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Rehabilitation treatment of female patients after uterine endoscopic surgery for infertility using complex physio- and hydrogen sulfide balneotherapy

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ABSTRACT

AIM: To evaluate the effectiveness of combined physiotherapy and hydrogen sulfide balneotherapy in patients who underwent endoscopic surgery on the fallopian tubes for tubal and uterine infertility.

MATERIALS AND METHODS: A total of 104 patients who had undergone endoscopic surgery on the fallopian tubes for tubal and uterine infertility were observed. Using simple randomization, the study population was divided into three groups. The control group (34 patients) received standard postoperative therapy, including conventional antibiotic treatment. The second group (32 patients) received a combination of pharmacotherapy, electro-magnetolaser therapy, and an anti-adhesion resorbable gel Mesogel (Russia). The main group (38 patients) underwent delayed rehabilitative treatment with hydrogen sulfide water therapy following combined pharmacological and electro-magnetolaser therapy. Patients were evaluated using standard clinical assessment methods, including clinical and immunological parameters, hysterosalpingography, pelvic ultrasound, and quality-of-life assessment.

RESULTS: The study assessed the restoration of reproductive function in women through physiotherapeutic and natural local treatments. The main group demonstrated significant alleviation of clinical symptoms ($p < 0.01$), improvement in immune status parameters ($p < 0.05$), restoration of fallopian tube patency ($p < 0.05$), and improved pelvic organs condition. A clinically significant difference in final outcomes was observed between the main and control groups ($p < 0.05$). The high therapeutic efficacy of the proposed rehabilitative treatment was confirmed, with pregnancy achieved in 48% of cases.

CONCLUSION: The obtained results suggest that the proposed rehabilitation method for patients after endoscopic surgery on the fallopian tubes for tubal and uterine infertility significantly enhances the effectiveness of standard therapy and leads to a substantial improvement in reproductive function.

Keywords: endoscopic surgery on the fallopian tubes for infertility; physical therapy; reproductive function; quality of life.

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Восстановительное лечение пациенток после эндоскопических операций на маточных трубах по поводу бесплодия с применением комплексной физио- и сероводородной бальнеотерапии

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АННОТАЦИЯ

Актуальность. Лечебные физические факторы способствуют повышению эффективности терапевтических мероприятий за счёт активации процессов саногенеза. При лечении трубно-перитонеального бесплодия необходимо не только устранение анатомической непроходимости маточных труб, но и проведение эффективной послеоперационной реабилитационной терапии, направленной на сохранение восстановленного функционального состояния труб и профилактику спайкообразования в отдалённом периоде.

Цель исследования — изучить эффективность комплексной физио- и сероводородной бальнеотерапии у пациенток с перенесёнными эндоскопическими операциями на маточных трубах по поводу бесплодия трубного и маточного происхождения.

Материалы и методы. Проведены наблюдения 104 пациенток с перенесёнными эндоскопическими операциями на маточных трубах по поводу бесплодия трубного и маточного происхождения. Методом простой рандомизации сформировано 3 группы: в контрольную группу вошли 34 пациентки, которым в раннем послеоперационном периоде проводили общепринятую базисную терапию, включающую стандартную антибиотикотерапию; 32 пациенткам назначили комбинированное применение лекарственных средств и электромагнитолазерной терапии и гель противоспаечный рассасывающийся «Мезогель» (Россия); в основной группе, куда вошли 38 пациенток, после проведённой комбинированной фармако- и электромагнитолазерной терапии выполняли отсроченное восстановительное лечение с применением сероводородных вод. Пациентки обследованы по общепринятой методике, включающей оценку клинических показателей и иммунного статуса, гистеросальпингографию, ультразвуковое исследование органов малого таза, оценку качества жизни.

Результаты. Рассмотрены результаты восстановления репродуктивной функции женщин с использованием физиотерапевтических и местных природных факторов. Выявлено, что у пациенток основной группы отмечено значимое нивелирование клинических проявлений ($p < 0,01$), улучшение показателей иммунного статуса ($p < 0,05$), восстановление проходимости фаллопиевых труб ($p < 0,05$), улучшение состояния органов малого таза. При этом обнаружена клинически значимая разница конечных показателей по отношению к группе контроля ($p < 0,05$). Доказан высокий терапевтический эффект разработанной технологии восстановительного лечения, позволивший добиться наступления беременности в 48% случаев.

Заключение. Полученные результаты позволяют считать, что предложенная методика реабилитации пациенток после эндоскопических операций на маточных трубах по поводу бесплодия трубного и маточного происхождения достоверно повышает эффективность проводимой стандартной терапии и обеспечивает значимое улучшение репродуктивной функции.

Ключевые слова: эндоскопические операции на маточных трубах по поводу бесплодия; физические методы лечения; репродуктивная функция; качество жизни.

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输卵管不孕症患者在内镜手术后采用综合物理治疗和硫化氢矿物疗法的康复治疗

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摘要

研究目的。 评估综合物理治疗和硫化氢矿物疗法在输卵管内镜手术治疗输卵管性和子宫性不孕症患者中的临床疗效。

材料与方法 本研究纳入 104 例因输卵管性或子宫性不孕接受输卵管内镜手术的患者，并采用简单随机化方法将其分为三组。对照组（ $n=34$ ）接受标准术后治疗，包括常规抗生素治疗。第二组（ $n=32$ ）在标准术后治疗的基础上，额外接受电磁激光治疗及抗粘连可吸收凝胶 Mesogel（俄罗斯）。主要研究组（ $n=38$ ）在接受联合药物和电磁激光治疗后，进一步接受硫化氢矿物疗法作为延迟康复措施。所有患者均接受标准化评估，包括临床及免疫学指标测定，子宫输卵管造影，盆腔超声检查及生活质量评估。

结果表明，物理治疗与天然矿物疗法在恢复女性生殖功能方面具有良好效果。主要研究组患者的临床症状显著缓解（ $p < 0.01$ ），免疫状态指标改善（ $p < 0.05$ ），输卵管通畅性恢复（ $p < 0.05$ ），盆腔器官状况改善。主要研究组与对照组终末指标的统计学差异具有显著性（ $p < 0.05$ ）。研究结果证实，提出的康复治疗方​​案疗效较高，其中 48% 的患者成功妊娠。

结论研究表明，在输卵管内镜手术治疗输卵管性和子宫性不孕症患者中，综合康复方案可显著增强标准治疗的疗效，并有效改善患者的生殖功能。

关键词： 输卵管内镜手术；物理治疗；生殖功能；生活质量。

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BACKGROUND

The last decade has seen significant progress in solving many scientific and practical issues of infertility and adverse reproductive outcomes. However, the improvement of contemporary therapies and rehabilitation of patients with infertility due to tubal-peritoneal factors and endometrial diseases, the development and scientific substantiation of treatment and rehabilitation programs and their prognostic efficacy criteria are still relevant [1–3].

One of the most common types of female infertility is tuboperitoneal infertility. Its treatment requires both to remove the anatomical fallopian tubal obstruction and to provide effective postoperative rehabilitation aimed at maintaining the restored function of the tubes and preventing adhesion in the long term [4, 5]. Considering the role of inflammation in the adhesion, various physiotherapy methods, desensitizing agents, enzyme agents, and bio- and immunostimulants of various origins are widely used in addition to antibacterial treatment to prevent postoperative adhesion [6, 7]. Some studies have shown that physical therapeutic factors contribute to increasing the efficacy of therapy by activating sanogenesis [8–13]. In addition, they neutralize side effects of drugs and potentiate their activity [14–18]. The Republic of North Ossetia-Alania has multiple natural healing factors that have been proven to be a necessary step in increasing the clinical efficacy of medical interventions for various diseases [19–22]. They are a promising component of medical rehabilitation programs for patients with gynecologic diseases postoperatively.

Aim

To evaluate the efficacy of combined physiotherapy and hydrogen sulfide balneotherapy in patients who underwent endoscopic surgery on the fallopian tubes for tubal and uterine infertility.

MATERIALS AND METHODS

Study design

Open, prospective, randomized, controlled clinical study. The study involved examination and medical rehabilitation of 104 patients after minimally invasive endoscopic pelvic interventions for tubal and uterine infertility. The inpatient treatment stage was conducted at the Central District Hospital of the Pravoberezhny District (Beslan); the outpatient stage was conducted at women's health clinics No. 1 and 3 in Vladikavkaz. The study protocol was approved by the Ethics Committee of the North Ossetian State Medical Academy (Minutes No. 6 dated April 8, 2020).

Inclusion criteria: female patients aged 20 to 44 years who have undergone endoscopic surgery on the fallopian tubes for tubal and uterine infertility (adhesiolysis, fimbriolysis, salpingo-ovariolysis, salpingotomy, salpingostomy); 2nd

day after surgery, and informed voluntary consent to participate in the study. It should be noted that the duration of the disease ranged from 2 to 14 years; 72% of women had a history of chronic salpingitis, ultrasound signs of adhesions were detected in 61.3%, external genital endometriosis was diagnosed in 30%; hysterosalpingography (HSG) showed that the fallopian tubes were blocked in 61.2% of patients; analysis of hysteroscopy and pathomorphologic findings in the endometrium showed a high frequency of chronic endometritis (34.1% of cases). Based on the laparoscopic findings, the most common anatomical pelvic abnormality was pelvic adhesion of various severity, including grade 1–2 in 66% of cases and grade 3–4 in 34% of cases. Menorrhagia was observed in 24.9% of cases, hypomenorrhea was observed in 68.2% of cases, dysmenorrhea was observed in 52.9% of cases, and intermenstrual bleeding was observed in 42.2% of cases.

Exclusion criteria: general contraindications to physiotherapy; intolerance to cellulose ethers; withdrawal at any stage of the study.

Three groups were created using a simple randomization method. The control group included 34 patients who received standard antibiotic therapy in accordance with clinical guidelines (cefazolin 1.0 g / cefuroxime 1.5 g, intravenously; during surgery and then the same dosage for 2 days). In the experimental group of 32 patients, a combined antibiotic therapy and electro-magnetolaser therapy was prescribed. In addition, an anti-adhesion resorbable gel Mesogel (registration certificate for a medical product FSR 2010/08895, Russia) was used by distributing a thin layer of the gel over the peritoneum, once during endoscopic minimally invasive pelvic interventions. The treatment group of 38 patients underwent medical rehabilitation in an outpatient setting using hydrogen sulphide waters after combined drug and electro-magnetolaser therapy.

Electro-magnetolaser therapy

Procedures using the KAP-ELM-01 AndroGyn device at the recovery stage of successive treatment. The procedures were performed 1–2 days after laparoscopic surgery. During electrotherapy, the patient was lying on her back with her legs spread and bent; the cavity electrode was inserted into the posterior vaginal fornix until tissue resistance, and the 6x9 cm plate electrode was positioned horizontally in the suprapubic region. It was advised to apply bursts (6 s excitation, 2 s pause) of asymmetric bipolar pulses with alternation of 10 min exposure to positive and negative polarity; mode 3; frequency: 10 Hz; deviation: 20%. For magnetolaser therapy, we used a transvaginal sensor in phase with electrical stimulation and continuously using a cutaneous sensor with the emitter located above the pubis. The cutaneous neurostimulator was positioned on the lumbar segments of the spinal cord; the intensity was selected individually (until the patient felt a slight tingling sensation). Chromotherapy was performed through special glasses by selecting colors based

on clinical presentations of the disease and psychophysiological disorders, with a light signal duration of 8 s. The total duration of the procedure was 20 min, once daily, 12 procedures per course of treatment.

Hydrogen sulphide balneotherapy

Chloride-sulphate-calcium mineral water from well No. 4-R of the Redantskoye deposit (a replacement of Sergievskie mineral waters), medium mineralization, hydrogen sulphide content of 90 mg/L, was used as a balneotherapeutic factor in the form of immersion baths and vaginal irrigations. Vaginal irrigations were performed daily on a gynecological examination chair using sterile glass tips, at a water temperature of 37–38 °C, for 10 min, 8 procedures per course of treatment. 30 min after the irrigation, the patients had an immersion bath at a temperature of 36–37 °C, for 15 min, 10 procedures per course of treatment.

The efficacy was monitored before and after medical rehabilitation based on changes in clinical manifestations of the disease and long-term observations (at 12 months). The immune status (helper T cells [CD₄ antigen], suppressor T cells (CD₈ antigen), and immunoregulatory balance [CD₄/CD₈]) was studied by the immunofluorescence method using monoclonal antibodies directed to the corresponding markers; interleukins (IL-1β, IL-6) and tumor necrosis factor α (TNF-α) were analyzed by solid phase enzyme immunoassay using Biokhimmak reagents (St. Petersburg). Pelvic ultrasound (US) examination was performed using a Medison SA-8000 XL ultrasound machine (South Korea) with a transabdominal sensor with a frequency of 4–9 MHz. To assess the fallopian tube patency on the 7th–11th day of the menstrual cycle, X-ray hysterosalpingography was performed on a PRESTILIX 1600X device using an aqueous Urografin® solution according to the generally accepted method. The women's quality of life was assessed by the validated NAIF (New Assessment and Information Form to Measure Quality of Life) questionnaire, where

the quality of life score approaches 100%, scores up to 75% are considered as a slight decrease, scores up to 50% are considered as a moderate decrease, scores up to 25% are considered as a significant decrease, and scores less than 25% are considered as a sharp decrease in quality of life.

Statistical analysis of the results was performed using generally accepted parametric and nonparametric statistics with the standard applied statistical analysis software STATGRAFICS FOR WINDOWS, a Russian STADIA software, and Excel. The differences were considered significant at $p < 0.05$.

RESULTS

Case follow-up during treatment showed that there was good tolerance, no discomfort or complications when using electro-magnetolaser therapy and balneotherapy (see Table 1).

Early postoperative rehabilitation, including simultaneous electro-magnetolaser exposure, had a sufficient analgesic effect reinforced by subsequent hydrogen sulfide balneotherapy in 18 out of 20 (90%) patients. The persistent effect is worth noting: only 1 (2.6%) patient in the treatment group experienced pain again during the observation period (12 months) after the rehabilitation program. In the experimental group, pain relief was observed in 82.4% of patients with the effect lasting for 12 months. In the control group, pain relief was observed in much less patients (only 61.1%) compared to the treatment group with this indicator increasing at 12 months.

Hypomenorrhea for 9–12 months in the treatment group was observed in only 1 (2.6%) patient, which was significant in relation to similar indicators in the control group. In the experimental group, there was also significant positive changes: 72.7% of patients did not have hypomenorrhea for 9–12 months.

Table 1. Dynamics of clinical manifestations of leveling

Clinical manifestations	Observation period	Treatment group (<i>n</i> =38) abs, %	Experimental group (<i>n</i> =32) abs, %	Control group (<i>n</i> =34) abs, %
Dysmenorrhea	Before	20; 52.6	17; 53.1	18; 52.9
	After	2; 5.3**	3; 9.4**	7; 20.5*
	At 9–12 months	1; 2.6***	5; 15.6**	10; 29.4*
Menorrhagia	Before	10; 26.3	8; 25.0	8; 23.5
	At 9–12 months	1; 2.6***	3; 9.4**	6; 17.6
Hypomenorrhea	Before	26; 68.4	22; 68.7	23; 67.4
	At 9–12 months	3; 7.9***	6; 18.8***	15; 44.1*
Intermenstrual bleeding	Before	17; 44.7	13; 40.6	14; 41.2
	At 9–12 months	***	3; 9.4***	7; 41.2**

Note: * and ** are statistically significant differences between pre-treatment $p < 0.05$ and $p < 0.01$ respectively; " — difference of parameters with data in CG — $p < 0.05$.

It is generally accepted that immune imbalance is a sign of prolonged inflammation and slow reparative processes and immune restoration is the criterion of treatment efficacy. The efficacy of integrated physiotherapy and hydrogen sulphide balneotherapy was evaluated before and immediately after the course of medical rehabilitation based on changes in the immune status (see Table 2). It should be noted that the combination of the anti-adhesive drug Mesogel (during laparoscopic intervention), electro-magnetolaser therapy, and hydrogen sulfide balneotherapy resulted in significant positive changes in immunogenesis in patients in the treatment and the experimental groups with intergroup differences with the control group. In the treatment group, it was observed that all studied immunogenesis parameters and the ratio of helper and suppressor T cells returned to reference values with the activation of the cellular component of immune system ($p < 0.01$), leading to the improved ($p < 0.01$) immunoregulatory balance. The standard drug therapy resulted in reliable changes in only a few cellular immunity indicators.

A follow-up ultrasound at the end of rehabilitation stages confirmed the anti-inflammatory and defibrosing effect of the therapeutic physical factors used, including the potentiation of the therapeutic benefits of the anti-adhesive resorbable drug Mesogel. Ultrasound after the course of treatment showed that patients in the treatment group had no signs of adhesion in the small pelvis, lower severity and frequency of endometrium abnormalities characteristic of infertility in chronic endometritis, thicker endometrium, and improved endometrial echostructures. In patients, the positive changes in pelvic ultrasounds were significantly lower ($p < 0.05$).

Hysterosalpingography at 12 months post-treatment showed reocclusion of the fallopian tubes in 29.4% of cases in the control group; whereas reocclusion was observed in 18.8% of cases in the experimental group, where the integrated drug and physiotherapy was used; in the treatment group with the additional use of hydrogen sulfide balneotherapy, reocclusion was observed in only 10.5% of cases.

A NAIF assessment of the quality of life at 9–12 months showed that the new technology we developed for the medical rehabilitation of patients after endoscopic minimally invasive pelvic interventions for infertility (treatment group) contributed to a significant improvement in all NAIF scores with the quality of life score increasing by 25.8% ($65.6 \pm 5.8\%$ compared to 88.4%; $p < 0.05$). Moreover, most women highlighted the improved psychoemotional state ($p < 0.05$), improved physical activity and performance ($p < 0.05$), self-confidence ($p < 0.05$), and increased sexual function ($p < 0.05$). This was significant ($p < 0.05$) compared with the changes in the control group, where only a tendency toward improving the quality of life was observed. In the experimental group, the quality of life score was only 8–10% lower compared to the treatment group.

An analysis of the long-term treatment outcomes in patients who had undergone endoscopic surgery on the fallopian tubes for infertility showed that the reproductive function restored in patients in the treatment group, who received integrated drug, physiotherapy, and hydrogen sulphide balneotherapy; 60.5% of patients got pregnant, which was significant compared to the control group, where pregnancy was detected in 38.2% of women. In the experimental group, where only drug therapy and simultaneous electro-magnetolaser therapy were used, 50% of women got pregnant.

Table 2. Dynamics of immune status indicators

Clinical manifestations	Observation period	Treatment group ($n=38$) M $\pm$ SD	Control group ($n=32$) M $\pm$ SD	Control group ($n=34$) M $\pm$ SD
Helper T cells (CD 4), %	Day 1	23.2 $\pm$ 2.8	24.1 $\pm$ 2.5	23.5 $\pm$ 2.7
	Day 21	35.6 $\pm$ 3.2**	34.1 $\pm$ 3.4*	26.3 $\pm$ 2.3
Suppressor T cells (CD 8), %	Day 1	12.3 $\pm$ 1.6	12.2 $\pm$ 1.7	12.6 $\pm$ 1.5
	Day 21	17.0 $\pm$ 1.0**	16.1 $\pm$ 1.1*	14.5 $\pm$ 1.4
Immunoregulatory balance (CD 4 / CD 8)	Day 1	1.4 $\pm$ 0.7	1.4 $\pm$ 0.6	1.5 $\pm$ 0.4
	Day 21	2.2 $\pm$ 0.8**	2.1 $\pm$ 0.6*	1.8 $\pm$ 0.4
Tumor necrosis factor α (TNF- α)	Day 1	49.8 $\pm$ 3.7	48.9 $\pm$ 3.5	48.4 $\pm$ 3.9
	Day 21	31.2 $\pm$ 2.5***	33.2 $\pm$ 2.4*	41.0 $\pm$ 3.7
Interleukin IL-1 β , pg/ml	Day 1	59.2 $\pm$ 4.3	58.9 $\pm$ 4.4	58.1 $\pm$ 4.6
	Day 21	37.8 $\pm$ 3.4***	40.0 $\pm$ 3.4*	50.3 $\pm$ 3.6
Interleukin IL-6, pg/ml	Day 1	1.2 $\pm$ 0.4	1.2 $\pm$ 0.3	1.2 $\pm$ 0.5
	Day 21	0.7 $\pm$ 0.3***	0.8 $\pm$ 0.2***	1.0 $\pm$ 0.3

Note: significance of differences with data before treatment * and ** — $p < 0.05$ and $p < 0.01$ respectively; significance of differences with the control group " — $p < 0.05$.

DISCUSSION

The new medical rehabilitation technology for patients who have undergone endoscopic surgery on the fallopian tubes for infertility with the integrated use of drug therapy, physiotherapy, and hydrogen sulphide balneotherapy contributed to the analgesic, anti-inflammatory, immunostimulating, defibrosing, and sedative effects. This resulted in the reduction of pain and inflammation, management of functional disorders of the fallopian tubes, prevention of adhesion, and improved immune resistance, which generally led to the improvement of reproductive function in patients and a significant improvement in their quality of life.

The staged rehabilitation and recovery after the endoscopic surgery on the fallopian tubes for infertility provides for a clear sequence of interrelated and interdependent actions with observance of all rehabilitation principles of [12, 18, 19] and relevance to the final outcome, i.e. restoration of reproductive health in this group of women.

Magnetolaser therapy is widely used in the treatment of gynecologic patients after surgery and, due to its pronounced anti-inflammatory and immunomodulatory effects, helps to relieve pain and inflammation and potentiate the therapeutic benefits of the anti-adhesive resorbable drug Mesogel and antibiotics [13, 20, 21].

There are isolated studies indicating positive experience in using hydrogen sulphide mineral water Redant-4R in the treatment of patients with chronic general salpingo-oophoritis [22–25]. The analyzed indicators showed that after staged magnetolaser therapy and hydrogen sulphide balneotherapy patients reported a reliably reduced severity of pain, depressive disorders, and increased energy and physical activity.

CONCLUSION

The obtained results suggest that the proposed rehabilitation method for patients after endoscopic surgery on the fallopian tubes for tubal and uterine infertility, including the integrated use of drug therapy, physiotherapy, and hydrogen sulphide balneotherapy, significantly enhances the efficacy of standard therapy and leads to a substantial improvement in reproductive function.

ADDITIONAL INFORMATION

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Authors' contribution. L.V. Tsallagova — concept, study design and editing of the final version of the manuscript; I.V. Kabulova — writing the text and partial statistical processing of the material; L.V. Maisuradze — concept, study design and editing of the final version of the manuscript; M.N. Sharipova — material collection, statistical processing; L.A. Gurtseva — material collection, statistical processing; K.M. Galyeva — material collection, statistical processing. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

Patients' consent. Written consent obtained from all the study participants before the study screening in according to the study protocol approved by the local ethic committee.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Вклад авторов. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией). Наибольший вклад распределён следующим образом: Л.В. Цаллагова — концепция, дизайн исследования и редактирование финальной версии рукописи; И.В. Кабулова — концепция, дизайн исследования и редактирование финальной версии рукописи; Л.В. Майсурадзе — научная редакция текста рукописи и обзор публикаций по теме статьи; М.Н. Шарипова — сбор материала, статистическая обработка; Л.А. Гурциева — сбор материала, статистическая обработка; К.М. Галуева — сбор материала, статистическая обработка.

Информированное согласие на участие в исследовании. Все участники до включения в исследование добровольно подписали форму информированного согласия, утверждённую в составе протокола исследования этическим комитетом.

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