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Research article

Antioxidant therapy of male infertility in patients with varicocele

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BACKGROUND: The study of the relationship between the presence of varicocele and male infertility is the subject of numerous studies, while many aspects of impaired spermatogenesis remain unclear. It has been established that after surgical treatment of varicocele, fertility is not restored in a significant number of patients. In this regard, the search for new and pathogenetically substantiated methods of treating such patients seems to be very relevant.

AIM: To evaluate the effectiveness of antioxidant therapy in spermatogenesis disorders in men with varicocele, prescribed both in combination with surgery and as monotherapy.

MATERIALS AND METHODS: Three groups of infertile men with varicocele were observed, who were treated with Speroton (a complex containing folic acid, L-carnitine, zinc, selenium, vitamin E) 1 sachet once a day, the duration of the course was three months. Patients of the first group (n = 43) were prescribed the drug after the Ivanissevich operation, the patients of the second group (n = 37) received antioxidant therapy during three months before the Ivanissevich operation and continued for three months after it. Patients of the third group (n = 21) did not undergo surgery, but received only antioxidant therapy for six months. The results of the combined treatment and conservative therapy with Speroton were compared with the results of treatment of 65 infertile patients who underwent only Ivanissevich's operation.

RESULTS: In patients with varicocele with initially pathological parameters of ejaculate, who were prescribed drugs with antioxidant properties in the postoperative period as an adjuvant treatment for 3 months, in 76.7% of cases there was a change in spermogram indicators towards improvement. The most significant changes were observed six months after the operation and subsequent adjuvant therapy. The indicators characterizing sperm motility underwent more noticeable changes. In patients who received only antioxidant therapy for six months, in all cases, there was a statistically significant ($p < 0.001$) improvement in sperm motility, which persisted for six months and exceeded these changes in groups of patients with adjuvant therapy and neo- and adjuvant therapy.

CONCLUSIONS: The results obtained allow us to conclude that there is no need for surgical treatment for varicocele in order to treat male infertility, since the operation itself can negatively affect the state of spermatogenesis, and conservative antioxidant therapy leads to better results in infertility treatment than the performed operation or any combination of it with antioxidant therapy.

Keywords: male infertility; varicocele; antioxidant therapy.

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Научная статья

Антиоксидантная терапия мужского бесплодия у пациентов с варикоцеле

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Актуальность. Изучение связи между наличием варикоцеле и мужским бесплодием — предмет многочисленных исследований, при этом многие аспекты нарушения сперматогенеза остаются неясными. Установлено, что после оперативного лечения варикоцеле фертильность не восстанавливается у значительного числа пациентов. В этой связи поиск новых и патогенетически обоснованных методов лечения таких больных представляется весьма актуальным.

Цель исследования. Оценить эффективность антиоксидантной терапии при нарушении сперматогенеза у мужчин с варикоцеле, назначаемой как в комбинации с операцией, так и в виде монотерапии.

Материалы и методы. Наблюдали три группы бесплодных мужчин с варикоцеле, которым проводили терапию препаратом «Сперотон» (комплекс, содержащий фолиевую кислоту, L-карнитин, цинк, селен, витамин Е) по 1 саше 1 раз в сутки, продолжительность курса 3 мес. Пациентам первой группы ($n = 43$) препарат назначали после произведенной операции Иваниссевича, пациентам второй группы ($n = 37$) антиоксидантную терапию проводили в течение 3 мес. перед операцией Иваниссевича и продолжали еще 3 мес. после нее. Больным третьей группы ($n = 21$) операцию не выполняли, а применяли только антиоксидантную терапию в течение полугода. Результаты комбинированного лечения и консервативной терапии препаратом «Сперотон» сравнивали с результатом лечения 65 бесплодных пациентов, которым проводили только операцию Иваниссевича.

Результаты. У пациентов с варикоцеле с исходно патологическими показателями эякулята, которым в послеоперационном периоде в качестве адъювантного лечения в течение 3 мес. назначали препараты, обладающие антиоксидантными свойствами, в 76,7 % случаев отмечено изменение показателей спермограмм в сторону улучшения. Наиболее значимые изменения наблюдались спустя полгода после проведенной операции и последующей адъювантной терапии. Более заметные изменения претерпели показатели, характеризующие подвижность сперматозоидов. У пациентов, которым проводилась только антиоксидантная терапия в течение 6 мес., во всех случаях отмечено статистически достоверное ($p < 0,001$) улучшение подвижности сперматозоидов, сохранявшееся в течение полугода и превосходившее эти изменения в группах пациентов с адъювантной терапией и нео- и адъювантной терапией.

Выводы. Полученные результаты позволяют сделать заключение об отсутствии необходимости оперативного пособия при варикоцеле с целью лечения мужского бесплодия, поскольку сама операция может негативно сказываться на состоянии сперматогенеза, а консервативная антиоксидантная терапия приводит к лучшим результатам лечения бесплодия, чем операция или любая комбинация ее с антиоксидантной терапией.

Ключевые слова: мужское бесплодие; варикоцеле; операция; антиксидантная терапия.

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ЭКО•ВЕКТОР

BACKGROUND

The main indication for surgical treatment of varicocele is its supposed effect on spermatogenesis, although this assumption is controversial [1], and surgery does not guarantee an improvement in the function of the testicles [2–4]. Fertility, regardless of the surgical interventions performed, is not restored in more than half of the patients, and in 28%–30% of cases, a progressive deterioration in spermatogenesis is reported [5–8]. The relatively low and unstable result of surgical treatment of varicocele in infertile men is largely caused by a lack of understanding of the mechanism of damage to spermatogenesis in these patients.

In recent years, an increase in the count of spermatozoa with a damaged DNA chain has been found to play a significant role in impaired spermatogenesis. Furthermore, overproduction of reactive oxygen species and the oxidative stress caused by them have been suggested to contribute to this [9–12]. To restore the fertilizing ability of spermatozoa, the function of the antioxidant system in the ejaculate should be normalized [13]. Numerous studies on the effect of antioxidant therapy in infertile men on the state of spermatogenesis have supported the treatment, since it leads to more frequent pregnancy in their intimate partners [14–17]. The credibility of the data obtained enables to recommend the use of antioxidants "in all cases of male infertility associated with oxidative stress" [18]. It has been noted that a stable improvement in spermogram parameters in men during such treatment occurs due to normalization of free radical oxidation processes in the ejaculate [19–21]. Moreover, a positive effect was noted from the use of a complex of biologically active substances, including antioxidants, comparable to surgery in patients with varicocele [22].

The gathered experience of effective treatment of idiopathic infertility, which pathogenesis comprises oxidative stress and DNA fragmentation of spermatozoa, and higher stimulation of the production of reactive oxygen species in the spermatozoa of infertile men with varicocele compared to that of men without varicocele [23–26] initiated the prescription of antioxidant therapy for spermatogenesis disorders in the postoperative period in men with varicocele [16, 27–30].

The present study aimed to evaluate the efficiency of antioxidant therapy for impaired spermatogenesis in men with varicocele, prescribed in combination with surgery and as monotherapy.

MATERIALS AND METHODS

The efficiency of antioxidant therapy in the postoperative period was investigated in 43 patients aged 21–36 years (mean age, 24.2 ± 1.0 years), who, after the Ivanissevich surgery, received Speroton (a complex containing folic acid, L-carnitine, zinc, selenium, vitamin E) 1 sachet once a day for 3 months (group 1). Additionally, 58 patients aged 23–31 years (mean, 25.1 ± 1.1 years) underwent a 3-month course of the abovementioned antioxidant therapy, after which they were distributed into two groups. One group included 37 patients who underwent the Ivanissevich surgery followed by (adjuvant) 3-month antioxidant treatment (group 2). The rest (21 patients) refused surgical treatment and continued conservative antioxidant therapy (group 3). The results of combined treatment and conservative therapy with Speroton were compared with the results of treatment of 65 infertile men aged 22–30 years (mean, 24.8 ± 2.1 years) who underwent only the Ivanissevich surgery.

Ejaculate tests, performed according to the WHO Guidelines for the examination and processing of human ejaculate (5th ed., 2012), were controlled at the beginning of the study and 3 and 6 months after the surgery. Moreover, in patients receiving conservative antioxidant treatment, the state of the ejaculate was assessed 3 and 6 months after the start of treatment. The results obtained were processed statistically and compared in groups. Statistical analysis of the study results was performed using Statistica 10.0, using commonly used methods of medical statistics; $p < 0.05$ was considered statistically significant.

STUDY RESULTS

The analysis of spermogram parameters in patients after the therapy and their comparison with the baseline indicators enabled to identify a certain dependence on the nature of the treatment. It was noted that in 33 patients (76.7%), the main indicators of the spermogram of patients after adjuvant antioxidant treatment differed significantly from the baseline toward improvement. In the remaining 10 patients, the spermogram parameters remained almost unchanged. The most significant changes were registered 6 months after the surgery and subsequent adjuvant antioxidant therapy for 3 months. This referred mainly to indicators characterizing sperm motility. Thus, the percentage of normally motile spermatozoa increased statistically significantly ($p < 0.05$) from 19.3% ± 0.13% to 34.8% ± 0.38%, whereas the percentage of spermatozoa with low motility decreased (from 25.55% ± 0.25% to 21.21% ± 0.21%), as well as the percentage of immobile spermatozoa (from 55.15% ± 0.95% to 43.99% ± 1.89%). Concurrently, no significant changes were registered in the indicator characterizing the morphology of spermatozoa. Although there was an increase in the percentage of spermatozoa with normal morphology in the spermogram of these patients, it was not statistically significant ($p > 0.05$) (Table 1).

In the patients who underwent 3-month neoadjuvant antioxidant treatment, before surgery for varicocele,

a therapeutic effect was noted on the part of all spermogram parameters, especially in indicators characterizing sperm motility (Table 2). A significant improvement in ejaculate parameters was observed in almost all patients (58 people), which enabled to refrain from the planned surgery in 21 men (patients who preferred to avoid surgery) and give them a second course of antioxidant therapy for 3 months. The remaining 37 patients underwent the Ivanissevich surgery supplemented with adjuvant therapy with antioxidants.

A study of the ejaculate of patients in this group 6 months after the Ivanissevich surgery (37 people) revealed a statistically significant improvement in spermogram parameters compared to baseline values (Table 3); however, these changes differed little from the values of the ejaculate parameters of patients who received only the adjuvant antioxidant therapy and were significantly better only in some cases (Table 4).

Thus, a comparative analysis of the results of neoadjuvant and adjuvant antioxidant treatment of

Table 1. Dynamics of spermogram indices in patients with varicocele after surgical treatment and adjuvant antioxidant therapy (group 1, *n* = 43)

Таблица 1. Динамика показателей спермограммы у пациентов с варикоцеле после хирургического лечения и адъювантной антиоксидантной терапии (1-я группа, *n* = 43)

Ejaculate indicator	Timing		
	before surgery	3 months after surgery	6 months after surgery
Volume, ml	3.12 ± 0.10	3.07 ± 0.03, $p > 0.05$	3.13 ± 0.03, $p > 0.05$
pH	7.37 ± 0.37	7.41 ± 0.01, $p > 0.05$	7.47 ± 1.46, $p > 0.05$
Sperm cell density, mln/ml	16.1 ± 0.36	**19.5 ± 0.35,** $p < 0.05$	**29.11 ± 1.38,** $p < 0.001$
Normal sperm motility, %	19.3 ± 0.13	**30.91 ± 0.21,** $p < 0.05$	**34.8 ± 0.38,** $p < 0.05$
Low sperm motility, %	25.55 ± 0.25	**20.10 ± 0.21,** $p < 0.05$	**21.21 ± 0.21,** $p < 0.05$
Nonmotile spermatozoa, %	55.15 ± 0.95	**48.99 ± 1.09,** $p < 0.001$	**43.99 ± 1.89,** $p < 0.001$
Morphologically normal spermatozoa, %	42.5 ± 0.65	42.91 ± 1.01, $p > 0.05$	46.45 ± 0.25, $p > 0.05$
Spermatozoa with head pathology, %	35.54 ± 0.24	34.14 ± 0.31, $p > 0.05$	29.93 ± 0.23, $p > 0.05$
Spermatozoa with midpiece pathology, %	13.52 ± 0.23	13.16 ± 0.26, $p > 0.05$	14.31 ± 0.31, $p > 0.05$
Spermatozoa with tail pathology, %	8.94 ± 0.19	9.79 ± 0.22, $p > 0.05$	9.31 ± 0.21, $p > 0.05$

Note. Bold font indicates postoperative parameters that differ significantly from baseline.

Table 2. Dynamics of spermogram indices in patients with varicocele after neoadjuvant antioxidant therapy (*n* = 58)

Таблица 2. Динамика показателей спермограммы у пациентов с варикоцеле после неоадъювантной антиоксидантной терапии (*n* = 58)

Ejaculate indicator	Timing		*p*
	baseline	after antioxidant therapy (3 months)	
Volume, ml	3.13 ± 0.13	3.16 ± 0.16	>0.05
pH	7.32 ± 0.02	7.43 ± 0.04	>0.05
Sperm cell density, mln/ml	16.1 ± 0.31	19.8 ± 0.38	>0.05
Normal sperm motility, %	21.99 ± 0.29	**26.11 ± 0.16**	<0.001
Low sperm motility, %	16.96 ± 0.26	**19.29 ± 0.19**	<0.005
Nonmotile spermatozoa, %	61.05 ± 0.95	**54.6 ± 0.56**	<0.005
Morphologically normal spermatozoa, %	45.1 ± 0.61	46.39 ± 1.19	>0.05
Spermatozoa with head pathology, %	31.01 ± 0.21	32.62 ± 0.32	>0.05
Spermatozoa with midpiece pathology, %	14.15 ± 0.15	15.15 ± 0.25	>0.05
Spermatozoa with tail pathology, %	9.74 ± 0.14	**5.84 ± 0.24**	<0.005

Note. Bold font indicates postoperative parameters that differ significantly from baseline.

spermatogenesis disorders in infertile men with varicocele revealed a higher therapeutic effect from neoadjuvant and adjuvant use of antioxidant drugs (in our case, the Speroton complex).

Furthermore, a study of the ejaculate in all 21 patients with varicocele who, after antioxidant therapy, did not receive surgical treatment and continued conservative treatment showed that the change in the main parameters of the spermogram 6 months after the end of therapy statistically significantly improved compared to the baseline (Table 5). A statistically significant ($p < 0.001$) increase in spermatozoa concentration from 16.1 ± 0.31 to 28.21 ± 1.31 million/ml was noted. Indicators of normal spermatozoa motility and spermatozoa with low motility increased statistically significantly ($p < 0.005$) due to a decrease in the count of immobile spermatozoa. A comparative analysis of these changes showed that in infertile men with varicocele, who received conservative treatment with antioxidant drugs instead of surgery, an improvement in spermogram parameters 6 months after

Table 3. Dynamics of spermogram indices in patients with varicocele after Ivanissevich's operation with neo- and adjuvant antioxidant therapy

Таблица 3. Динамика показателей спермограммы у пациентов с варикоцеле после операции Иваниссевича с нео- и адъювантной антиоксидантной терапией

Ejaculate indicator	Timing		*p*
	baseline (*n* = 58)	6 months after surgery (*n* = 37)	
Volume, ml	3.13 ± 0.13	3.16 ± 0.16	>0.05
pH	7.32 ± 0.02	7.43 ± 0.04	>0.05
Sperm cell density, mln/ml	16.1 ± 0.31	23.8 ± 0.33	>0.05
Normal sperm motility, %	21.99 ± 0.29	**36.16 ± 0.16**	<0.001
Low sperm motility, %	16.96 ± 0.26	**29.29 ± 0.19**	<0.005
Nonmotile spermatozoa, %	61.05 ± 0.95	**34.55 ± 0.56**	<0.001
Morphologically normal spermatozoa, %	45.1 ± 0.61	45.99 ± 1.09	>0.05
Spermatozoa with head pathology, %	31.01 ± 0.21	30.62 ± 0.32	>0.05
Spermatozoa with midpiece pathology, %	14.15 ± 0.15	13.15 ± 0.25	>0.05
Spermatozoa with tail pathology, %	9.74 ± 0.14	10.24 ± 0.24	>0.05

Note. Bold font indicates postoperative parameters that differ significantly from baseline.

Table 4. Dynamics of spermogram indices in patients with varicocele six months after Ivanissevich's operation with neo- and adjuvant and adjuvant antioxidant therapy

Таблица 4. Динамика показателей спермограммы у пациентов с варикоцеле через 6 мес. после операции Иваниссевича с нео- и адъювантной и адъювантной антиоксидантной терапией

Ejaculate indicator	Type of treatment		*p*
	after adjuvant therapy (*n* = 43)	after neo- and adjuvant therapy (*n* = 37)	
Volume, ml	3.13 ± 0.03	3.16 ± 0.16	>0.05
pH	7.47 ± 1.46	7.43 ± 0.04	>0.05
Sperm cell density, mln/ml	29.11 ± 1.38	23.8 ± 0.33	<0.001
Normal sperm motility, %	34.8 ± 0.38	36.16 ± 0.16	<0.005
Low sperm motility, %	21.21 ± 0.21	29.29 ± 0.19	<0.001
Nonmotile spermatozoa, %	43.99 ± 1.89	34.55 ± 0.56	<0.001
Morphologically normal spermatozoa, %	46.45 ± 0.25	45.99 ± 1.09	>0.05
Spermatozoa with head pathology, %	29.93 ± 0.23	30.62 ± 0.32	>0.05
Spermatozoa with midpiece pathology, %	14.31 ± 0.31	13.15 ± 0.25	>0.05
Spermatozoa with tail pathology, %	9.31 ± 0.21	10.24 ± 0.24	>0.05

the start of treatment was statistically significantly better than similar parameters of the spermogram of patients who received neoadjuvant and adjuvant antioxidant therapy (Table 6).

Therefore, if the concentration of spermatozoa in patients after the Ivanissevich surgery and adjuvant therapy with antioxidant agents virtually did not differ from the concentration of spermatozoa in the semen of patients who received antioxidant therapy without surgery, then the indicator of normal spermatozoa motility in the ejaculate of nonoperated patients was statistically significantly higher ($p < 0.001$) than in that of operated men who received adjuvant antioxidant therapy (41.8% ± 0.18% versus 34.8% ± 0.38%). Additionally, the percentage of immotile spermatozoa was statistically significantly ($p < 0.001$) lower in patients from the group of nonoperated patients and amounted to 36.08% ± 1.8% versus 43.99% ± 1.89% in patients receiving adjuvant antioxidant therapy after surgery for varicocele.

Since the main indicator of efficiency of infertility treatment for varicocele is pregnancies in the wives and intimate partners of patients, this indicator was analyzed in married couples over a period of 3 years. This considered the presence of pregnancies and childbirth that

Table 5. Dynamics of spermogram indices in patients with varicocele after conservative antioxidant therapy

Таблица 5. Динамика показателей спермограммы у пациентов с варикоцеле после консервативной антиоксидантной терапии

Ejaculate indicator	Timing		
	baseline ($n = 58$)	after 3 months ($n = 58$)	after 6 months ($n = 21$)
Volume, ml	3.13 ± 0.13	3.16 ± 0.16, $p > 0.05$	3.11 ± 0.01, $p > 0.05$
pH	7.32 ± 0.02	7.43 ± 0.04, $p > 0.05$	7.41 ± 1.41, $p > 0.05$
Sperm cell density, mln/ml	16.1 ± 0.31	19.8 ± 0.38, $p > 0.05$	28.21 ± 1.31, $p < 0.001$
Normal sperm motility, %	21.99 ± 0.29	26.11 ± 0.16, $p < 0.001$	41.8 ± 0.18, $p < 0.001$
Low sperm motility, %	16.96 ± 0.26	19.29 ± 0.19, $p < 0.005$	22.12 ± 0.21, $p > 0.05$
Nonmotile spermatozoa, %	61.05 ± 0.95	54.6 ± 0.56, $p < 0.005$	36.08 ± 1.8, $p < 0.001$
Morphologically normal spermatozoa, %	45.1 ± 0.61	46.39 ± 1.19, $p > 0.05$	47.05 ± 0.15, $p > 0.05$
Spermatozoa with head pathology, %	31.01 ± 0.21	32.62 ± 0.32, $p > 0.05$	30.23 ± 0.23, $p > 0.05$
Spermatozoa with midpiece pathology, %	14.15 ± 0.15	15.15 ± 0.25, $p > 0.05$	15.31 ± 0.31, $p > 0.05$
Spermatozoa with tail pathology, %	9.74 ± 0.14	5.84 ± 0.24, $p < 0.005$	7.41 ± 0.11, $p > 0.05$

Note. The *p*-value indicates the significance of differences compared to the baseline.

Table 6. Comparative characteristics of spermogram indices in patients with varicocele 6 months after treatment

Таблица 6. Сравнительная характеристика показателей спермограммы у пациентов с варикоцеле через 6 мес. после проведенного лечения

Ejaculate indicator	Type of treatment			p_{1-2}	p_{1-3}
	after adjuvant therapy ($n = 43$)	after neo- and adjuvant therapy ($n = 37$)	after conservative therapy ($n = 21$)		
Volume, ml	3.13 ± 0.03	3.16 ± 0.16	3.11 ± 0.01	>0.05	>0.05
pH	7.47 ± 1.46	7.43 ± 0.04	7.41± 1.41	>0.05	>0.05
Sperm cell density, mln/ml	29.11 ± 1.38	23.8 ± 0.33	28.21 ± 1.31	<0.001	>0.05
Normal sperm motility, %	34.8 ± 0.38	36.16 ± 0.16	41.8 ± 0.18	<0.005	<0.001
Low sperm motility, %	21.21 ± 0.21	29.29 ± 0.19	22.12 ± 0.21	<0.001	>0.05
Nonmotile spermatozoa, %	43.99 ± 1.89	34.55 ± 0.56	36.08 ± 1.8	<0.001	<0.001
Morphologically normal spermatozoa, %	46.45 ± 0.25	45.99 ± 1.09	47.05 ± 0.15	>0.05	>0.05
Spermatozoa with head pathology, %	29.93 ± 0.23	30.62 ± 0.32	30.23 ± 0.23	>0.05	>0.05
Spermatozoa with midpiece pathology, %	14.31 ± 0.31	13.15 ± 0.25	15.31 ± 0.31	>0.05	>0.05
Spermatozoa with tail pathology, %	9.31 ± 0.21	10.24 ± 0.24	7.41 ± 0.11	>0.05	>0.05

Note. The p_{1-2} value indicates the significance of differences in patients after adjuvant therapy and after neo- and adjuvant therapy; the p_{1-3} value indicates the significance of differences in patients after neo- and adjuvant therapy and after the conservative therapy.

Table 7. Reproductive function of patients with varicocele within 36 months after treatment

Таблица 7. Репродуктивная функция пациентов с варикоцеле в течение 36 мес. после проведенного лечения

Follow-up groups	Pregnancy in the intimate partner		Birth of a child	
	n	%	*n*	%
Ivanissevich surgery (*n* = 65)	17	26.15	8	12.3
Conservative treatment with antioxidants for 6 months (*n* = 21)	13	61.9	11	52.38
Ivanissevich surgery + adjuvant treatment with antioxidants (*n* = 34)	14	41.17	10	29.41
Ivanissevich surgery + neoadjuvant and adjuvant treatment with antioxidants (*n* = 30)	13	43.33	10	33.33

occurred after conservative treatment of infertility or surgical treatment of varicocele with adjuvant conservative therapy with antioxidants. By the time of the study, all patients from the conservative treatment group had been married for more than 1 year (1–4.5 years); in the group of patients with neoadjuvant and adjuvant treatment, 30 men had wives or permanent intimate partners and did not use contraceptives, and in the group of patients receiving adjuvant antioxidant therapy, 34 men were married for 1–3 years. Throughout the entire follow-up period, in the families of patients who underwent Ivanissevich surgery with adjuvant antioxidant therapy, pregnancies occurred in 14 families, ending in term births in 8 cases and preterm births of healthy children in 2 cases (at 35 and 36 weeks of gestation) (29.41%) (Table 7). In patients who received neoadjuvant (for 3 months before surgery) and adjuvant treatment with antioxidants, pregnancies occurred in 13 families, and in 10 cases (33.3%), they ended in term delivery of healthy children. The best result was noted in patients with varicocele who did not undergo surgical treatment, but were treated for 6 months using a complex of drugs containing antioxidant agents. Thus, out of 21 married couples during the 3-year follow-up period, 13 women had pregnancies, 11 (52.38%) of which ended in the birth of a healthy child at term. It should be noted that 17 men from this group underwent annually a 3-month course of antioxidant therapy during the follow-up period.

CONCLUSION

This study revealed that in patients with varicocele with initially pathological indicators of ejaculate, who received drugs with antioxidant properties in the postoperative period as an adjuvant treatment for 3 months, deterioration of spermogram parameters was not noted in any of the patients, and their change toward improvement occurred in 76.7% of cases. The most significant changes could be seen 6 months after the surgery and subsequent adjuvant therapy. Indicators characterizing the motility of spermatozoa showed more noticeable changes. Moreover, the percentage of normally motile spermatozoa increased statistically significantly ($p < 0.05$), and the percentage of spermatozoa with low mobility and proportion of immobile spermatozoa decreased. A significant improvement in ejaculate parameters was noted in almost all patients who received a 3-month treatment with antioxidants as a neoadjuvant therapy before surgical treatment. However, 6 months after surgical treatment and subsequent adjuvant therapy, changes in the parameters of the ejaculate of these patients did not differ significantly from changes in the ejaculate parameters of patients who received adjuvant treatment with antioxidants after surgical treatment of varicocele. Concomitantly, in patients (21 people) who received only antioxidant therapy for 6 months, in all cases, a statistically significant ($p < 0.001$) improvement in sperm motility was observed, which persisted for 6 months and exceeded these changes in groups of patients with adjuvant therapy and neoadjuvant and adjuvant therapy.

The evaluation of the results of male infertility treatment based on the frequency of pregnancy and childbirth in the families of patients, depending on the therapy, showed the best results of conservative therapy with antioxidants. In this study, during the 3-year follow-up period, the birth of healthy children was noted in the wives of the patients in 52.38% of cases compared with 12.3% in patients after the Ivanissevich surgery, in 29.41% of cases in patients after adjuvant antioxidant therapy, and in 33.3% of cases of patients after neoadjuvant and adjuvant antioxidant therapy. The results indicated that surgical intervention for varicocele to treat male infertility is not required, since the surgery itself can affect adversely the state of spermatogenesis, and conservative antioxidant therapy leads to better results in infertility treatment than surgery or any combination of it with antioxidant therapy.

ADDITIONAL INFORMATION

Author contributions. All authors confirm that their authorship complies with the international ICMJE criteria (all authors have made a significant contribution to the development of the concept, research, and preparation of the article and read and approved the final version before its publication).

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