

ВОЗМОЖНОСТИ САНАТОРНО-КУРОРТНЫХ МЕТОДИК В РЕАБИЛИТАЦИИ ПАЦИЕНТОК С РАННИМИ ГЕСТАЦИОННЫМИ ПОТЕРЯМИ

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Реферат. Введение. Ранние репродуктивные потери являются актуальной проблемой современного акушерства. Основную сложность для клинициста представляет поликаузальность и коморбидность невынашивания беременности малых сроков. Ключевыми этиопатогенетическими звеньями могут являться эндокринные, иммунные, гематологические нарушения, эндометриальная дисфункция, что обуславливает необходимость разностороннего, комплексного подхода к преемственной подготовке. **Цель исследования** – оценка эффективности применения санаторно-курортных методик в реабилитации пациенток с ранними гестационными потерями. **Материалы и методы.** Проанализирована результативность курса лечебно-реабилитационных процедур (климатотерапия, бальнео-, пелоидо-, физио- и фитотерапия в санаторно-курортных условиях города Белокуриха Алтайского края у 79 пациенток с ранней репродуктивной потерей в анамнезе. **Результаты:** улучшение физического и психического здоровья, уменьшение ультразвуковых маркеров хронического эндометрита, наступление беременности в первый год после лечения в 70,9%, завершившейся срочными родами в 92,8% случаев. Обсуждение: высокая эффективность предлагаемой программы реабилитации, обусловлена разнонаправленным потенцирующим действием природных факторов, оказывающих мощный иммуномодулирующий, противовоспалительный и регенерирующий эффекты. **Заключение.** Комплекс санаторно-курортных процедур в сочетании с продленным курсом фитотерапии пациенткам с ранними репродуктивными потерями способствует эффективному восстановлению их психосоматического и репродуктивного здоровья, что позволяет рекомендовать данную программу для практического внедрения.

Ключевые слова: ранние репродуктивные потери, санаторно-курортные методики, фитотерапия.

Для ссылки: Яворская С.Д., Ремнёва О.В., Чернова А.Е., и др. Возможности санаторно-курортных методик в реабилитации пациенток с ранними гестационными потерями // Вестник современной клинической медицины. – 2023. – Т.16, вып.4. – С.71-77. DOI: 10.20969/VSKM.2023.16(4).71-77.

SPA AND RESORT POSSIBILITIES IN REPRODUCTIVE HEALTH RECOVERY IN PATIENTS WITH EARLY GESTATIONAL LOSSES

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Abstract. Introduction. Early pregnancy loss is still an unresolved problem in obstetric and gynecology. The pathogenesis is based on the comorbidity of pathological factors such as subclinical hormonal, immune, psychoneurotic disorders and endometrial pathology. It requires complex rehabilitation pregnancy planning programs for such patients. Aim. **Aim** of research is to optimize treatment and rehabilitation measures in patients with the history of early pregnancy lost using the Belokurikha's spa and resort clusters. **Material and methods.** 79 patients with early reproductive lost

history underwent a course of medical and rehabilitation treatment in the «Altai Castle» spa and resort (Belokurikha, Altai Region). Complex spa treatment included climatotherapy and combination of various methods: balneo-, peloid-, physiotherapy and a prolonged course of herbal medicine. **Results and discussion.** Women with a history of early pregnancy loss had significant improvement in physical and mental health, ultrasound chronic endometritis markers were decreased. The first year onset pregnancy occurred in 70.9% after rehabilitation and most of them (92.8%) delivered at term. Proposed rehabilitation program is highly efficient due to the multidirectional potentiating action of natural factors that have powerful immunomodulatory, anti-inflammatory and regenerating effects. **Conclusion.** A complex rehabilitation program for patients with a history of early pregnancy lost in Belokurikha's spa and resort with a prolonged course of herbal medicine helps to make rapid psychosomatic and reproductive health recovery.

Key words: early pregnancy loss, health resort, herbal medicine.

For reference: Yavorskaya SD, Remneva OV, Cpernova AE, et al, Spa and resort possibilities in reproductive health recovery in patients with early gestational losses. The Bulletin of Contemporary Clinical Medicine. 2023; 16(4): 71-77.

DOI: 10.20969/VSKM.2023.16(4).71-77.

Introduction. One of the modern medical and social problems of Russian society is to save reproductive health [1]. The Russian Government has made several measures for increasing the birth rate but nevertheless natural population growth rate still remains at a low level in our country [1]. The most significant factor for reduced population growth rate is to delay reproductive issues to older age when the both partners already have somatic, gynecological, androgenic diseases which significantly reduces their reproductive health or cause infertility, miscarriage and other obstetrics complications [2].

Partners genital tract infection is one of the most frequent causes of infertility and miscarriages [3]. According to several researches, the chronic endometritis rate is up to 70-80% in the population and it can be only the one etiological factor for infertility in 20% and miscarriage up to 50% of cases [4,5]. However reproductive dysfunction is a multi-etiological pathology where a combination of factors such as subclinical hormonal, immune and psychoneurotic disorders are existing [6]. Treatment of only one etiological factor leads to success in only 30% of cases [7]. It needs to search for new integrated ways for diagnostics and reproductive health recovery treatment with the help of spa resort clusters and Russian herbal medicine.

Aim of research. Treatment and rehabilitation optimization in patients with the history of early reproductive losses using the Belokurikha's spa and resort clusters.

Materials and methods. A study design was developed in the Obstetrics and Gynecology Department of Altai State Medical University. A prospective cohort study was made in one group (single group study) to evaluate results before and after treatment rehabilitation methods of the Belokurikha's spa clusters. The cases were collected between 2019 to 2020 years in the City Pregnancy Planning Center which is a part of Maternity House №2 (Barnaul, Altai Region, Russia). All women have miscarriage history and their aim was to get a special reproductive recovery program. The study group contains 79 patients with the history of missed pregnancy during a year, chronic endometritis ultrasound signs with the following histological and immunohistochemical confirmation, having ovulatory cycles and husband's semen analysis is fertile. Exclusion criteria were recurrent pregnancy loss, acute pelvic inflammatory diseases history,

hormone-dependent gynecological disorders, fibroid, endometriosis, sub- and decompensation somatic diseases.

The research was performed in accordance with the requirements of the World Medical Association Declaration of Helsinki (2013). Research protocol was approved by local Ethnic Committee of Altai State Medical University. All the patients signed written agreement for participating in research.

Firstly all the patients were examined. Ultrasound was performed on the 21-24th menstrual cycle day. Irregular external endometrium contour, thickened and heterogeneous endometrium, hyperechoic inclusions in the basal layer, endometrial thickness < 7 mm are used as ultrasound criteria of chronic endometritis [8]. Pipelle biopsy specimens were taken in the first phase of the menstrual cycle (5-7th day). After the tissue was collected, it was immediately immersed in 10 % neutral formaldehyde for fixation. It was done according to the standard Hematoxylin and Eosin stain protocol with following quantitative morphological chronic endometritis severity evaluation [9]. Immunohistochemistry was performed by following detailed procedures of the kit using monoclonal antibodies ((clone L26) Ventana (USA)) and the CD138+ phenotype using polyclonal antibodies (Spring (USA)). The results were evaluated by a quantitative method with calculation of positive cells in a field of view microscope at x400 [10].

Complex rehabilitation was the 1st step for new pregnancy planning and was carried out in Belokurikha (Altai Region) on the basis of the Altai Castle Spa and Resort. The treatment course activities lasted 14 days and consisted of manipulations aided at general recovery, central and vegetal neural systems regeneration, immune homeostasis normalization. Uterine post-inflammatory changes elimination and endometrial reception to ovarian steroids recovery were the main aims. Procedures for general psychosomatic status recovery included climatotherapy. The Resort is surrounded by a mountain zone which leads to the absence of strong winds because of what the air contains a large number of pine phytoncide fractions [11]. Patients had dosed physical activity, swimming in the pool, music therapy using the program of resonant acoustic oscillations patented by the sanatorium [12]. Detoxification and immunomodulatory therapy included intestinal lavage, treatment in the mini-sauna «Siberian

health resort UN-1» (Cedar barrel) at temperature +65 °C for 15 minutes using the patented product «Liopante» («Altai-Med», RF) in the form of slices with a natural lyophilized cut of the antlers of the Altai deer, patented underwater physiotherapy massage [13]. The bath is filled with thermal mineral-nitrogen-siliceous water with a low content of radon (5.4 nCu/dm³) directly coming from the Belokurikha wells №4E. Natural water temperature is about 38 °C. The bath duration is 15 minutes. Patients had 7 procedures. Underwater vacuum physiotherapy massage with low content radon water for the lower abdomen, suprapubic and sacral areas leads to organs and tissues microcirculation increasing, has a lymphatic drainage effect and activates the reflexogenic zones [13]. The low radon containing water has a beneficial health effect on the hypothalamic-pituitary-ovarian system function and helps to normalize sex steroid hormones ratio [14].

For uterus rehabilitation after inflammation were used preformed physical factors and pelotherapy. This combination make it possible to achieve several effects, such as analgesia and anti-inflammatory influence, improvement of blood circulation in the genital organs because of anticoagulant, disaggregating and fibrinolytic effects; normalization of the pituitary hormones balance, mild stimulation of ovaries steroidogenesis and endometrial reception recovery [15]. As physical factors were used, electrical stimulation on the electro-laser-magnetic therapy complex KAP-ELM-01 «Andro-Gyn» (7 procedures). Natural salt-saturated medium sulfide silt therapeutic mud applications (extracted from Lake Marmyshanskoye, Romanovsky district, Altai Region) on the lower abdomen and the sacral area were used for pelotherapy. Applications were laid on for 20 minutes at 38-40 °C (a course of 7 procedures).

The 2nd step therapy was a prolonged phytotherapy treatment with a certified herbal products: «Alfit-8» tea in briquettes for morning / evening intake (Alfit, Altai Territory, Russia) and phytocapsules «Gyneconorm» (Pharmzavod Galen, Altai Territory, Russia). The main components of herbal tea «Alfit-8» are bergenia, shepherd's purse, yarrow, nettle, red root. These herbs have haemostatic, immunomodulatory and anti-inflammatory effects. Motherwort has a sedative effect in the evening part. Ortilia one-sided is a part of Gyneconorm phytocapsules and has a vasodilating

effect and helps to restore the endometrial receptors [15]. The effectiveness of spa and resort treatment was evaluated in three steps. The 1st one (quick result) is before and after the course of rehabilitation. Participants were tested using the Russian version of the SF-36 questionnaire (SF-36 Health Status Survey) [16]. The 2nd step is the menstrual cycle estimation and ultrasound endometrium examination before and in 3 months after the treatment. The 3d stage is observation during a year for onset pregnancy and its outcomes.

All results were gathered in the Excel table and then statistical analysis was performed with the Statistica SPSS Version 11.0 software package. We used the method of descriptive statistics with finding the arithmetic mean, variance and calculation of the 95% confidence interval. Student's t-test was used in normal distribution. U - Mann-Whitney test (for independent samples) and T - Wilcoxon test (for related samples) were used when the outcome is not normally distributed. Nonparametric χ^2 test was used with a Yates correction for continuity to compare qualitative features. All the following conclusions are based on the statistical analysis results with the reliability conformation $p < 0,05$ [17].

Results. Patients' age ranged from 25 to 37 years old, the average age was 34.1±1.8 years. It is known that menarche age is a main reproductive function development indicator. The menarche started at 12.2 ± 1.2 years old in patients with a history of early pregnancy loss, which corresponds to the general population in Russia [18]. Among somatic diseases were found a high chronic urinary system disease frequency (cystitis, urethritis, pyelonephritis) - 63.3% and thyroid dysfunction (autoimmune thyroiditis - 16.4%). All patients had a normal hormonal status according to laboratory tests. However, every third (29.1%) woman has noticed that miscarriage has changed the menstrual cycle (oligomenorrhea, polymenorrhea, a decrease in the duration of the desquamation phase). Ultrasound examination was performed at the 21-24th menstrual cycle day and it showed the chronic endometritis markers in all examined patients. It contained irregular external endometrium contour, thickened and heterogeneous endometrium, hyperechoic inclusions in the basal layer, and endometrial thickness did not correspond to the day of menstrual cycle (table 1).

Table 1

Ultrasound characteristics of the endometrium before and after rehabilitation measures

Ultrasound parameters	Main group (n=79)		p Before and after treatment
	Before treatment %	After treatment %	
Irregular external endometrium contour	39,2	18,9	0,008
Irregularity of the line of closure of the anterior and posterior endometrium sheets	84,8	37,9	<0,001
Thickened and heterogeneous endometrium	78,5	50,6	<0,001
Hyperechoic inclusions in the basal layer	100,0	75,9	<0,001
Endometrial thickness < 7 mm (21-24 menstrual cycle day)	17,7	3,79	0,02

All patients before the rehabilitation treatment underwent standard morphological and immunohistochemical examination for diagnosis verification. Diffuse inflammatory infiltrates were found in 39.2.0% cases, focal had 60.7% women. Infiltrates were presented by monocytes, neutrophils, plasma cells, macrophages. Focal stromal fibrosis was found in every second patient (49.4%). Fortunately diffuse stromal fibrosis was not detected. Stroma periglandular and perivascularly single lymphoid cells were found in 80.5% of cases. Lymphoid cells were formed clusters perivascularly and periglandular in the stroma and

were determined in 20,5 % of all cases. Hypoplastic variant of chronic endometritis is the most problematic for recovery and it was diagnosed in 12.6% of cases. Histochemical examinations detected subpopulation composition of lymphocytes, CD138+ and CD20+ phenotypes in 100% of cases. In all cases the chronic endometritis morphological and histochemical signs were regarded as mild or moderate ones more rarely. There were no histological signs of severe inflammation in the endometrium in the patients of the studying group.

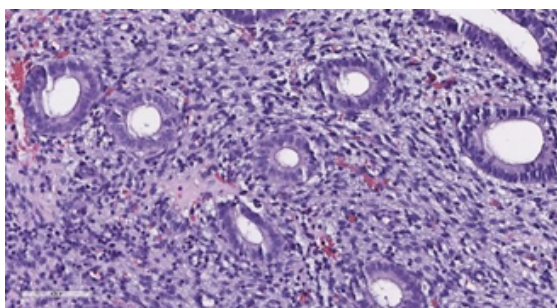


Fig.1. Endometrium with focal moderate lymphoid infiltration, mild stromal fibrosis. H&E, x320

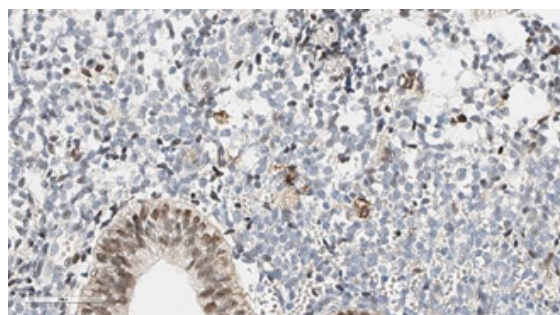


Fig.2. Accumulation of three plasma cells in the stroma. Histochemical examination CD138, x400

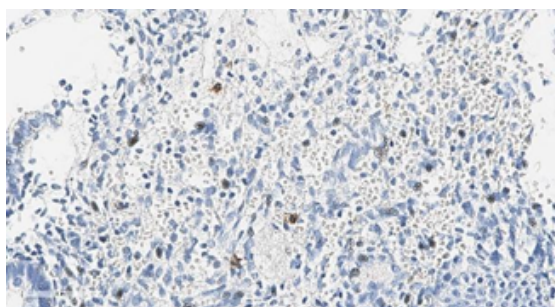


Fig.3. B-lymphocytes in the stroma. Histochemical examination CD20, x400

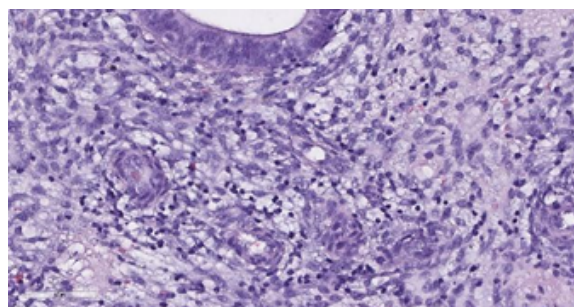


Fig.4. Perivascular lymphoid infiltration. H&E, x320

Ultrasound was performed in three months in "implantation window" time and showed a significant improvement in all criteria (table1).

We tested the patients before and on the last day of the rehabilitation course with quality of life scale SF-36 to assess the clinical effectiveness of a spa and resort

health rehabilitation course for patients with an early pregnancy loss history (table 2).

The results of analysis have shown that many assessed indicators exceeded the average values characteristic of the Russian population [19]. However, role indicators physical and emotional functioning

Table 2

Quality of life indicators on the SF-36 scale before and after a course of rehabilitation course

Index	Before course	After course	Average population indicators
Physical functioning (PF)	84,2	83,6	77,02
Role physical functioning (RP)	51,0	95,0	53,80
Pain intensity (BP)	70,9	83,1	61,30
General health (GH)	69,0	80,8	56,56
Vital activity (VT)	58,6	72,8	55,15
Social functioning (SF)	70,5	82,5	69,67
Role emotional functioning (RE)	53,3	100,0	57,23
Mental health (MH)	63,5	74,7	58,82

was below the population average. It means that their daily activities were limited due to their physical and emotional state. All the estimated indicators were not only higher than the average population, but also significantly increased compared to the initial data at the end of the rehabilitation course. This data suggests a rapid positive effect of the health-improving course on the physical and psychological health of patients with a history of early reproductive loss. Menstrual cycle normalization was noted in 3 months after the end of the rehabilitation course and it is a primary evaluation test of the hypothalamic-pituitary-ovarian system work. The frequency of oligo- and polymenorrhea was decreased (29.1% and 7.6%; $p < 0.001$).

During a year of onset pregnancy occurred in the majority of patients (56 women, 70,9%) who underwent a course of rehabilitation activities in Belokurikha spa and resort. The most fertile were the first three months after the end of the rehabilitation planning pregnancy course (median - 2.24 months). But the onset of pregnancy is only the first step in solving the reproductive issues. We analyzed pregnancy outcomes and found that early pregnancy loss occurred in 7.2% of cases, which is lower than in the general population [7], term labor happened in 92.8% of cases. Patients after an episode of early pregnancy loss have a reduced physical and mental health. Our complex rehabilitation program in Belokurikha spa and resort allows us to quickly reduce the level of stress, clean the body from toxins, normalize immune system functioning and rehabilitate the endometrium inflammation injury and, namely increase the overall level of psychosomatic and gynecological health. The long-term (three monthly courses) phytotherapy use allows to consolidate the rehabilitation effects in the planning pregnancy stage and helps to restore reproductive health with onset successful pregnancies in 70.9% during a year after the case of reproductive loss.

Discussion. Complex rehabilitation in spa and resort centers of patients with a history of early reproductive loss and chronic endometritis contributes to the rapid recovery of the physical and mental status of patients. The onset pregnancy rate has reached 70.9% during the first year after treatment and term deliveries rates have been very high up to 92.8%. Such applied treatment and rehabilitation program effectiveness is probably due to the multidirectional therapeutic effect of the applied natural physical factors, such as radon therapy and mud therapy, and preformed factors (electro-laser-magnetic therapy) [20, 21]. Ultrasound and endometrium histological dates have demonstrated the prevalence of chronic inflammatory lesions of the endometrium among patients with early reproductive loss. The results of the control ultrasound examination and its combination with the clinical result (percentage term deliveries) confirm the high immunomodulatory and anti-inflammatory efficacy of the methods used in the program. Previously, a number of authors have already shown the clinical results of such immunomodulatory and anti-inflammatory procedures as immunocytotherapy, intravenous administration of fat emulsions [22], the use of copper electrophoresis in

combination with laser and magnetic therapy [23]. Our method differs from others by minimally invasiveness and a more expanded arsenal of clinical effects: normalization of steroidogenesis, fibrinolytic, lymphatic drainage and detoxification effects. Prolonged herbal medicine (2-3 months) leads to the balneotherapy and pelotherapy therapeutic effects consolidation. It is the additional mechanism for long-term activation of the body's regulatory systems (neurotropic, immunotropic and hormonal), which contributes to the complete restoration of the psychosomatic and reproductive health of women.

Conclusion. Early reproductive loss remains an unresolved and relevant problem in the doctors' clinical work. It is still continuing the scientific search for effective methods of rehabilitation and pregnancy planning methods in patients with early pregnancy loss history. In our treatment and rehabilitation program we tried to combine the use of methods that have a positive effect on various etiological and pathogenetic pathways leading to reproductive losses. The results of the study allow us to recommend a complex rehabilitation of patients with early pregnancy lost in Belokurikha spa and resort with the using climatotherapy, radon therapy, detensor therapy, intestinal lavage, a program of resonant-acoustic oscillations, mud applications and herbal medicine in a wide clinical practice

Conflict of interest. *The authors declare no conflict of interest.*

Research transparency. *The authors are solely responsible for providing the final version of the manuscript for publication. The research was carried out on the basis of the Department of Obstetrics and Gynecology ASMU as a part of the dissertation research «Pregravid preparation of patients with reproductive losses using natural physical factors (clinical and experimental study)».*

Financing. *All authors participated in the concept, study design and in writing the manuscript development and didn't receive a research fee. The final version of the manuscript was approved by all authors. The research was carried out as part of a Government Grant "Providing a grant for conducting scientific research on developing regional natural healing resources and developing methodologies for their use, reservation and searching promised land for the spa and resort industry development in Altai Region". Financing was partly made from the grand resources. Particularly, endometrium immunohistochemical examination was realized on the grand support.*

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