

THE ROLE OF HYPERPROLACTINEMIA IN THE REMODELING OF JOINT STRUCTURES IN RHEUMATOID ARTHRITIS IN WOMEN

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ABSTRACT	KEYWORDS
In 61 women with RA of reproductive age, an increase in blood prolactin levels was found in 72.1% of cases, compared with healthy women. As the disease progresses, the amount of prolactin in the patients' blood increases, and as its level increases, the radiological signs of the disease progress. At the same time, fluctuations in its level in the blood are accompanied by the progression of osteitis, an increase in the number and volume of erosions in the joints, which indicates the involvement of hyperprolactinemia in the early remodeling of joint structures.	Rheumatoid arthritis, prolactin, reproductive age.

Introduction

Musculoskeletal disorders are an important public health problem and are among the leading causes of disability and poor quality of life (5). As one of the diseases accompanied by damage to the musculoskeletal system, rheumatoid arthritis (RA) is a pressing issue in modern medicine, driven by rising morbidity, deteriorating quality of life, and significant socio-economic losses for society (6). According to modern concepts, this disease is characterized by the disruption of auto-tolerance, which is the primary factor in the pathogenesis of RA and leads to a systemic immune-inflammatory process (2, 3). Potential targets for immune aggression can be not only the tissues of joint structures but also various antigens of the endocrine system (7, 14).

As is known, the immune system, in addition to its specific functions, maintains the body's homeostasis in conjunction with the endocrine system. Therefore, in RA, along with the main manifestations, there are also various endocrine symptoms caused by immune influences (14). This means that homeostasis during inflammation is achieved through the balance between cytokines and hormones. Among the hormones, prolactin plays an important role in the interaction and regulation of immune system cell activity—a universal hormone secreted not only by the anterior lobe of the pituitary gland but also by immune cells (3, 11).

In autoimmune diseases, hypersecretion of prolactin (1,4) is often observed. In particular, literature data indicate the presence of interaction between prolactin and the immune system in RA (1, 11). Thus, prolactin enhances the expression of several genes encoding pro-inflammatory cytokines (IL-6, IL-8,

IL-12 β , TNF) and increases the production of IL-6, IL-8, and IL-12 β by macrophages (10). Hormonal disorders accompanied by disruptions in the cytokine profile can affect their ability to alter all structural-functional and adaptive processes in the joints. Consequently, remodeling is possible, i.e., a change in the properties of the morphological substrate in the joint structure associated with hyperprolactinemia. Therefore, studying the relationship between hyperprolactinemia and indicators reflecting the structural state of joint tissue in women with RA of reproductive age is promising.

The purpose of this study was to study the relationship between changes in blood prolactin levels and structural disorders in joints in women with rheumatoid arthritis of reproductive age.

Research materials and methods

A comprehensive examination of 61 women of reproductive age with RA was conducted. RA (9) was diagnosed based on the criteria of the American College of Rheumatology and European Alliance of Associations for Rheumatology (ACR/EULAR, 2010). The study included women aged 38.1 ± 9.8 years, with a disease duration of 7.1 ± 2.2 years, who provided voluntary informed consent to participate in the study. Exclusion criteria from the study were severe somatic pathology; pregnancy; use of drugs (including glucocorticosteroids and cytostatic drugs) that affect hormone metabolism and disrupt their absorption within 6 months before admission to the hospital; previous pelvic surgeries. The activity of RA was determined by assessing DAS-28 (13).

All patients underwent X-ray, ultrasound, and magnetic resonance imaging (MRI) of the joints. The study of prolactin levels in the blood was conducted using enzyme immunoassay (ELISA). The results obtained during the study were subjected to statistical processing using the Microsoft Office Excel 2021 software package and established statistical processing methods.

Results and discussion of the obtained data

Analysis of the characteristics of menstrual cycle disorders showed that before the development of RA, the vast majority of women (85.2%) noted the timely establishment of menarche (13.4 ± 3.2 years), regular menstrual rhythm, and normal duration of the menstrual cycle and menstrual bleeding. Menstrual cycle disorders were diagnosed in 73.8% of women. Analysis of prolactin levels in the blood showed that the proportion of patients with elevated levels was 72.1%. In turn, the analysis of blood prolactin levels depending on the stage of the disease, as shown in Figure 1, indicated the presence of a progressive trend curve as the disease progresses. Thus, in the initial stage of the disease, its level was 16.2 ± 2.5 ng/ml compared to 12.4 ± 4.7 ng/ml in healthy women ($p > 0.05$) and increases significantly in the advanced stage of RA to 22.2 ± 2.5 ng/ml ($p < 0.05$) and its maximum value is observed in the late stage of the disease - 32.4 ± 3.3 ng/ml ($p < 0.02$).

Assessment of the clinical course of RA in women of reproductive age showed the same characteristics as in the general population (8). The identified clinical signs indicated heterogeneity and the presence of destructive disorders in joint structures. At the same time, the clinical course of the joint syndrome was veiled by the duration of the disease. Thus, in women with RA in the late stage of the disease, the severity of the joint syndrome was characterized by significant structural disorders, as the frequency of joint deformation ($p < 0.01$) and ankylosis ($p < 0.001$) in them exceeded 70%, while elbow joint contracture ($p < 0.01$) and ulnar deviation ($p < 0.01$) were identified in nearly >70% of patients.

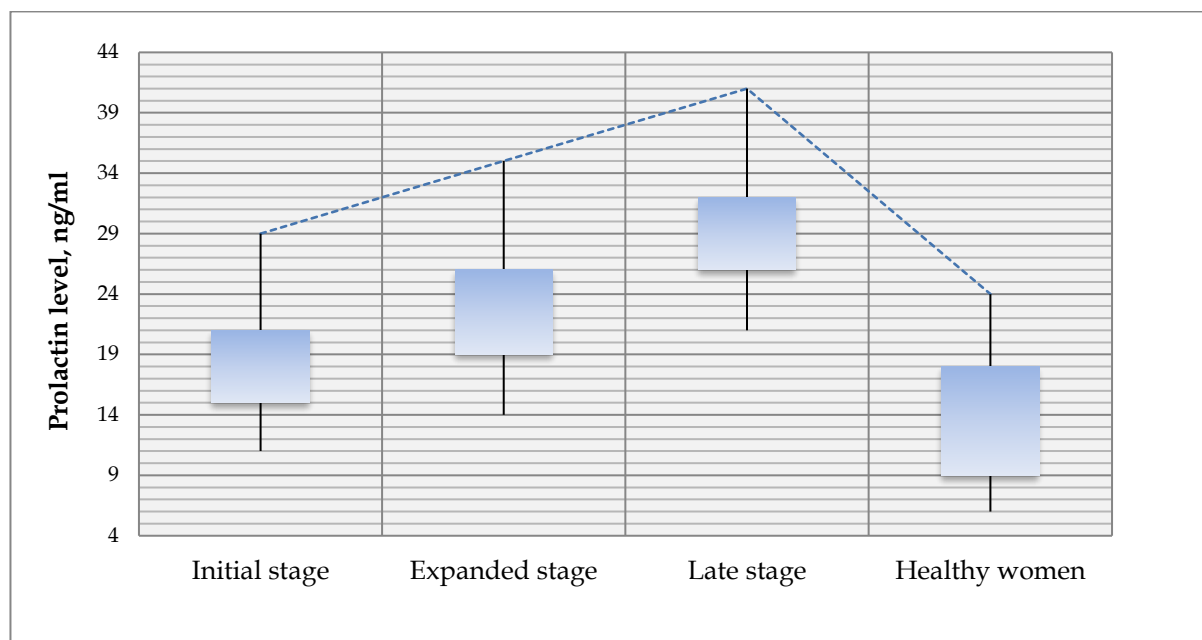


Figure 1. Prolactin levels in the blood depending on the stage of RA in women with RA of reproductive age.

As mentioned above, against the background of the immune-inflammatory process, varying degrees of disorders occur in all categories of joint tissue structures. Considering that there is a correlation between the immune system and hormones, it is obvious that this can lead to various degrees of disruption in the remodeling of joint structures. Consequently, what is the role of hyperprolactinemia in remodeling and structural disorders in joint tissue during this disease? The results of our studies reflect the features of the radiological picture of joint structures depending on the level of prolactin in the patients' blood.

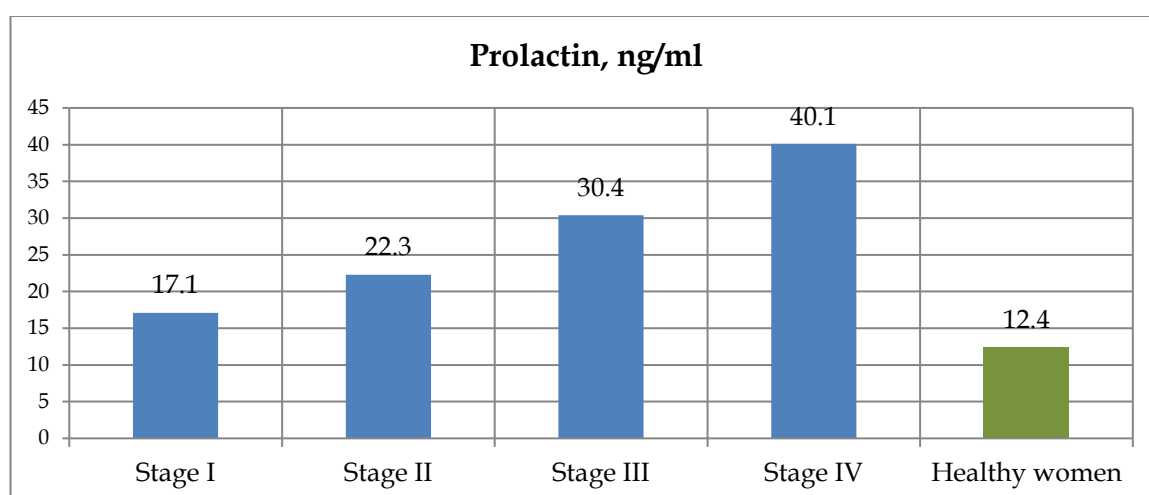


Figure 2. Prolactin levels in the blood of RA women depending on the radiological stages of RA.

As shown in Figure 2, as the radiological (R^o) picture of RA progressed, prolactin levels changed significantly. Thus, in patients with stage R^o I RA, the prolactin level showed no statistically significant differences ($p > 0.05$) compared to the indicators of healthy women. However, starting from stage R^o II

of the disease, a significant ($p<0.05$) increase is observed, and in stage R°IV, its level is almost 3 times higher compared to the indicators of women with stage R°I.

It is well known (13) that structural changes in joints in RA begin with damage to the synovial membrane, and as the process progresses, specific changes such as erosion and pannus are observed, followed by disorders in other joint tissues. As reflected above, hyperprolactinemia in women with RA is accompanied by the progression of radiological signs; the use of ultrasound and MRI research methods expands the possibilities for assessing soft and other types of tissues in the joint. Therefore, it is of scientific interest to study the presence of a correlation between fluctuations in prolactin levels and indicators reflecting structural disorders in the joints, taking into account ultrasound and MRI.

Correlation analysis showed that in women with RA, hyperprolactinemia is accompanied by specific remodeling of the knee joint structure. As shown in Figure 2, it participates in the alteration of the soft structure and bone tissue of the knee joint. At the same time, their role in the development of osteitis is noticeable, as fluctuations in prolactin levels and its volume had a direct correlation ($r=0.81$; $p<0.05$). At the same time, an increase in its level is accompanied by an increase in the volume and quantity of erosion, as a positive correlation ($r=0.79$; $p<0.05$) was identified between them, indicating the role of hyperprolactinemia as a predictor of early remodeling of joint structures.

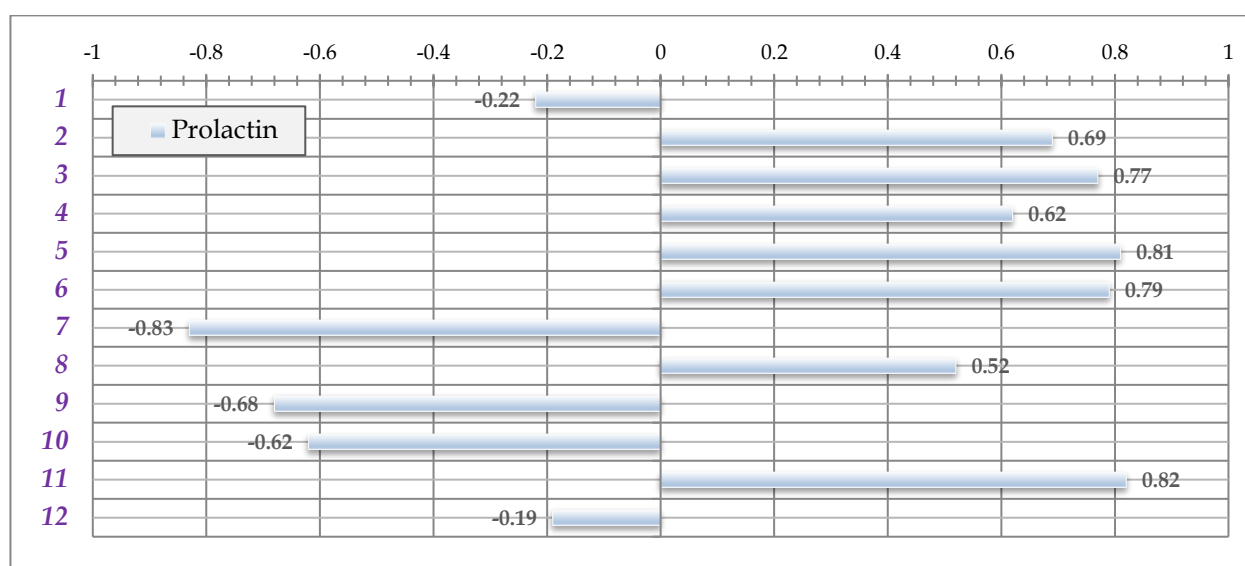


Figure 2. Correlation between prolactin fluctuations and structural changes in the knee joint (r) in RA women. Conditional signs: 1 - osteoporosis in the lateral parts of the bone; 2 - osteoporosis in the subchondral parts of the bone; 3 - osteoporosis of the bone epiphysis; 4 - thickness of the synovial membrane; 5 - volume of the osteitis; 6 - volume and amount of erosion; 7 - size of the interarticular space; 8 - subchondrial osteosclerosis; 9 - volume of the defect on the cartilage surface; 10 - volume of the defect in the cartilage at the site of attachment to the bone tissue; 11 - resorption volume; 12 - expansion of the pannus.

In turn, a positive correlation was also identified between fluctuations in prolactin levels and osteoporosis volume indicators in the subchondral parts of the bone and bone epiphysis ($r=0.69$ and $r=0.77$, respectively; $p<0.05$). In addition to the above, the concentration of prolactin in the blood had a significant negative correlation with the size of the interarticular space ($r=-0.83$; $p<0.05$). It was

established that with an increase in prolactin levels, an expansion of resorption volume occurs in bone tissue ($r=0.82$; $p<0.05$).

Conclusion

Thus, an increase in prolactin levels is an unfavorable prognostic marker of the autoimmune process in RA, which is reflected in its role in the early remodeling of joint structures. At the same time, as the prolactin level increases, the radiological signs of the disease progress.

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