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CHANGES IN SPERM DENSITY CAUSED BY VARICOCELE AND THEIR TREATMENT BY MEANS OF SCLEROEMBOLIZATION OR HIGH SPERMATIC VEIN LIGATION

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Summary. *The incidence of varicocele in the male population is 15-20% and its contribution to infertility is 30-50%. In this study, the treatment of varicocele included high spermatic vein ligation. Fifty male patients were treated and checked up postoperatively. Their sperm density increased postoperatively from 27.35 million per ml to 50.30 million per ml, while after the scleroembolization it increased from 27.25 to 49.68 million per ml. A statistically significant increase was not noticed in both of the examined groups. Very little motile sperm was evident in both groups preoperatively. A statistically significant increase in sperm motility in the postoperative period, in comparison with the previous values, was recorded in both examined groups at every postoperative checkup over a period of 9 months, and 12 months after the scleroembolization. The high pregnancy rate (66% and 62%, respectively) indicates the necessity of treating male infertility caused by varicocele.*

Key words: *Varicocele, scleroembolization, ligature, v. testicularis*

Introduction

The presence of varicocele in the general male population is 15-20% (1). Varicocele causes infertility in 30-50% of all marriages (2,3). Our research has confirmed that it causes reduced sperm density, as well as reduced sperm motility. Both the operation and the radiological intervention treatment of varicocele contributed to the fertility of men who had oligoasthenospermia. The increase in sperm density and motility after surgery was 54 - 78% (4), and the pregnancy rate was 34 - 53% (5). Damage to spermatogenesis, caused by the negative influence of varicocele, occurs as the result of the unified effect of increased testicular temperature and the slower flow and stagnation of blood in the pampiniform plexus due to the effect of prostaglondine and seronine. The question, however, exists as to the very effects of the treatments of varicocele and infertility caused by it, as well as whether ligation or scleroembolization could result in the improvement of sperm parameters and infertility. In this study, we tried to estimate the efficiency of the surgery and scleroembolization in treating infertile men with varicocele. In addition, we tried to see if any difference exists between the methods of treatment. In the pathogenesis of varicocele, gradual damage is done to the germ cell epithelia and Leydig cells. Changes occur in both the testicles which are not always of the same degree of seriousness. The initial changes in the testicles are due to the onset of varicocele. The reduced number of mobile spermatozoids and the increased number of abnormal ones are the result of the spermatogenesis caused by varicocele (6).

A prolonged vein hypertension will cause distortion and atrophy of the big blood vessel medium. The hypoxemic testicle on the side of varicocele becomes smaller and softer while the contra lateral one remains protected (undamaged). The reduced number of spermatozoids, their reduced mobility of below 50%, and the increasing rate of pathological forms of above 35% show the effect of varicocele and its damage to the contra lateral testicle as well. Damage to the tubular basal membrane enables the penetration of spermatozoids and their particles into the interstitium which, in contact with lymphocytes, results in the appearance of circulating antispermatozoid antibodies. This can lead to a decrease in spermatozoids of 1mil/ml and in the percentage of motility to below 40%, while pathological forms stay above 50% followed by a dominance of micro cephalic spermatozoids.

Patients and Methods

For the purpose of the study, we selected patients with long lasting sterility (≥12 months), aged 23 to 42, with obvious and/or palpable varicocele and a positive Valsalva maneuver. At anamneses, none of the patients had serious kidney or liver diseases, nor were they under any long-lasting infertility treatment. The patients had obtained the pathological findings of their spermograms (taken at least three times with a one-month

pause) in accordance to the criteria of WHO (7), and were suffering from a decreasing number of spermatozoids <20mil/ml or their decreasing motility <50%. None of the patients had urogenital infections, their rectum findings were normal, the number of leukocytes in their ejaculate was < 1mil/ml and there were no changes in the secretion of the accessory gland. Their hormone levels (FSH, LH, and testosterone) were normal. The hormone levels were evaluated by means of the RIA method.

In the period from 1990 to 2004, 100 patients with varicocele and the resulting infertility were divided into two groups. One group of 50 men (Group A) underwent high spermatic vein ligations, and the remaining 50 men (Group B) were treated with the radiological scleroembolization of the testicular vein at the Institute for Radiology. After a complete examination of their fertility status (sperm density carried out 3 times, hormonal status, clinical state, sperm culture and tests for possible infections), we performed high spermatic vein ligations employing the Ivanissevich method or scleroembolization. After the intervention, all of the patients were checked up every three months over a period of one year, and the analyses of sperm and hormone levels were performed for both groups. During the study, we kept records of the time interval between the intervention and the pregnancy.

Results

There were no significant differences between the two groups with respect to the following values: the mean of the patients' ages, the duration of the infertility prior to the patients' participation in our study program, and their hormone levels (FSH, LH, prolactin, testosterone) (Table 1).

Table 1. Patient profile before the treatment

Patient number	Group A 50	Group B 50
Age	30.48 ± 4.43 *	30.68 ± 3.52
Infertility / months	25.60 ±11.70 *	26.30 ± 13.5
FSH (iu/l)	9.86 ± 4.66	11.43 ± 6.37
LH (iu/l)	10.04 ± 3.53	10.60 ± 3.85
Testosterone (Nmol/l)	7.31 ± 3.28	7.77 ± 4.22

* levels with the mean value ± SD

No differences were noted in the number of spermatozoids between the patients of both treated groups at the beginning of the study, as well as during the checkup period of 12 months (Table 2).

The increasing number of sperm was statistically significant in both groups of patients at every checkup in the given periods of time, compared to the previous value for group A in the period up to 9 months, and for group B up to 12 months after the intervention (Table 3), regardless of the method used in the treatment of varicocele.

Table 2. Average values of the number of sperm/ml

Parameter	Group A	Group B	Statistic
Before treatment	24.79 ± 19.14	27.25 ± 17.32	z = –0.986; p = 0.324 n.s.*
After 3 months	36.77 ± 20.65	35.61 ± 19.17	z = –0.343; p = 0.733 n.s.
After 6 months	43.00 ± 21.16	41.08 ± 20.30	z = –0.362; p = 0.717 n.s.
After 9 months	49.31 ± 22.57	45.41 ± 22.38	z = –1.251; p = 0.211 n.s.
After 12 months	50.30 ± 22.67	49.68 ± 23.21	z = –0.014; p = 0.989 n.s.

*Mann-Whitney U - Wilcoxon Rank Sum W Test

Table 3. The statistical analysis of the number of sperm

Compare	Statistics*	
	Group A	Group B
0 month – 3 months	z = –6.093; p <0.001	z = –6.057; p < 0.001
3 months – 6 months	z = –5.735; p < 0.001	z = –5.874; p < 0.001
6 months – 9 months	z = –5.508; p < 0.001	z = –5.532; p <0.001
9 months – 12 months	z = –1.680; p = 0.093 n.s.	z = –5.652; p < 0.001

* Wilcoxon Matched-Pairs Signed-Ranks Test

The decreased number of motile sperm is the dominant parameter in the pathological results of the spermogram of most of the patients with varicocele. Table 4 shows the average value ±50 percent of mobile sperm before the intervention and during the three-month period during which both groups were under observation. All the results were compared statistically.

Table 4. The average percent of mobile sperm

	Group A	Group B	Statistic
Before treatment	36.28 ± 12.57	39.63 ± 11.54	z = –0.984; p = 0.325 n.s.**
After 3 months	56.10 ± 16.01	52.10 ± 10.98	T = 1.46; p = 0.148 n.s.*
After 6 months	65.06 ± 14.18	61.40 ± 9.69	T = 1.51; p = 0.135 n.s.
After 9 months	73.76 ± 12.50	68.90 ± 10.27	T = 2.12; p = 0.036<0.05
After 12 months	75.00 ± 11.34	75.70 ± 9.09	T = 0.34; p = 0.734 n.s.

* t – test * * Mann-Whitney U - Wilcoxon Rank Sum W Test

There was no significant difference between these two groups with respect to the sperm motility values obtained after two different methods used in the treatment of varicocele. After the treatment, the sperm checkup analysis showed that there were no differences in sperm mobility in regards to the implemented procedure, except in the period after 9 months when an effect was achieved due to surgical treatment.

We noticed a statistically significant increase of sperm motility at every regular three-month checkup: in group

A – 9 months after surgery, in group B – 12 months after scleroambolization (Table 5).

Table 5. The statistical comparison of sperm mobility during a three-month period

Compare	Statistics*	
	Group A	Group B
0 month – 3 months	z = –5.844; p < 0.001	z = –5.675; p < 0.001
3 months – 6 months	z = –5,131; p < 0.001	z = –5.734; p < 0.001
6 months – 9 months	z = –5.736; p < 0.001	z = –4.934; p < 0.001
9 months – 12 months	z = –1.094; p = 0.274 n.s.	z = –5.326; p < 0.001

*Wilcoxon Matched-Pairs Signed-Ranks Test

Twelve months after the high spermatic vein ligation or scleroembolization there was a significant increase in the number of sperm and their mobility, which resulted in an increased number of pregnancies, in group A 33/50 (66%) and in group B 31/50 (62%). The sperm parameters showed a significant increase during the first six months after the intervention.

Discussion

The relation between varicocele, either left or bilateral, and abnormal sperm parameters is generally noticed but not as yet fully accounted for. According to WHO (7), the infertility of a great number of couples is caused by varicocele, which is the main cause of male infertility (30-50%). An abnormal spermogram is more frequent in men with varicocele than in those with normal parameter findings (3,8). Different results were recorded and ascribed to the effects of the varicocele correction, that is, the qualitative and quantitative improvement of the spermogram (4,5), leading to a greater number of pregnancies (10). Some patients were still infertile despite the operation or scleroembolization. The success of varicocele treatment and the improvement of the spermogram were influenced by: age, testicular volume, whether the varicocele was unilateral or bilateral, grade, the incidence of the increasing values of FSH or the final damage done to the spermatogenesis with a presence of terato or necrospermia. According to some authors, pregnancies occurred in 34-53% of the cases (2,4,5). Other authors, however, did not obtain such good results and they expressed their doubts as to the efficiency of varicocele treatment in combating infertility. The failure to obtain promising results could be the consequence of an inadequate selection of patients for varicocele treatment, therapy regimes, and the period of infertility or pathological state in some of the female partners. Much of the previous research was retrospective, as opposed to ours which is prospective, controlled, and aimed at two complementary methods for the treatment of varicocele. Upon selection of patients, two groups were formed depending on the choice of method used in the treatment of varicocele. Both groups were similar in regards to age, difference in the number and motility of spermatozoids, or the absence of statistically significant differences, or differences in hormone parameters. A significant decrease in sperm mobility and the original values was achieved in both treated groups. Other authors were able to obtain similar results (9). In group A, an improvement was noticed in the first 9 months of observation, while in group B it occurred during the first 12. The high pregnancy rate in group A 33/35 (66%), and group B 31/50 (62%) after one year of observation coincides with the observations of Madgar (10), according to whom the highest pregnancy rate occurred during the first year after the treatment of varicocele. Such a high pregnancy rate was the result of well-determined criteria in the selection of patients for varicocele treatment and the unique criteria for sperm evaluation before and after the treatment. The fact that there is no statistically significant difference in sperm density, mobility and pregnancy rate between the groups shows that the choice of method in the treatment of varicocele is not the crucial issue. Improvement in all the sperm parameters and the pregnancy rate shows that varicocele might be present in the majority of infertile couples and should be treated as soon as possible to avoid irreversible damage to the testicular parenchyma.

The improvement of the sperm parameters after the intervention, even in the case of couples where a pregnancy was not recorded, shows the effectiveness of varicocele treatments and suggests that treatment should start as soon as possible, sometimes even as a preventive measure (11). Varicocele is associated with a decrease in fertility and testicular functions. Correction of varicocele in most patients improves sperm parameters and increases the rate of fertility. If varicocele is a consequence of a congenital lack in the vein drainage of the testicular grove, it can appear between the ages of 13 and 15 (13) and its occurrence is caused by the presence of vein reflux (14). Even though the left-sided varicocele is dominant (15), it is also very important to locate bilateral varicocele by contemporary means of diagnosis (16,17) and to start treatment in order to decrease residual varicocele. Most authors confirm the importance of an early diagnosis and treatment of varicocele (6,18) for preventive reasons, and they also confirm that the progressive effect of varicocele should not be related to the age of a patient (19,20). The postoperative increase in the number of sperm to a value of above 40 million per ml contributes to pregnancy (14). Other authors think that the increase in the number of sperm up to 20 million per ml causes a 50% increase in pregnancies, which is the result of a timely operation. The normal state of the spermogram in both groups (2/3 of patients) was achieved during the first 6 months after treatment. The conclusion is that varicocele treatment is necessary and that it increases the pregnancy rate.

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PROMENE U SPERMOGRAMU USLOVLJENE POSTOJANJEM VARIKOCELE I TRETIRANE VISOKOM LIGACIJOM ILI SKLEROEMBOLIZACIJOM SPERMATIČNE VENE

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Kratak sadržaj: *Varikocela se sreće u opštoj populaciji muškaraca 15 do 20%, a kod 30 do 50% brakova, neplodnost je uslovljena postojanjem varikocele. Tretman varikocele sastojao se u hirurškoj visokoj ligaciji spermatične vene ili njenoj radiološkoj skleroembolizaciji. Ispitivanjem je obuhvaćeno po 50 muškaraca koji su kontrolisani 12 meseci nakon tretmana. Porast broja spermatozoida nakon operacije bio je sa 24,79 na 50,30 miliona po ml. dok je nakon skleroembolizacije broj porastao sa 27,25 na 49,68 miliona po ml. Statistiški značajan porast broja spermatozoida bio je kod obe tretirane grupe. Preoperativno, kod obe ispitivane grupe je dominirao smanjen broj pokretnih spermatozoida. Statistički značajno povećanje pokretljivosti spermatozoida nakon tretmana, u odnosu na vrednosti pre procedure zabeleženo je u obe posmatrane grupe pri svakoj kontroli do 9 meseci nakon operacije i 12 meseci iza skleroembolizacije. Visok procenat trudnoća (66% odnosno 62%) kod seksualnih partnerki ukazuje na neophodnost tretmana muškog infertiliteta uslovljenog varikocelom.*

Ključne reči: *Varikocela, skleroembolizacija, ligatura v. tesicularis*