

Pathogenetic substantiation of medical immunocorrection in parous women with endometriosis cysts of the ovaries

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The objective: to identify effective treatment in parous women with ovarian endometriomas based on the characteristics of their immune status.

Patients and methods. 50 healthy non-pregnant women (control), 15 women with a confirmed diagnosis of ovarian endometrioma treated with a conventional treatment, 15 women with the same diagnosis who received comprehensive treatment, including immunomodulators and adaptogens. There were studied phagocytic activity of blood (NBT-test, stimulated NBT-test); myeloperoxidase activity of neutrophils; content of cationic proteins in neutrophils. Determination of subpopulations of lymphocytes was carried out using monoclonal antibodies against antigens CD₃⁺, CD₄⁺, CD₈⁺, CD₁₆⁺, CD₁₉⁺. Determination of humoral immunity IgA, IgM, IgG was performed using monospecific sera against these immunoglobulin. Statistical data processing performed using computer software package STATISTICA (StatSoftStatistica v.6.0).

Results. In parous women with endometriomas on pretreatment stage irregularities were detected in the immune system, manifested by incomplete phagocytosis, decreased neutrophil microbicidal potential, increase in the number of B-lymphocytes and immunoglobulins of basic groups, indicating a violation of the immune mechanisms of protection of the woman's body and confirmed their participation in the pathogenesis of the disease.

Conclusion. At the end of the traditional course of treatment microbicidal capacity of neutrophils has still been reduced and observed activation of humoral immune system, indicating the need for pathogenetic substantiation of medical immunocorrection. Following a comprehensive treatment the normalization of immunohomeostasis of body was observed.

Key words: endometrioma, pregnancy, immunotherapy, immunodiagnosics.

The presence of tumor-like formations of ovaries is one of the leading problems of modern gynecology and occurs in 20% of women of reproductive age. It was found that in 30-40% of cases in this pathology is observed infertility, which is not absolute, but dramatically reduces the chances of getting pregnant [1-4].

For the majority of women diagnosed with endometrial ovarian cysts that are configured on the birth of their second child, the most pressing issue is the possibility of the next pregnancy.

Despite the negative outlook, endometriosis does not always cause problems with conception. A certain percentage of women suffering from this disease can become pregnant without treatment (depending on the stage of the disease) and bear a child.

For many years, pregnancy was considered and is considered a natural method of treatment of this disease. However, a complete cure in pregnancy and lactation occurs only possible remission and suppression of lesions without reverse development of endometriotic cysts i.e. after birth, these women need to be treated.

This time, the proposed methods of treatment of ovarian

cysts are not effective enough, so the tactics of these patients, according to some researchers, remains controversial.

One of the main and perhaps the leading role in the pathogenesis of endometriosis play immunological disorders [5-8], which affects the process of ovulation. Identification of these disorders is important, especially for therapeutic (surgical and non) point of view, since in previously parous women endometriotic lesions often are not local, their dimensions are not always sufficient for surgical manipulation (which in turn may lead to a decrease in ovarian reserve and stipulate further inefficient assisted reproductive technologies), and the results of clinical studies indicate that the use of only drugs that suppress estrogen synthesis, gives a high rate of relapse [9, 10].

In this regard, currently remains urgent to improve the results of treatment of women with previously realized reproductive function, taking into account the state of the immune system, which was the goal of our work: to identify the effectiveness of different treatments of ovarian tumor-like formations in previously parous women, taking into account the features of the immunological status.

The objective: was to identify effective treatment in parous women with ovarian tumor-like formations based on the characteristics of their immune status.

PATIENTS AND METHODS

We examined 80 women aged 17-40 years who gave written informed consent to participate in the study. The study was approved by the Bioethics Committee of the SI «Zaporozhye Medical Academy of Postgraduate Education of Ministry of Health of Ukraine» and conforms to the ethical, moral and legal requirements according to the Order of the Ministry of Health of Ukraine № 281 from 01.11.2000.

The first group (control) consisted of 50 healthy non-pregnant women of reproductive age, at the time of the survey with no signs of gynecological and chronic somatic pathology, applied to the facility on the choice of contraception.

Women of the 2nd group, with a confirmed diagnosis of endometrioid ovarian cyst are not treated with after pregnancy that ended in a live birth, were divided into 2 groups according to the treatment.

Group 2 A consisted of 15 women who have previously given birth with a confirmed diagnosis of endometrioid ovarian cyst treated with conventional treatment.

Group 2 B consisted of 15 women who have previously given birth to a confirmed diagnosis of endometrioid ovarian cyst treated with comprehensive treatment. Comprehensive treatment consisted of supplemental drugs with immunomodulatory and adaptogenic action: galavit and indogreen.

Treatment efficiency was assessed after 3 months of starting treatment.

In all patients were studied indicators of nonspecific and specific parts of the immune system.

To investigate the non-specific immune reactivity was held

Table 1

State of functional-metabolic status of neutrophils in parous women with endometriosis, depending on the applied treatment Me (75%Q – 25%Q = RQ)

Indicator, values	Group 1, n=50	Group 2, n=30	Group 2A, n=15	Group 2B, n=15
NPI on 30 min, %	67,5 (74,2-49,1=25,1)	64,1* (81,7-42,2=39,5)	65,7 (83,4-41,3=42,1)	69,4*,** (86,7-51,0=35,7)
NPN on 30 min, c.u.	3,1 (6,5-1,3=5,2)	3,3 (5,0-1,3=3,7)	3,2 (5,7-1,5=4,2)	3,1 (6,2-1,7=4,5)
NPI on 120 min,%	58,4 (68,3-39,8=28,5)	57,4 (60,1-30,8=29,3)	57,4 (62,3-36,7=25,6)	58,2 (67,6-37,2=30,4)
NPN on 120 min, c.u.	5,7 (6,1-4,0=2,1)	5,3 (7,1-3,4=3,7)	5,5 (7,4-3,9=3,5)	5,8 (6,7-4,2=2,5)
NBTsp, c.u.	1,2 (1,3-1,0=0,3)	1,5* (2,5-0,7=1,8)	1,3 (2,0-0,6=1,4)	1,2 (1,4-0,9=0,5)
NBTst, c.u.	1,3 (2,2-0,8=1,4)	1,4 (2,3-0,6=1,7)	1,4 (2,1-0,9=1,2)	1,3 (2,0-0,7=1,3)
CP, c.u.	2,2 (3,0-1,4=1,6)	1,9 (2,7-0,4=2,3)	2,0 (2,9-0,8=2,1)	2,1 (2,9-1,1=1,8)
MP, c.u.	2,3 (3,4-0,7=2,7)	2,0 (2,9-0,6=2,3)	2,1 (3,1-0,9=2,2)	2,2 (3,0-0,7=2,3)

Notes: * – statistically significant differences (p<0,05) relative to the control group; ** – Statistically significant differences (p<0,05) relative to Group 2, NPI – neutrophils phagocytic index, NPN – neutrophils phagocytic number.

Table 2

State of cell immunity in parous women with endometriosis, depending on the applied treatment, Me (75% Q - 25% Q = RQ)

Indicator, values	Group 1, n=50	Group 2, n=30	Group 2A, n=15	Group 2B, n=15
CD ₃ ⁺ , %	63,7 (67,1-59,8=7,3)	62,9 (67,7-56,2=11,5)	63,9 (68,2-57,7=10,5)	63,9 (67,9-58,5=9,4)
CD ₄ ⁺ , %	38,7 (44,2-31,8=12,4)	38,2 (43,4-30,3=13,1)	39,5** (46,3-31,7=14,6)	39,7* (45,1-32,6=12,5)
CD ₈ ⁺ , %	25,6 (39,0-21,3=17,7)	23,8* (33,1-20,4=12,7)	24,7 (37,2-20,6=16,6)	25,0** (38,4-21,7=16,7)
CD ₁₆ ⁺ , %	16,5 (24,6-11,9=12,7)	16,0 (22,5-12,3=10,2)	16,5 (24,9-11,3=13,6)	16,9 (25,1-12,6=12,5)

Notes: * – statistically significant differences (p<0,05) relative to the control group; ** – statistically significant differences (p<0,05) relative to Group 2.

definition: phagocytic activity of blood neutrophils, based on the method of determining the absorption and digest their ability in relation to a microbial culture test after a joint preincubation [11]; oxygen-depending metabolism of neutrophils (NBT-test) and functional reserve of cells (stimulated NBT-test) [12]; myeloperoxidase activity (MPO) of neutrophils [13]; content of cationic proteins (CP) in neutrophils [14].

Determination of subpopulations of lymphocytes was carried out using monoclonal antibodies against antigens CD₃⁺ (total number of T-lymphocytes), CD₄⁺ (T-helper), CD₈⁺ (T-suppressors), CD₁₆⁺ (NK cells), CD₁₉⁺ (B cells) produced by NPO «Granum» (Kharkiv).

Determination of humoral immunity IgA, IgM, IgG was performed using monospecific sera against said immunoglobulin [15].

Statistical data processing performed using computer software package STATISTICA (StatSoftStatistica v.6.0). Assessment of the nature of the distribution of the analyzed indicators by criterion consent of Kolmogorov-Smirnov determined that most of them are not subject to the normal law. Statistical significance compared parameters are set using a series of criteria Wald-Wolfowitz at a significance level of P < 0.05. The analyzed data are presented as the median (Me) and quartile range (RQ), which represents the difference between the values of the 75th and 25th percentiles (RQ = 75% UQ - 25% LQ), where UQ - the upper quartile; LQ - bottom quartile.

RESULTS

Earlier, in study of the immune status of women with ovarian tumor-like formations were identified changes that were characterized by incomplete phagocytosis of neutrophils in the

background of maintaining the functional-metabolic reserve, reduced microbicidal capacity retention of the number of T-lymphocytes and their subpopulations, a slight increase in the number of B-lymphocytes, hyperglobulinaemia.

Based on these results, a comparative analysis of the immune status of women treated with traditional and complex treatment consists of an immunomodulatory therapy.

In assessing the indicators characterizing the functional and metabolic status of neutrophils in the 2a group were found statistically insignificant, but clinically significant changes in the absorption and digestive ability, as well as the functional activity of neutrophils with respect to both the control group and the comparison group (from 2% to 5%). Functional-metabolic reserve, characterized by an indicator of spontaneous and stimulated NBT test was increased by 8% and 7% compared to the control group and the matched comparison group parameters (Table 1).

Indicators of microbicidal system – cationic protein and myeloperoxidase (CP, MPO) were reduced by 9% and 8% relative to the control group and increased by 5% and 5% relative to the comparison group.

Women in the treatment group 2 A conventional techniques level indicators of T-cell and NK-system cells – CD₃⁺, CD₄⁺, CD₈⁺, CD₁₆⁺ values substantially matched control group and the comparison. All the changes were not statistically significant, but clinically significant (Table 2).

When evaluating the performance of humoral immunity level CD₁₉⁺ was increased relative to the control group by 10% and nearly match the value of the comparison group. Showed an increase in the concentration of Ig A, M, G relative control group by 11%, 54%, 48% and decreased relative to the compari-

Table 3

State of humoral immune system in parous women with endometriosis, depending on the applied treatment, Me (75% Q – 25% Q = RQ)

Indicator, values	Group 1 (n = 50)	Group 2 (n = 30)	Group 2 A (n = 15)	Group 2 B (n = 15)
CD19+, %	17,2 (23,1-15,6=7,5)	19,4* (25,3-16,1=9,2)	19,0 (24,7-15,7=9,0)	18,2** (23,9-14,8=9,1)
IgA, g/l	1,8 (2,3-0,9=1,4)	2,4 (2,7-1,8=0,9)	2,0 (2,5-1,6=0,9)	2,0 (2,6-1,4=1,2)
IgM, g/l	1,1 (2,5-0,4=2,1)	1,9 (3,1-0,7=2,4)	1,7* (2,9-0,6=2,3)	1,4** (2,6-0,5=2,1)
IgG, g/l	10,2 (13,1-6,7=6,4)	11,3 (13,4-7,8=5,6)	11,0 (12,8-7,3=5,5)	11,0 (13,0-7,1=5,9)

Notes: * – statistically significant differences (p<0,05) relative to the control group; ** – Statistically significant differences (p<0,05) relative to Group 2.

son group at 17%, 11% and 3% of that in the subsequent case is not statistically significant, but clinically significant (Table 3).

Thus the presence of immune disorders after conventional therapy (which is fraught with the development of secondary bacterial infections), activation of humoral immune system, prove the necessity of using of immunomodulators that is pathogenetically substantiated.

Based on these results seemed necessary to extend the traditional treatment by appointment of immunomodulatory drugs.

The drug of choice for this group of patients was galavit (aminodioksotetragidroftalazindion sodium), the main targets of action of which are phagocytosis and antibody response (especially the synthesis of IgG). Which was appointed by 0.1 g 2 times a day, the course of 20 days. Comprehensive treatment was complemented by appointment of a small immunomodulator indole-3-carbinol – 300 mg per day during meals, course of 3 months.

In assessing the indicators characterizing the functional and metabolic status of neutrophils in group 2 B indicators characterizing the absorption and digestive ability is not much different from the values of the control group were increased by 8% and 2% of the comparison group, in the latter case is not statistically significant, but clinically significant. Indicators of functional activity of neutrophils for 30 min and 120 min correspond to the index of the control group at 30 min were reduced by 6% at 120 min – increased by 9% compared to the comparison group parameters. Indicators of functional metabolic reserve (NSTsp and NSTst) corresponded to those of the control group and were reduced relative to the comparison group by 20% and 7% respectively.

Indicators of microbicidal system CP, MPO – were reduced by 5% and 4% relative to the control group and increased by 10% and 10% relative to the comparison group (Table 1).

Women 2 B group in complex treatment the indicators of cellular immunity CD3+, CD4+, CD8+ – corresponded the values of control and comparison groups. The level of CD16+ almost

matched the values of the control group, exceeding the value of the comparison group at 6%, respectively (Table 2).

Status indicators for humoral immunity, CD19+ – exceed the value of the control group and 6% were reduced relative to the comparison group at 6%. Showed an increase in the concentration of Ig A, M, G – 11%, 27% and 7% compared to the control group and decreased by 17%, 26%, 43%, relative to the comparison group (Table 3).

Using the therapy proposed by us drugs – galavit and indogrineen, observed recovery of microbicidal potential of phagocytic system, as well as normalization of humoral immunity.

Thus, the effect of the proposed method of treatment was achieved by assignment of immunomodulators and adaptogens, leading to the restoration of physiological values of parameters of the immune status.

CONCLUSION

In parous women with ovarian tumor-like formations in pre-treatment stage, irregularities were detected in the immune system, manifested by incomplete phagocytosis, decreased neutrophil microbicidal potential, increase in the number of B-lymphocytes and immunoglobulins of basic groups, indicating a violation of the mechanisms of immune protection of women and confirmed their participation in the pathogenesis of the disease.

At the end of the traditional course of treatment still remains reduced microbicidal capacity of neutrophils and observed activation of humoral immune system, indicating the need of substantiation of medical immunocorrection, based on the impact on key pathophysiological processes. Following a comprehensive treatment, including the appointment of immunomodulators and adaptogens – galavit and indole-3-carbinol and the normalization of immune homeostasis of body, which indicates an increase in the effectiveness of the treatment and possible recommendations of this scheme for future use.

использованием моноспецифических сывороток против указанных иммуноглобулинов. Статистическая обработка полученных данных выполнена с использованием компьютерных программ пакета STATISTICA (StatSoftStatistica v.6.0).

Результаты. У рожавших женщин с эндометриозами яичников на долеченом этапе были выявлены нарушения в иммунной системе, проявляющиеся незавершенным фагоцитозом, снижением микроbicидного потенциала нейтрофильных гранулоцитов, увеличением количества В-лимфоцитов и основных групп иммуноглобулинов, что указывало на нарушение механизмов иммунной защиты организма женщины и подтверждало их участие в патогенезе заболевания.

Заключение. После окончания проведения традиционного курса лечения по-прежнему был снижен микроbicидный потенциал нейтрофильных гранулоцитов, а также наблюдалась активация гуморального звена иммунной системы, что указывало на необходимость применения обоснованной иммунокоррекции, основанной на воздействии на ключевые патофизиологические процессы. После проведенной комплексной терапии отмечена нормализация иммуногемостаза организма.

Ключевые слова: эндометриоз, беременность, иммунокоррекция, иммунодиагностика.

Патогенетическое обоснование лечебной иммунокоррекции у рожавших женщин с эндометриозными кистами яичников О.С. Шаповал, Л.Л. Воронцова

Цель исследования: определение эффективных методов лечения у рожавших женщин с эндометриозными кистами яичников с учетом особенностей их иммунного статуса.

Материалы и методы. Обследовано 50 здоровых небеременных женщин (группа контроля), 15 женщин с подтвержденным диагнозом «эндометриозная киста яичников», получавших традиционное лечение, 15 женщин с тем же диагнозом, получавших комплексное лечение, включающее применение иммуномодуляторов и адаптогенов. Проведено определение: фагоцитарной активности нейтрофильных гранулоцитов крови (НСТ-тест, стимулированный НСТ-тест); активности миелопероксидазы нейтрофильных гранулоцитов; содержания катионных белков в нейтрофильных гранулоцитах. Определение субпопуляционного состава лимфоцитов проводили с использованием моноклональных антител к антигенам CD3+, CD4+, CD8+, CD16+, CD19+. Определение показателей гуморального иммунитета IgA, IgM, IgG проводили с

Патогенетичне обґрунтування лікувальної імуноткорекції у жінок, які народили, з ендометріодними кістами яєчників
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Мета дослідження: визначення ефективних методів лікування у жінок з ендометріодними кістами яєчників, які народили, з урахуванням особливостей їхнього імунного статусу.

Матеріали та методи. Обстежено 50 здорових невагітних жінок (група контролю), 15 жінок з підтвердженим діагнозом «ендометріодна кіста яєчників», які отримували традиційне лікування, 15 жінок з тим самим діагнозом, які отримували комплексне лікування, що включає застосування імунотмодуляторів і адаптогенів. Проведено визначення: фагоцитарної активності нейтрофільних гранулоцитів крові (НСТ-тест, стимульований НСТ-тест); активності мієлопероксидази нейтрофільних гранулоцитів; змісту катіонних білків у нейтрофільних гранулоцитах. Визначення субпопуляційного складу лімфоцитів проводили з використанням моноклональних антитіл до антигенів CD3+, CD4+, CD8+, CD16+, CD19+. Визначення показників гуморального імунітету IgA, IgM, IgG проводили з використанням моноспецифічних си-

роваток проти зазначених імуноглобулінів. Статистичне оброблення отриманих даних виконано з використанням комп'ютерних програм пакета STATISTICA (StatSoftStatistica v.6.0).

Результати. У жінок з ендометріомами яєчників, які народили, на долікувальному етапі були виявлені порушення в імунній системі, що проявляються незавершеним фагоцитозом, зниженням мікробіцидного потенціалу нейтрофільних гранулоцитів, збільшенням кількості В-лімфоцитів і основних груп імуноглобулінів, що свідчило про порушення механізмів імунного захисту організму жінки і підтверджувало їхню участь у патогенезі захворювання.

Заключення. Після закінчення проведення традиційного курсу лікування, як і раніше, був знижений мікробіцидний потенціал нейтрофільних гранулоцитів, а також спостерігалася активація гуморальної ланки імунної системи, що свідчило про необхідність застосування обґрунтованої імуноткорекції, заснованої на впливі на ключові патофізіологічні процеси. Після проведеної комплексної терапії відзначена нормалізація імуногемостазу організму.

Ключові слова: ендометріоми, вагітність, імуноткорекція, імунодіагностика.

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