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Endometriosis and Serum Hepcidin Levels

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Abstract: ***Aim: Endometriosis is a benign disease which takes third place in gynecological morbidity after inflammatory disease and uterine myoma. We tried to evaluate serum iron and hepcidin levels and search for a connection in occurrence of endometriosis. Data: For serum hepcidin quantification we used ELISA assay. 40 women, average age 25.4 ± 4.3 were included. They were divided into two groups – women with endometriosis (EM) and control group. The samples were taken in the University Hospital "Michin Dom" for a period of one year, 2014. We measure serum iron levels, ferritin and calculate transferrin saturation. Pearson's coefficient and Student's t-test were used for evaluation of correlation and statistical significance. Results: We found statistically significant differences in serum hepcidin levels between measured groups: women with endometriosis had higher concentrations – 57.4 ± 8.5 µg/L vs control group – 20.7 ± 2.8 µg/L (r = -0.174, P < 0.001). Serum ferritin levels showed significant differences between two groups: EM – 18.3 ± 9.6 ng/mL vs control – 68.99 ± 16.1 ng/mL(r = -0.203, P < 0.001). Serum iron levels were statistically different: for EM 48.9 ± 4.9 µmol/L compared to 11.6 ± 1.7 µmol/L in control group (P < 0.001). Conclusions: We conclude that our results support the thesis that iron overload and elevated serum hepcidin levels takes an important role into pathogenesis of endometriosis.***

Keywords: endometriosis, hepcidin, iron overload, ferritin, inflammation

1. Introduction

Endometriosis is a benign disease for which it is assumed that covers about 10-25% of women. Endometriosis is an estrogen-driven inflammatory disease that causes pelvic pain, painful menstrual periods, and infertility (1). It is characterized by the growth of endometrial tissue at extrauterine sites, mainly on the ovaries and peritoneum. In the structure of gynecological morbidity endometriosis ranks third, after inflammatory disease and uterine myoma.

There is uncertainty about the causes of the disease, its etiology. There are several hypotheses:

- Retrograde (with reverse flow) menstruation and implantation of endometrium outside the uterine cavity. In menstrual blood are found still viable endometrial cells, which under appropriate conditions can develop into endometrial glands;
- hematogenic (blood-borne) and lymphogenic (lymphatic time) distribution of endometrial cells;• transformation (metaplasia) cells of the peritoneum in endometrial due to constant estrogen stimulation;
- Genetic predisposition;
- Dissipation of endometrial cells during the surgery.

The most important condition for the development and progression of endometriosis is the presence of menstrual function and related cyclic hormonal stimulation of the target (target) authorities. This disease does not occur before the onset of first menstruation (menarche), while the menopause endometriotic foci spontaneously regress (undergo regression).

This iron accumulation leads to an excessive production of free radicals enhances the activity of pro-inflammatory cytokines, chemokines, adhesion molecules, growth factor, and angiogenic factor, supporting the inflammatory response, resistance to apoptosis, and cell proliferation in endometriotic lesions (2,3). It stimulates an inflammatory response, which promotes the proliferation and survival of ectopic endometrial cell (4).

2. Materials and Methods

For a period of one year we determined serum hepcidin levels using ELISA assay in 40 women; average age 25.4 ± 4.3. The samples were taken in the University Hospital "Michin Dom". The patients included were divided into two groups – women with endometriosis (EM) and control group. Demographic parameters are shown in Table 1.

We measure serum iron levels, ferritin and calculate transferrin saturation. Pearson's coefficient and Student's t-test were used for evaluation of correlation and statistical significance. We measure hepcidin levels using verified ELISA method (5). For iron quantification we used AAS

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(Perkin Elmer) and for serum ferritin levels – ECLIA method (Roche Diagnostics).

3. Results

Age distribution of included women in this trial is shown in Table 1.

Table 1: Age distribution of included women

	Control group	With endometriosis
n	20	20
mean (age)	25.1	25.8
SD (age)	3.5	5.1

Patients were signing the informed consent according to the Declaration of Helsinki (Directive 2001/20 / EC).

We found statistically significant differences in serum hepcidin levels between measured groups: women with endometriosis had higher concentrations – 57.4 ± 8.5 µg/L vs control group – 20.7 ± 2.8 µg/L (r = -0.174, P < 0.001) (Fig. 1). Serum ferritin levels showed significant differences between two groups: EM – 18.3 ± 9.6 ng/mL vs control – 68.99 ± 16.1 ng/mL(r = -0.203, P < 0.001). Serum iron levels were statistically different: for EM 48.9 ± 4.9 µmol/L compared to 11.6 ± 1.7 µmol/L in control group (P < 0.001) (Fig. 2).

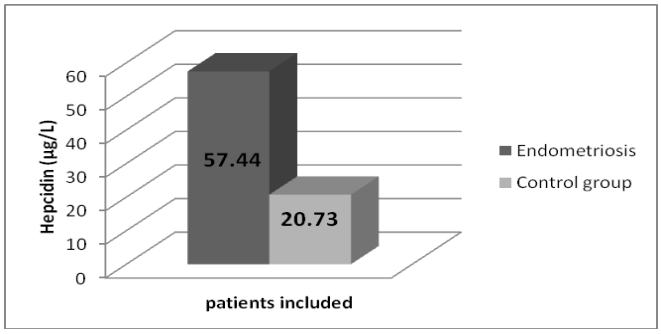

Figure 1: Measured serum hepcidin levels in two groups

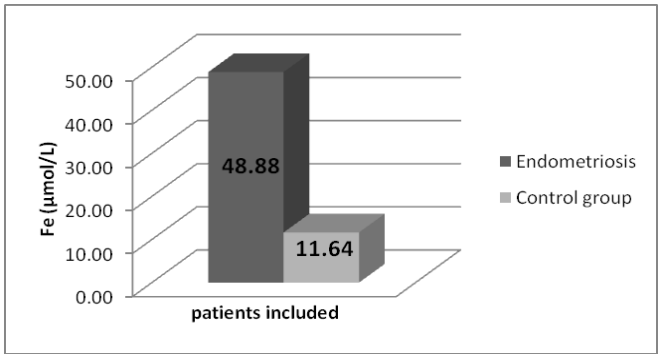

Figure 2: Serum iron concentrations in women with endometriosis and control group

Serum hepcidin levels correlated negatively to ferritin concentrations in endometriosis group r = -0.420, P < 0.001 (Fig. 3) and positively in control group r = 0.225, P < 0.001. We found that there is a significant correlation between serum hepcidin levels and iron concentration in both groups (P < 0.001).

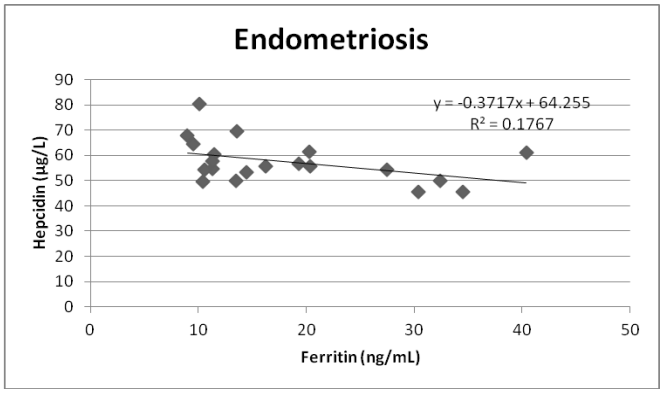

Figure 3: Correlaion between serum ferritin and hepcidin levels in patients with endometriosis

4. Discussion

It is known that the accumulation of iron in the body causes a cytotoxic effect, breaking the balance between the formation of free radicals and antioxidant protection. This condition is known as oxidative stress; it is suggests that it plays a role in the etiology of endometriosis. Oxidative stress is involved in the pathogenesis of many other diseases, such as malignancies, atherosclerosis, neurodegenerative diseases, preeclampsia (6). The presence of the super-imposition of iron was found in the peritoneal cavity in patients with endometriosis (7). The process of iron accumulation in macrophages in peritoneal cavity leads to the development of chronic inflammation (8), which influences the secretion of hepcidin. Elevated serum hepcidin levels in turn lead to changes in the intestinal absorption of iron by the interaction between hepcidin and the only known intracellular iron exporter - ferroportin (9,10).

5. Conclusion

Choosing the right therapeutic management of impaired homeostasis of iron still remains a challenge in routine work of gynecologists. On the one hand iron overload can cause fetal harm and disrupt the normal course of pregnancy. On the other hand, iron deficiency also has its adverse effects on the course of pregnancy. Serum hepcidin quantification may be a part of the algorithm for endometriosis patients' treatment, in which it will be easier to make the right choice between either the iron therapy to correct anemic syndrome or to avoiding further iron disposition, preventing organism intoxication, which is quite similar to patients in rheumatoid arthritis (11).

6. Acknowledgement

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