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Role of insulin and insulin-like growth factor I receptor expression in the pathogenesis of genital endometriosis

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BACKGROUND: Growth factors play an important role in the pathogenesis of genital endometriosis. Insulin and insulin-like growth factors are involved in mitosis and differentiation in the endometrium during the menstrual cycle and early pregnancy, and are likely to indirectly affect the invasion of the endometrium during retrograde menstruation and the development of pain syndrome in endometriosis. However, the available literature data on insulin-like growth factors and insulin in the endometrium and endometrioid heterotopies in patients with genital endometriosis are scarse and contradictory.

AIM: The aim of this study was to investigate the expression of insulin receptors and insulin-like growth factor I receptors in the eutopic endometrium and endometrioid heterotopies of patients with genital endometriosis.

MATERIALS AND METHODS: This cross-sectional study included immunohistochemical analysis of surgical material obtained from two groups of women in the proliferative phase of the menstrual cycle: patients with endometriosis who received surgical treatment (endometrium and endometrioid heterotopies) and patients without endometriosis who were examined due to infertility (endometrium). The study also included investigation of carbohydrate metabolism (glucose tolerance test) and determination of blood serum insulin-like growth factor I, insulin and sex hormone levels. The material was stained to detect the expression of insulin receptors and insulin-like growth factor I receptors. Then, the relative area and optical density of the receptor expression were determined and the obtained data were analyzed statistically.

RESULTS: We analyzed the examination results of 131 women matched in age and weight and height characteristics: 101 patients with genital endometriosis and 30 patients in the control group. Carbohydrate metabolism was characterized by a 2.1-fold increase in glucose-stimulated insulin secretion in patients with genital endometriosis compared with the control subjects. The blood level of insulin-like growth factor I did not differ in the study groups. Statistically significant differences in receptor expression were obtained between the groups. In the endometrium of patients with genital endometriosis, the optical density of insulin receptors was lower ($p = 0.007$) and the expression of insulin-like growth factor I receptors higher ($p = 0.002$) compared to the endometrium of the control subjects. The median values of insulin receptor expression in endometrioid heterotopies were decreased compared to the endometrium of the control group ($p < 0.001$). The expression of insulin-like growth factor I receptors in endometrioid heterotopies was reduced compared to the endometrium of the same patients ($p < 0.001$).

CONCLUSIONS: The data obtained indicate significant features in the functioning of the insulin / insulin-like growth factor I system in patients with genital endometriosis: glucose-*stimulated insulin* secretion and relative endometrial insulin resistance due to the decreased expression of insulin receptors and the increased expression of insulin-like growth factor I receptors in the endometrium.

Keywords: endometriosis; insulin; insulin receptors; insulin-like growth factor I receptors; immunohistochemistry.

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Роль системы инсулин/инсулиноподобный фактор роста в патогенезе генитального эндометриоза

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Обоснование. В патогенезе наружного генитального эндометриоза значительную роль играют ростовые факторы. Инсулин и инсулиноподобные факторы роста участвуют в пролиферации и децидуализации эндометрия во время менструального цикла и на ранних сроках беременности, вероятно, опосредованно влияют на инвазию эндометрия при ретроградной менструации и формирование болевого синдрома при эндометриозе. Однако литературные данные об инсулиноподобном факторе роста и инсулине в эндометрии и эндометриоидных гетеротопиях у пациенток с наружным генитальным эндометриозом немногочисленны и противоречивы.

Цель — изучить роль системы инсулина и инсулиноподобного фактора роста 1 в патогенезе наружного генитального эндометриоза.

Материалы и методы. Проведено поперечное исследование, включавшее изучение углеводного обмена (глюкозотолерантный тест), определение уровней инсулиноподобного фактора роста 1, инсулина и половых гормонов в сыворотке крови и иммуногистохимический анализ операционного материала, полученного от женщин в пролиферативную фазу менструального цикла: пациенток с эндометриозом (эндометрий и эндометриоидные гетеротопии) и без эндометриоза (эндометрий). Материал окрашивали для выявления экспрессии рецепторов инсулина и инсулиноподобного фактора роста 1. Затем вычисляли относительную площадь и оптическую плотность экспрессии рецепторов и с помощью статистического анализа изучали различия данных показателей между группами.

Результаты. Были проанализированы результаты обследования 131 пациентки. Женщины были сопоставимы по возрасту и весо-ростовым характеристикам: 101 больная с наружным генитальным эндометриозом и 30 женщин контрольной группы. Углеводный обмен характеризовался повышением уровня стимулированного инсулина в 2,1 раза у пациенток с наружным генитальным эндометриозом по сравнению с женщинами контрольной группы. Уровень инсулиноподобного фактора роста 1 в крови в исследуемых группах не отличался. Получены статистически значимые отличия в экспрессии рецепторов между группами. В эндометрии пациенток с наружным генитальным эндометриозом оптическая плотность рецепторов инсулина была снижена (p = 0,007), а уровень экспрессии рецепторов инсулиноподобного фактора роста I был повышен по сравнению с эндометрием пациенток контрольной группы (p = 0,002). При оценке экспрессии рецепторов инсулина медианные значения в эндометриоидных гетеротопиях были снижены по сравнению с эндометрием контрольной группы (p < 0,001). Экспрессия рецепторов инсулиноподобного фактора роста 1 в очагах эндометриоза была снижена по сравнению с эндометрием этих же пациенток (p < 0,001).

Заключение. Результаты исследования указывают на наличие значимых особенностей в функционировании системы инсулин/инсулиноподобный фактор роста 1 у больных наружным генитальным эндометриозом, в том числе на повышение уровня стимулированного инсулина, относительную инсулинорезистентность эндометрия за счет снижения экспрессии рецепторов к инсулину и увеличение в эндометрии рецепторов к инсулиноподобному фактору роста 1 — мощному ростовому фактору.

Ключевые слова: эндометриоз; инсулин; рецепторы инсулина; рецепторы инсулиноподобного фактора роста 1; иммуногистохимия.

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BACKGROUND

Endometriosis is a chronic disease but remains underinvestigated. Owing to the combination of genetic predisposition, hormonal deregulation, and immunological susceptibility, endometrium-like tissue can propagate and exist outside the uterine cavity [1]. Although epidemiological data vary widely, endometriosis is estimated to affect up to 10% of women of reproductive age. The manifestations of endometriosis can vary but usually include pelvic pain, dysmenorrhea, dyspareunia, infertility, and miscarriage, as well as gastrointestinal and urinary manifestations, which reduce significantly the quality of life of most patients [2]. Endometriosis is involved in many immune-mediated processes and is associated with systemic inflammation and increased oxidative stress [2, 3], which can adversely affect other body systems. According to epidemiological data, external genital endometriosis (EGE) is associated with certain body characteristics such as tall stature and low weight and body mass index (BMI) both at birth and adolescence and at the time of diagnosis [4, 5]. However, despite such a favorable structure and the knowledge that endometriosis is characterized by absolute or relative hyperestrogenemia, the disease is associated with several pathological atherogenic changes in the lipid profile of patients and an increased risk of cardiovascular complications [6, 7] and endocrine disorders [8, 9].

Insulin and insulin-like growth factors (IGFs) form a complex system consisting of peptide hormones (such as insulin, insulin-like growth factors 1 and 2 [IGF-1 and IGF-2, respectively]), receptors on the cell surface, and circulating proteins, binding these hormones. IGF-1 and IGF-2 promote cell growth and differentiation in mammals, whereas insulin primarily controls metabolism [10]. However, their functions can overlap, which is emphasized by the high homology between insulin and IGF-1 receptors, which form hybrid heterodimers in many cells and share many signaling pathways [11]. Acting jointly, these components control important biological mechanisms such as cell growth, proliferation, differentiation, migration, and anti-apoptotic mechanisms. The processes in which these substances are involved are directly related to the formation and remodeling of tissues, bone growth, brain development, and energy metabolism, which ultimately affect the growth and life expectancy of the organism. This close interaction between insulin and IGF-1 probably contributes to the relationship between hyperinsulinemia and some types of pathological hyperproliferative processes, including malignant ones [12].

Recent studies have revealed that IGF-1 may be involved in the pathogenesis of pain syndrome in endometriosis, by acting as a neurotrophic and sensitizing factor. Several studies have found that the concentration of IGF-1 in the peritoneal fluid of patients with endometriosis is significantly increased compared with its concentration in women without endometriosis [13], and this increase is positively correlated with the severity of pain syndrome ($r = 0.44$, $p = 0.03$) [14]. The use of inhibitors of IGF-1 in an experimental mouse model of endometriosis led to a decrease in pain syndrome [14].

The concept of insulin resistance was first introduced by Himsworth [15], who noted that the simultaneous administration of glucose and insulin to patients with diabetes gives one or other results. Several patients with diabetes responded with stable or low blood glucose levels, and they have been considered insulin-sensitive. In other patients, blood glucose levels increased significantly, and this group was considered insulin-resistant. At present, the second group of patients exhibited insulin resistance typical of metabolic syndrome, as at normal plasma insulin levels, target tissues are unable to provide a normal coordinated glucose-lowering response, including suppression of endogenous glucose production, lipolysis, cellular uptake of available plasma glucose, and glycogenesis [16].

Insulin resistance leads to a compensatory increase in insulin secretion; therefore, fasting plasma insulin levels increase [17]. The real-time feedback response that links insulin sensitivity and insulin secretion makes it difficult to find a causal relationship in identifying the primary disorder. Changes in the signaling pathways of both insulin target tissues and pancreatic β-cells are essential for the development of fasting hyperglycemia and type 2 diabetes mellitus [18]. Chronic hyperinsulinemia leads to a decrease in insulin sensitivity at the receptor level [19]. With a decrease in the expression of insulin receptors on the cell surface, the rate of the cell's response to insulin decreases, but because of the "reserve" receptors, the maximum response does not decrease, unless the content of insulin receptors on the cell surface drops to 5%–10% of the normal [20]. Thus, insulin resistance is not a binary shutdown of insulin signaling, which makes hyperinsulinemia an effective compensatory mechanism for mild to moderate insulin resistance [21].

The literature presents almost no data on the level of IGF-1 expression in the endometrium of healthy women. A study published in 1993 examined 10 endometrial specimens obtained during hysterectomy for unspecified reasons and reported no difference in the IGF-1 expression during the menstrual cycle, but the expression of insulin receptors was more pronounced in the endometrium in the secretory phase of the menstrual cycle [22].

In our review of literature data, no study has reported on the level of insulin or its receptors in the endometrium and endometrioid heterotopies of patients with endometriosis.

In 1994, a study examined the IGF-1 and IGF-2 systems, their receptors, and proteins binding them and determined

the expression of messenger RNA. As a result of analysis of two samples of the endometrium in the proliferative phase and eight samples of the endometrium in the secretory phase of the menstrual cycle, the growth factors themselves were determined only in the stromal component of the endometrium, and the expression of IGF-1 was more pronounced in the endometrium in the proliferative phase, and the expression of IGF-2 was more pronounced in the secretory phase. Expression of receptors of types 1 and 2 did not depend on the phase of the menstrual cycle and was present in both the epithelial and stromal components of the endometrium but was more pronounced in the epithelial component [23].

Immunohistochemical study of IGF-1 expression in the endometrium of healthy women (n = 14) revealed more intense staining during the proliferation phase compared with the secretion phase. In the eutopic endometrium of women with endometriosis (n = 8, 4 samples each of the proliferative phase and secretory phase of the menstrual cycle), a decrease in staining was noted when assessing IGF-1, while intense immunostaining was recorded in the epithelial cells of fibrous adhesions of the peritoneum. Based on the immunohistochemical study of IGF-2 in the endometrium of healthy women, a more intense expression was revealed during the secretory phase in both stromal and epithelial cells [24].

This study aimed to investigate the role of insulin and IGF-1 system in the pathogenesis of genital endometriosis.

MATERIALS AND METHODS

This cross-sectional study enrolled 131 women who presented to the D.O. Ott Research Institute of Obstetrics, Gynecology, and Reproductology (Department of Gynecology and Endocrinology, Laboratory of Immunohistochemistry, Department of Morbid Anatomy). The obstetric and gynecological anamnesis was studied in all patients, and weight and height characteristics were measured. In 102 women of reproductive age (82 patients had previously laparoscopically confirmed endometriosis, 20 patients comprised the control group), carbohydrate metabolism was additionally evaluated by performing an oral glucose tolerance test to determine the level of basal and stimulated insulin. Moreover, the endocrine profile [follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, and prolactin] and serum IGF-1 levels on days 2–5 of the menstrual cycle were assessed. The levels of FSH and LH were determined by enzyme-linked immunosorbent assay using Alkor-Bio test systems (Russia), and the estradiol levels were assessed using DRG Diagnostics test systems (Germany). An enzyme-linked immunosorbent assay using reagents manufactured by DRG Instruments GmbH (Germany) was used to determine the level of IGF-1 in the blood serum. Insulin and prolactin levels were assessed using an enzyme-linked immunosorbent assay with enhanced chemiluminescence on an Access 2 analyzer (Beckman Coulter, USA).

During the study, the endometrium and endometrioid heterotopies obtained intraoperatively from 29 women were analyzed. Ten of these patients without endometriosis were included in the control group (only the endometrium), and 19 patients were diagnosed with EGE of varying degrees of generalization. The diagnosis of EGE was confirmed based on laparoscopy and results of histological examination of the endometriosis foci. All intraoperative samples were taken in the proliferative phase from day 7 to day 12 of the menstrual cycle; the menstrual phase was confirmed by the results of histological examination of the endometrium. For immunohistochemical studies, endometrial samples were obtained in the control group, and endometrial samples and excised endometrioid heterotopies were obtained in the EGE group. The study did not include women with concomitant gynecological (such as polycystic ovary syndrome, uterine fibroids, polyps, or endometrial hyperplasia) and endocrine (such as diabetes mellitus and impaired glucose tolerance) pathology or severe somatic diseases.

The relative area and optical density of the expression of the β-subunit of insulin receptors (reagent ab983, Abcam, USA) and IGF-1 receptors (reagent ab39398, Abcam) were calculated in all samples during the immunohistochemical study according to the standard one-stage protocol with antigen retrieval.

Morphometry, database construction, and statistical processing were performed using ImageJ, Microsoft Excel, and Jamovi programs. The Shapiro–Wilk test was used to check the normal distribution of the data. Normally distributed data were described using the mean and standard deviations M (SD), and data with a non-normal distribution were described using the median and interquartile range Me (Q_1; Q_3). To compare the two samples, depending on the nature of distribution, the Student t-test or Mann–Whitney test was used. Paired t-test and Wilcoxon test were applied for pairwise comparison of data obtained during the oral glucose tolerance test. Data among the three groups (endometrium of the control group, endometrium of the EGE group, and endometrioid heterotopy group) with abnormal distribution were compared using Kruskall–Wallis rank analysis of variations with subsequent multiple pairwise comparisons using the Dwass–Steel–Critchlow–Fligner method. With normal data distribution, a one-way analysis of variance was performed with the clarification of the equality of sample variances using the Leaven test. For unequal variances, Welch's modification was used, followed by a posteriori analysis by the Games–Howell method. Differences were considered significant at $p < 0.05$.

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RESULTS

No significant differences were found in terms of age and BMI between the EGE group and control group. In the immunohistochemical study, the average age of the EGE group was 35.4 (6.05) years and that of the control group was 33.9 (5.45) years. Patients were also comparable in terms of BMI, with 24.1 (3.42) kg/m^2 in the EGE group and 23.6 (3.95) kg/m^2 in the control group. In the assessment of carbohydrate metabolism, the average age and BMI of the EGE group were 32.4 (5.13) years and 23.8 (2.28) kg/m^2, respectively. In the control group, the average age and BMI were 29.8 (4.37) years and 22.7 (3.41) kg/m^2, respectively.

The results of the carbohydrate metabolism analysis are presented in Table 1.

In the control group, the oral glucose tolerance test revealed no disorders in the carbohydrate metabolism; while in the EGE group, 4% of the patients showed impaired glucose tolerance and 3% had impaired fasting glycemia. Average fasting plasma glucose and basal insulin levels in the EGE group [5.13 (0.48) mmol/l; 6.72 (2.89) μU/ml] did not differ significantly in comparison with that in the control group [4.74 (0.39) mmol/L; 5.61 (2.67) μU/ml], $p_{glucose}$ = 0.052, $p_{insulin}$ = 0.178.

Two hours after administration of 75 g of glucose, the plasma glucose level did not change significantly either in the control group (p = 0.648) or in the EGE group (p = 0.068).

The insulin level increased significantly in both groups (p < 0.001), but the difference in indicators was significantly greater in the EGE group than in the control group, namely, 30 (95% CI 16.3; 111.1) versus 11.5 (95% CI 7.46; 24.5), p = 0.021. The level of stimulated insulin in the blood of patients with endometriosis was 2.1 times higher than that in the control group.

No correlation was found between the results of the oral glucose tolerance test, BMI, age, or level of the studied hormones (Table 2).

No differences were found in the serum IGF-1 concentration of patients with endometriosis compared with women without endometriosis (p = 0.69).

Table 1. Results of the oral glucose tolerance test to determine basal and stimulated insulin levels in the control group and EGE group

Indicator	EGE group		Control group		*p*
	M (*SD*)	*Me* (Q_1; Q_3)	*M* (SD)	*Me* (Q_1; Q_3)	
Fasting glucose, mmol/l	5.13* (0.48)	5.1 (4.86; 5.55)	4.74* (0.39)	4.75 (4.5; 5.1)	0.052
Postload glucose, mmol/l	6.3 (1.59)	5.9* (5.35; 7.17)	4.88* (1.12)	4.7 (3.95; 5.45)	0.077
Average difference	0.5 (95% CI –0.06; 0.85)		0.173 (95% CI –0.65; 0.99)		
p	0.068		0.648		
Fasting insulin, mIU/L	6.72* (2.89)	6.58 (4.41; 9.37)	5.61* (2.67)	5.08 (3.71; 7.63)	0.178
Postload insulin, mIU/l	53.5 (59.3)	40.3* (22.9; 47.5)	19.6 (11.9)	19.1* (10.5; 21.0)	**0.003**
Average difference	30 (95% CI 16.3; 111.1)		11.5 (95% CI 7.46; 24.5)		**0.021**
p	**<0.001**		**<0.001**		
Insulin resistance index, homeostatic model assessment	1.59* (0.729)		1.2* (0.614)		0.366

Note. EGE, external genital endometriosis. * data distribution indicated.

Table 2. Results of the endocrine examination and determination of the levels of insulin-like growth factor 1 in the blood serum

Indicator	Main group	Control group	*p*
Estradiol, pmol/l	231 (107; 320)	149 (120; 202)	0.455
FSH, IU/L	7.49 ± 2.9	7.34 ± 1.13	0.363
LH, IU/L	5.04 ± 1.6	4.68 ± 0.54	0.779
Prolactin, mIU/L	253 (181; 335)	233 (205; 397)	0.876
IGF-1, ng/ml	136 (117; 162)	148 (120; 159)	0.701

Note. FSH, follicle-stimulating hormone; LH, luteinizing hormone; IGF-1, insulin-like growth factor 1.

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Table 3. Expression of insulin receptors and IGF-1 in the endometrium and in endometrioid heterotopies of the external genital endometriosis group in comparison with the endometrium of the control group

Localization	Relative area of expression, %		Optical density	
	IGF-1 receptor	insulin receptor	IGF-1 receptor	insulin receptor
Eutopic endometrium (n = 19)	12.8 (9.95; 15.2)	13.8 (5.21; 18.2)	0.132 (0.0477)	0.133 (0.0551)
Endometrioid heterotopies (n = 19)	3.02 (0.528; 5.22)	4.65 (2.70; 6.25)	0.117 (0.0738)	0.143 (0.0502)
Endometrium (control group) (n = 10)	5.50 (2.70; 6.87)	23.9 (17.0; 28.5)	0.157 (0.00792)	0.172 (0.0096)
Comparison between groups	**p < 0.001**	**p < 0.001**	**p = 0.017**	**p < 0.001**
Pairwise comparison	**$p_{1–2}$ < 0.001** **$p_{1–3}$ = 0.002** $p_{2–3}$ = 0.372	$p_{1–2}$ = 0.068 $p_{1–3}$ = 0.051 **$p_{2–3}$ < 0.001**	$p_{1–2}$ = 0.745 $p_{1–3}$ = 0.091 $p_{2–3}$ = 0.085	$p_{1–2}$ = 0.083 **$p_{1–3}$ = 0.007** **$p_{2–3}$ = 0.026**

Note. IGF-1, insulin-like growth factor 1.

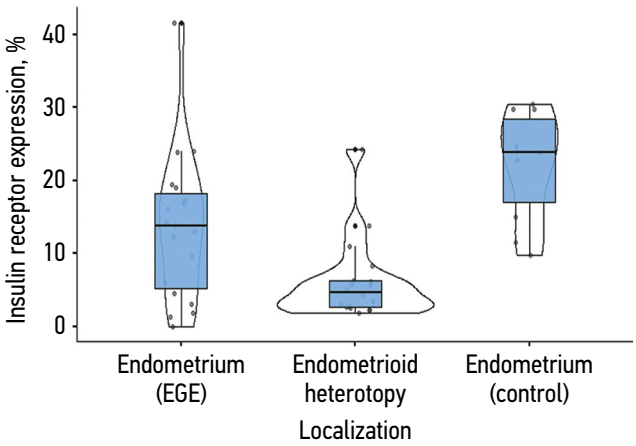

Fig. 1. Expression of insulin receptors (relative area, %) in the endometrium of patients in the EGE and control groups and in endometrioid heterotopia. EGE, external genital endometriosis

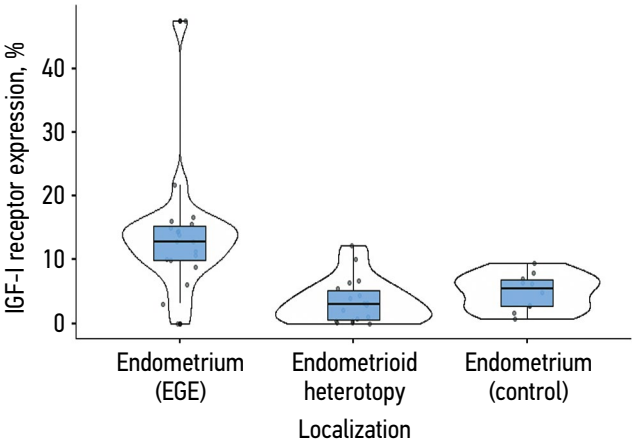

Fig. 3. Expression of insulin-like growth factor 1 (IGF-1) receptors (relative area, %) in eutopic endometrium of the external genital endometriosis (EGE) group and control group, and in endometrioid heterotopias

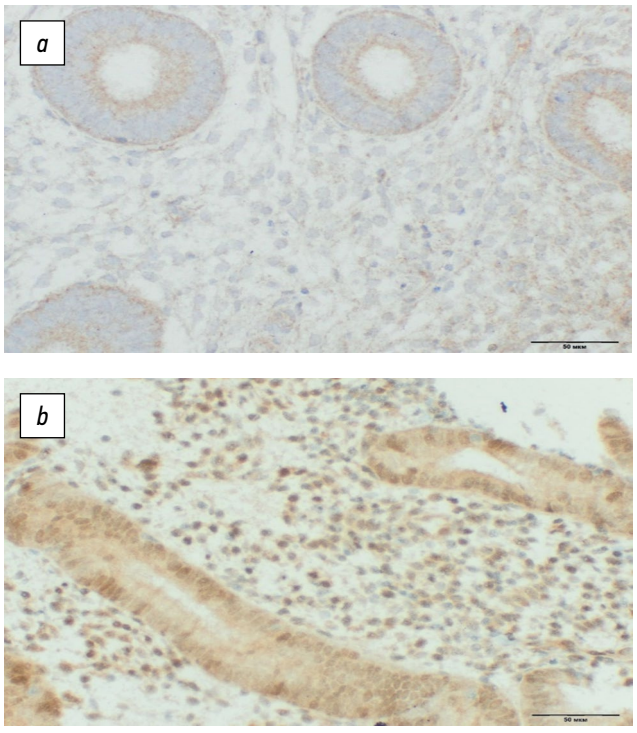

Fig. 2. Expression of insulin receptors in the endometrium of a patient with endometriosis (*a*) and in the endometrium of a patient without endometriosis (*b*). × 400

The results of the immunohistochemical study are presented in Table 3.

The relative area of expression of insulin receptors (Fig. 1) in the endometrium of the proliferation phase in the control group was five times higher than that in endometrioid heterotopies (p < 0.001). The expression of insulin receptors in the endometrium of women in the control group was 73% higher than that in the endometrium of patients with endometriosis, but the differences were below the threshold of significance (p = 0.051) (Fig. 2). Data on the optical density of insulin receptors in the endometrium of the two groups confirm these results. The maximum level of optical density (0.172) was also noted in the endometrium of the control group (0.0096), and it was significantly higher than similar indicators in the endometrioid heterotopia 0.143 (0.0502) (p = 0.026) and in the endometrium with 0.133 (0.0551) (p = 0.007) of the EGE group.

The highest expression level (12.8%) of IGF-1 receptors (Figs. 3, 4) was registered in the eutopic endometrium of patients with endometriosis (9.95; 15.2), which is 2.3 times higher than the expression in the endometrium of the patients in the control group (p = 0.002) and 4.2 times higher than that in the endometrioid heterotopia (p < 0.001).

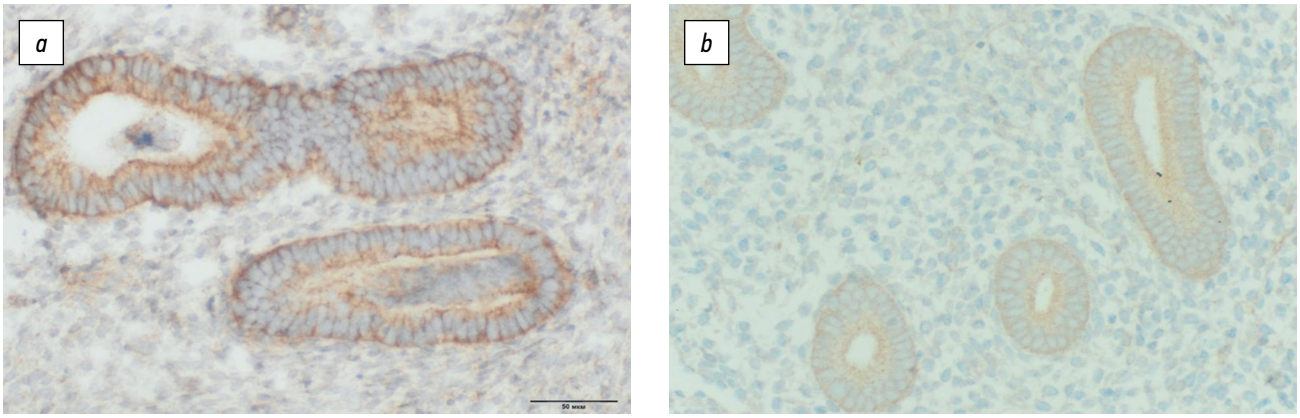

Fig. 4. Expression of insulin-like growth factor 1 receptors in the endometrium of a patient with endometriosis (*a*) and in the endometrium of a patient without endometriosis (*b*). × 400

The optical density of the expression of IGF-1 receptors was not significantly different in the pairwise comparison between the groups.

DISCUSSION

In this study, carbohydrate metabolism is characterized by an increase in the level of stimulated insulin in the EGE group when compared with the level in the control group by 2.1 times ($p = 0.003$), and the changes are not associated with BMI, age, or hormone levels (FSH, LH, estradiol, and prolactin) [25].

In patients with endometriosis, the relative area and optical density of the expression of insulin receptors in the eutopic endometrium were reduced compared with that in the control group. One of the possible causes for this decrease was postprandial hyperinsulinemia. As mentioned, the maximum effect of insulin decreases only when the number of receptors decreases by 5%–10% of the normal, while the decrease in the studied samples was 47.7% when compared with that in the control group, which may explain why the patients with endometriosis are not characterized by typical manifestations of insulin resistance and metabolic syndrome.

The current literature data do not cover sufficiently issues in the expression of insulin and IGF receptors in the endometrium of healthy patients and their changes in patients with gynecological and somatic diseases.

IGF-1 studies in endometriosis are focused on the analysis of blood plasma, peritoneal fluid, and polymorphism of genes encoding the synthesis of this growth factor. The level of IGF-1 in the peritoneal fluid of patients with EGE was increased, and it was assumed to be involved in the development of pain syndrome in endometriosis. However, the only IGF-1 study in the endometrium and endometrioid heterotopias, conducted in 1997, was exploratory and had an ambiguous small-group design ($n = 4$) [22].

Data on the expression of insulin receptors in patients with endometriosis are not presented in the literature.

The expression level of the IGF-1 receptor, which is a powerful growth factor, is increased significantly in the endometrium of patients with endometriosis. Possibly, cross-connections of insulin with IGF-1 receptors represent one of the causes of the pathological proliferative ability of the endometrium in patients with endometriosis.

However, the cause of the decreased expression of insulin and IGF-1 receptors in endometrioid heterotopias is not clear; therefore, continued research in this field is warranted.

CONCLUSIONS

The effect of insulin, the system of growth factors, and their receptors on the endometrium remains controversial. Literature data confirm the stimulating effect of IGF-1 on the proliferation of epithelial cells, its active synthesis in endometrial tissues, and its changes during the menstrual cycle. Its involvement in the pathogenesis of pain in endometriosis is suggested.

However, the functions of the insulin/IGF-1 system and their receptors in patients with endometriosis are underinvestigated. Moreover, no study has studied the expression of IGF-1 receptors, as well as insulin and its receptor in the endometrium and endometrioid heterotopies of patients with EGE.

Our results show that patients with endometriosis are characterized by certain aspects of carbohydrate metabolism, manifested by a significant increase in the level of stimulated insulin. Moreover, no significant differences were found in the levels of IGF-1 in the blood serum between the EGE group and control group. Significant differences were detected in the expression of insulin/IGF-1 receptors in patients with endometriosis, characterized by relative endometrial insulin resistance due to a decrease in the expression of insulin receptors and an increase in the level of expression of IGF-1 receptors in the endometrium.

Thus, changes in the insulin and IGF-1 system can play an important role in the pathogenesis of genital endometriosis, which necessitates further studies to comprehensively analyze the level of insulin and IGF-1 in the eutopic endometrium, endometriosis foci, peripheral blood, and peritoneal fluid in patients with endometriosis compared with the indices of the control group.

ADDITIONAL INFORMATION

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