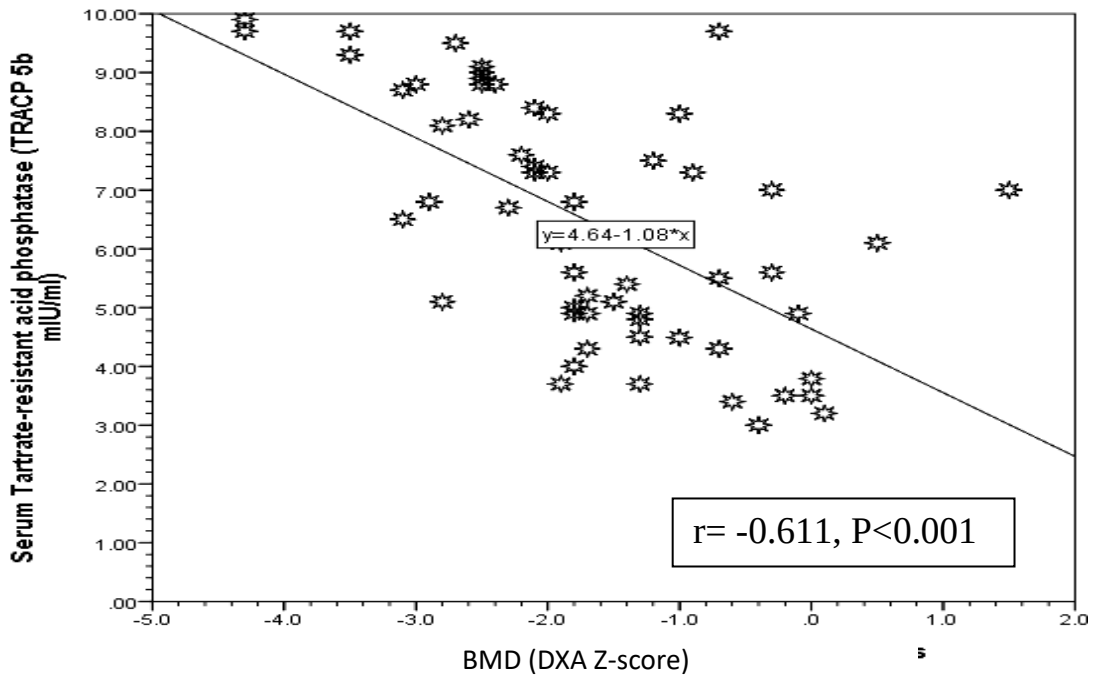

Figure 1-Scatter diagram with fitted regression line showing the linear correlation between serum tartrate-resistant acid phosphatase (TRACP 5b mlU/ml) and BMD (DXA Z score) among AS male patients.

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