Assessment of Serum Prolactin Level in Patients Women with Rheumatoid Arthritis

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Abstract:

The prolactin hormone played role in the many autoimmune disorders. To determine the importance of high levels of prolactin in triggering rheumatoid arthritis, thirty patient's women with hyperprolactinemia aged (20-45) years old have been investigated and compared with twenty five healthy individuals. All the studied groups were carried out to measure the concentration of citrulinated peptide(CCP) by enzyme linked immunosorbent assay(ELISA), antikeratin antibodies (AKA)and antinuclear antibodies(ANA) by indirect fluorescent assay IFAT. There was a significant elevation of CCP concentration compared with control groups ($P< 0.05$). The percentage of antikeratin antibodies and antinuclear antibodies was (20%, 10%) respectively, and there were significant differences ($P< 0.05$) between incidences percentage of antikeratin and antinuclear antibodies compared with control groups . This study indicated that women with rheumatoid arthritis may play a role as triggering factor of hyperprolactinemia

Key words: Women, High level prolactin, Rheumatoid Athritis

Introduction:

Prolactin (PRL) is one of the hormones that may play a role in regulating immune function. It is mainly produced in the anterior pituitary gland and consists of a single peptide chain of 198 amino acids, with a molecular weight of 23,500 Da[1]. Prolactin secretion is stimulated by thyrotropin releasing hormone (TRH), oxytocin , serotonin, and vasoactive intestinal peptide. Cytokines probably also participate in this regulation. In *vitro* studies have shown that IL-1, IL-2 and IL-6 are able to stimulate prolactin production[2]. IFN-gamma can inhibit prolactin production, while TNF- α has been found to increase as well as to decrease secretion of prolactin[2,3]. Prolactin levels are higher in women than in men, though there is a considerable overlap in the ranges, prolactin levels rise in response to stress .It has been suggested that prolactin enhance inflammatory responses[4,5].In human ,raised levels of prolactin have been reported in some autoimmune diseases such as Rheumatoid arthritis(RA) ,Systemic lupus erythematous (SLE), multiple sclerosis (MS), Sjogern syndrome(SS) [6,7]. Rheumatoid arthritis is a chronic, autoimmune inflammatory disease with a worldwide prevalence of 1% to 2% autoimmunity followed by the articular infiltration of leukocytes and hyperplasia of synovial cells lead to the development of an invasive inflammatory pannus that destroys the adjacent cartilage and bone. Locally produced cytokines are crucial for initiating the inflammatory process and destroying articular tissue, among these cytokines, TNF-α, IL-1β, and IFN-gamma stimulate both chondrocyte apoptosis and cartilage extracellular matrix degradation, and

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their inhibition ameliorates joint destruction. [8,9,10].Transgenic mice expressing TNF-α, a model of polyarthritis ,display chondrocyte apoptosis before the onset of full arthritis, suggesting that cytokine-induced chondrocyte apoptosis is a primary cause of, rather than an event secondary to, cartilage matrix breakdown[11].Prolactin acts both as a circulating hormone and a cytokine to regulate the function of a wide variety of tissues, including cartilage. PRL and the PRL receptor are expressed in chondrocytes where this hormone can promote differentiation and survival. [12, 13].Prolactin stimulates the synthesis of proteoglycans and type II collagen by bone marrow–derived chondrocytic mesenchymal cells ,and it inhibits the apoptosis of articular chondrocytes that induced by serum deprivation, suggesting the action of PRL on chondrocyte survival may be relevant in RA [14]. Prolactin is present in RA synovial fluid which produced by RA synovial cells, and can influence cartilage survival by exerting immuno regulatory effects. The PRL receptor is a member of the hematopoietin/cytokine receptor superfamily and is expressed in a variety of immune cells, in which this hormone can be pro inflammatory or anti inflammatory by regulating proliferation, survival, and the release of inflammatory mediators [15,16].The aim of the present study was to determine the relationship of rheumatoid arthritis in women patients with hyperprolactinemia.

Materials and Methods:

The study include (30) patients women with hyper prolactinemia of ages (20-45) years from Baghdad hospital, AL-Yarmoik hospital and (25) health blood donor taken as a healthy control group. All the study groups carried out to measure cyclic citrulinated peptile (CCP) by using ELISA test, antikeratin Ab and antinuclear Abs(ANA) by using indirect immunoflourescent(IFAT) test as shown in the leaflet of the kit [17].

Statistical analysis:-

Comparison of paired data from the group of subject was done using t-test (t), while correlation between groups were analyzed using person chi-square .The computer program which used was Spss V.II.5 [18].

Results and Discussion:

The results of the present study showed that there were a significant elevation of CCP concentration (5.131_+0.426) compared with control groups (3.380+_0.242) P< 0.05, the incidences percentage of antikeratin Abs and antinuclear Abs tests were [20%,10%] respectively, figure (1,2 and 3).

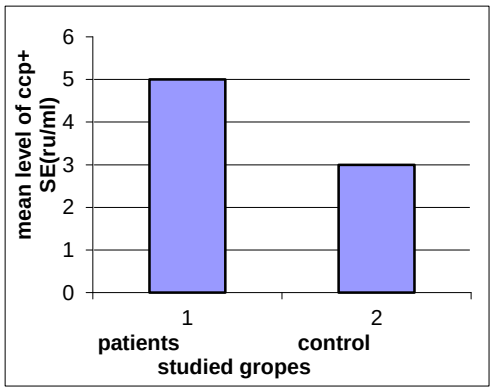


Fig (1): Mean level of CCP(RU/ml) in the sera of women with hyperprolactinemia and control groups.

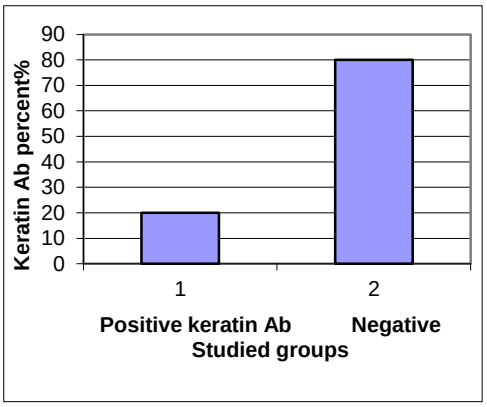


Fig (2): Anti-keratin Ab in sera of women with hyperprolactinemia

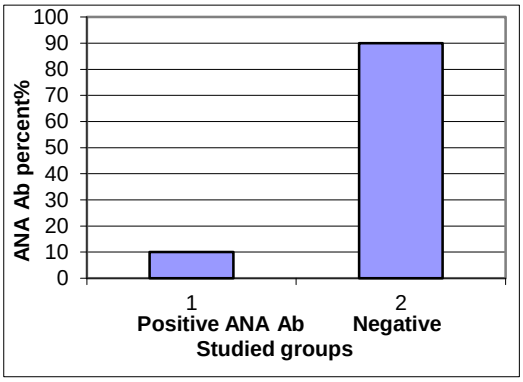
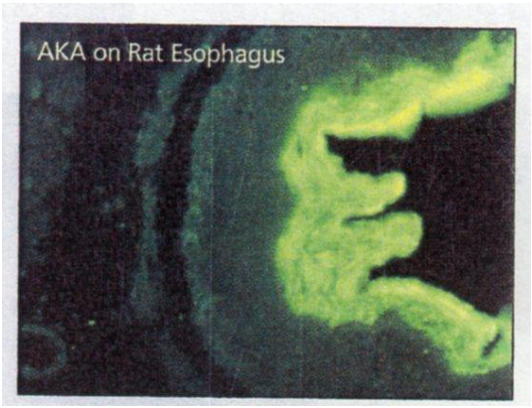


Fig (3):Anti-ANA Ab in sera of women with hyperprolactinemia

Also, there were significant differences ($P<0.05$) between percentage of antikeratin and antinuclear antibodies compared with control groups, Figure (4, 5).



Fig(4):Positive anti-Keratin Ab by IFAT

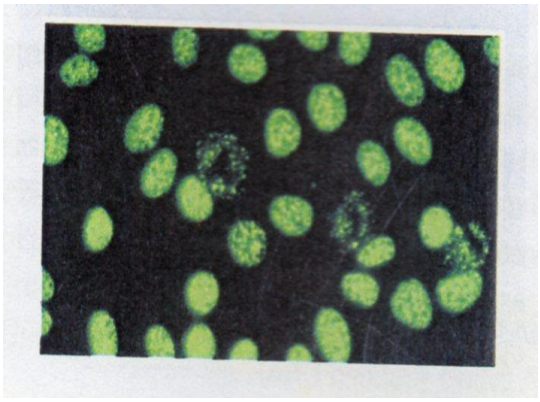


Fig (5): Positive anti-Nuclear Ab(ANA) by IFAT

Several studies reported higher serum prolactin concentration in women with rheumatoid arthritis compared with control [19]. A recent study shows an increase of prolactin in serum and synovial fluid from subjects affected with RA perhaps indicating that cytokines acts as a pro-inflammatory factor to increase disease severity and joint damage in RA, while others studies demonstrates that prolactin inhibits cytokine- and arthritis-driven chondrocyte apoptosis. This effect involves the reduced expression of pro-inflammatory cytokines in joints tissue and the blockage of their proapoptotic effect at the chondrocyte level [20]. Other research showed there is an increased level of prolactin in patient with RA and an abnormal increase of prolactin level after surgery [21].Non-steroid anti-inflammatory drugs (NSAIDs) can also influence prolactin secretion has not been studied extensively, but one study in humans showed a decrease in plasma prolactin levels during prostaglandin E2 PGE2 infusion and an increase after use of NSAIDs , more clearly after the use of indomethacin than after naproxen[22]. Another observation which has raised interest in a role of prolactin in RA activity is the fact that pregnancy is known to influence the course of RA in women, a

characteristic feature of RA is remission of disease during gestation and exacerbation in the post partum period. During pregnancy prolactin levels start to rise during the second trimester, preparing the breasts for lactation, and reach their peak at the end of pregnancy, which has been related to the post partum exacerbation of RA[1]. Furthermore, a higher incidence of RA development has been found in the post partum period, particularly when the mother breast feeds[23].Another indication of a role of prolactin in the post- partum flare of RA comes from a study in mice, in which bromocriptine, a prolactin secretion inhibitor, administered shortly after parturition, led to a reduction of the post-partum flare of arthritis ,however, during pregnancy and after delivery, there are many hormonal changes also involving hormones of the hypothalamus pituitary -axis, which makes it very difficult to clearly show a relation of RA activity with one of these, if enhanced levels of prolactin are a pro-inflammatory factor in RA, reduction of prolactin levels might improve disease outcome in RA, reduction normal levels of prolactin could still be beneficial in arthritis as it was shown in animal studies that normal levels were necessary to induce autoimmune arthritis[23,24].Prolactin has a role in immunomodulation and it has been proposed that prolactin is a risk factor for development of autoimmunity, however it remain unclear whether the higher porlactin concentration are the cause or consequence of RA.[25]. Although the role of endogenous prolactin in autoimmune diseases has generated controversies, some study reveals that elevating serum prolactin levels significantly attenuates cartilage death and joint inflammation in inflammatory arthritis, this strategy may be comparable to the well-established use of glucocorticoid in patients with rheumatoid arthritis in which levels of the endogenous hormones appear insufficient to control the disease, While prolactin is not essential for normal immune system development and function, it is a major stress-related hormone balancing immune system homeostasis in the context of stress, trauma, and inflammation [26, 27, 28].Previous studies of prolactin concentration in patients with rheumatoid arthritis have had inconsistent results the values being either increased, decreased, or unchanged, there could be several explanation for the contradictory reports; **first,** it is possible that non-steroidal anti- inflammatory drugs(NSAIDS) may influence prolactin levels, **second**, treatment with glucocorticoid may influence prolactin concentrations, **third**, disease modifying anti rheumatic drugs (DMARDS) may influence prolactin levels [29,30].

Conclusions:

This study indicated that women with rheumatoid arthritis may play a role as triggering factor of hyperprolactinemia

References:

1- Jara, L.J.; Lavalle , C. and Fraga, A. 1991.Prolactin, immunoregulation, and autoimmune diseases. Semin .Arthri. Rheum.20: 273-284.

2- Lopez, F.J. 1989. Role of dopamine and vasointestinal peptide in the control of the pulsatile prolactin release. Endocrin. 124:527-535.

3- Chikanza ,I.C. 1999. Prolactin and neuroimmunomodulation: *In vitro* and *in vivo* observations. Ann. N.Y. Acad .Sci . 876:119-130.

4- Matera, L.; Mori, M.; Geuna, M.; Buttiglieri, S. and Palaestro, G. 2000. Prolactin in autoimmunity and antitumor defence. J Neuro. Immunol. 109:47-55.

5- Ram , S.; Blumberg , D.; Newton, P .; Anderson , N.R . and Gama , R. 2004. Raised serum prolactin in rheumatoid arthritis: genuine or laboratory artifact?.Rheumatol.43:1272-1274.

6- Mok , C .C.; Lau, C.S. and Tam, S.C.F. 1997. Prolactin profile in a cohort of chinese systemic lupus erythematosus patients. J. Br. Rheumatol. 36:986-989.

7- Straub , R.H.; Zeuner, M.; Lock ,G.;Schölmerich, J. and Lang, B. 1997. High prolactin and low dehydroepiandrosterone sulphate serum levels in patients with sever systemic sclerosis. J.Br. Rheumatol. 36:426-432.

8-McInnes , I . B.and Schett, G. 2007. Cytokines in the pathogenesis of rheumatoid arthritis. Nat. Rev. Immunol. 7(6):429-442.

9-Schuerwegh , A.J. 2003. Influence of pro-inflammatory (IL-1 alpha , IL-6 , TNF- alpha , IFN- gamma) and anti-inflammatory(IL-4) cytokines on chondrocyte function. Osteo. Arthri. Carti.11(9): 681-687.

10-Goggs , R. 2003. Apoptosis and the loss of chondrocyte survival signals contribute to articular cartilage degradation in osteoarthritis. J. Vet . 166(2):140-158.

11- Christodoulou, C . and Choy , E . H.2006. Joint inflammation and cytokine inhibition in rheumatoid arthritis . Clin. Exp. Med. 6(1) :13-19.

12-Macotela, Y. 2006. Matrix metaloproteases from chondrocyte generate an antiangiogenic 16kDa prolactin. J. Cell. Sci. 119(9):1790-1800.

13-Zermeno, C.2006. Prolactin inhibits the a poptosis of chondrocytes induced by serum starvation. J. Endocrinol. 189(2): R1-R8.

14-Ogueta , S. 2002. Prolactin is a component of the human synovial liguid and modulates the growth and chondrogenic differentiation of bone marrow-derived mesenchymal stem cell. Mol. Cell.Endocrinol. 190(2):51-63.

15- Rovensky , J. 2005. Hormone concentration in synovial fluid of patients with rheumatoid arthritis . Clin. Exp. Rheumatol. 23(3):292-296.

16-Adan , N.; Guzman-Morales , J .; Ledesma- Colunga , M.G.; Perales-canales , S .I .; Quintanar-stephano , A .; Lopez-Barrera, F .; Mendez , I .; Moreno- Carranza , B .; Triebel , J .; Binart , N .; Martinez ,G.; Thebault , S . and Clapp , C. 2013. Prolactin promotes cartilage survival and attenuates inflammation in inflammatory arthritis . J.Clin. Invest . 123(9): 3902-3913.

17- Gaalen , V. 2004. Diagnostic significance of immunological markers of Rheumatoid arthritis. Arthri. Rheum.50(3).709-715.

18-McCullough , B .D. and Wilson , B. 2005. On the accuracy of statistical procedures in Microsoft Excel 2003. Computational statistics and Data A is. 49: 1244-1252.

19-Orbach , H. and Shoenfeld , Y.2007. Hyperprolactinemia and autoimmune disease. Autoimmun. Rev. 6: 537-542.

20-Fojtikova , M.; Tomasova, S.J.; Filkova , M.; Lacinova , Z .; Gatterova , J. and Pavelka , K.2010. Elevated prolactin levels in patients with rheumatoid arthritis: association with disease activity and structural damage .Clin. Exp. Rheumatol.28:849-854.

21-Harvey , S,; Aramburo , C . and Sanders , E.J.2012.Extrapituitary production of anterior pituitary hormones: an overview. Endocrine. 41:19-30.

22-Toppozada , M.; Gerges , F .; Khalil ,H .; Marzouk, S . and Kholeif, A. 1992. Effect of

prostaglandin E2 or prostaglandin synthesis inhibitors on human gonadotrophins and prolactin. Eicosanoids.5:23-27.

23- Bernichtein , S.; Touraine , P. and Goffin , V .2010.New concepts in prolactin biology. J.Endocrinol. 206:1-11.

24-Sierakowski, S. and Cutolo , M. 2011.Morning symptoms in rheumatoid arthritis: a defining characteristic and marker of active disease. Scanda. J. Rheumatol. 125:1-5.

25-Cutolo , M.2012.Chronobiology and the treatment of rheumatoid arthritis.Curr. Opin . Rheumatol. 24:312-318.

26-Hardy , R.S.; Raza , K.and Cooper , M.S. 2012. Endogenous glucocorticoids in inflammation: contributions of systemic and local responses. Swiss.Med.Wkly.142:136-150.

27-Rohner, E. 2012. Inflammatory synovial fluid drives primary human chondrocytes to actively take part in inflammatory joint diseases. Immunol. Res. 52(3):169-175.

28-Eijsbouts , A.M.M.; Hoogen, F.H.J.; Laan , R.F.J.; Sweep , C.G.J.; Hermus , A.R.M.M. and Deputte , L.B.A. 2005. Decreased prolactin response to hypoglycaemia in patients with rheumatoid arthritis: Correlation with disease activity. Ann. Rheum. Dis. 64:433-437.

29-Pool, A.J.; Whipp, B.J.; Skasick , A.J.; Alavi , A.; Bland , J.M . and Axford , J.S. 2004. Serum cortisol reduction and abnormal prolactin and CD4+/CD8+ T-cell response as a result of controlled exercise in patients with rheumatoid arthritis and systemic lupus erythematosus despite unaltered muscle energetics.Rheumatol.43:43-48.

30-Dinan , T.G.; Scott , L.V.; Thakore , J .; Naesdal , J . and Keeling , P.W. 2001.Impact of cortisol on buspirone stimulated proactin release: a double blind placebo-controlled study.Psycho.Neuro.Endocrinol.26: 751-756.

تقييم مستوى البرولاكتين المصلي الحليب في مصول النساء المصابات بالتهاب المفاصل الرثوي

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الخلاصه:

يلعب هرمون الحليب دورا في العديد من المتلازمات الذاتية المناعة ولغرض التحري عن أهمية هذا الهرمون في قدح مرض التهاب المفاصل الرثوي، تم التحري عن (30) امرأة تعاني من ارتفاع مستوى هرمون الحليب بأعمار تتراوح من(25-40) سنة وتمت المقارنة مع (25) امرأة سليمة كمجاميع سيطرة . خضعت جميع عينات الدراسة لقياس مستوى أضداد الببتيد الحلقي الستر وليني بواسطة تقنية الامتزاز المناعي المرتبط بالانظيم، وقياس مستوى أضداد الكيراتين وأضداد الأجسام المضادة النووية باستخدام تقنية التالق المناعي الغير مباشر. لوحظ هنالك ارتفاعا معنويا في تركيز أضداد الببتيد الحلقي الستر وليني ($P< 0.05$) مقارنة بمجاميع السيطرة الأصحاء، وكانت نسبة انتشار أضداد الكيراتين والأجسام المضادة النووية (20%و10%) على التوالي، بينما لوحظ أن هنالك فرقا معنويا ($P< 0.05$) بين نسب وجود أضداد الكراتين والأجسام المضادة النووية مقارنة بمجاميع السيطرة. تشير الدراسة بان النساء المصابات بالتهاب المفاصل الرثوي يمكن ان تلعب دورا كعامل قدح لارتفاع مستوى هرمون الحليب