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The influence of varicocelectomy on semen parameters and fertility

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Abstract

Introduction. Varicocele is an abnormal dilation of the spermatic veins within the pampiniform plexus of the spermatic cord. This pathology is diagnosed in 25% of infertile men. There is some data that confirms varicocelectomy improves semen parameters and fertility potential in men with clinically diagnosed varicocele and impaired semen parameters. The aim of our study was to determine the influence of laparoscopic varicocelectomy on semen parameters and evaluation of spontaneous pregnancy rate.

Material and methods. We retrospectively reviewed the data of 60 consecutive patients subjected to laparoscopic varicocelectomy between November 2010 and December 2016 due to clinical varicocele, impaired semen parameters and infertility.

Results. The average age was 31 +/- 7. Compared with baseline semen parameters, sperm count, sperm concentration, morphology and progressive motility at 3 and 6 months. We did not observe changes in semen volume and semen pH during follow-up. A total improvement in semen parameters was observed in 64% and 70% of patients after 3 and 6 months after surgery. In 4 patients deterioration of semen parameters was noticed. Spontaneous pregnancy was achieved in 30% of couples. Two pregnancies were unsuccessful due to spontaneous abortion. A total of 16 children were born. The surgery- to- conception time was 7.7 +/- 7 months.

Conclusions. Laparoscopic varicocelectomy in a patient who has suffered from infertility and confirmed semen parameters and fertility potential of men.

Key words: varicocele, male infertility, infertility treatment, laparoscopic varicocelectomy, varicocelectomy, semen abnormalities.

Introduction:

Infertility (according to WHO) is the inability of a sexually active, non-contracepting couple to achieve pregnancy in one year.[1]. About 15% of sexually active couples are unable to conceive a child and require infertility treatment, 1/8 of couples have difficulties in conceiving the first child, and 1/6 of couples in conception of the second [2]. Amongst 50% of infertile couples, men have improper semen parameters [3] .Male fertility is influenced by following factors: congenital or acquired genitourinary disorders, cancers, urogenital infections, increased scrotal temperature (for example as a result of varicocele), endocrine disorders, genetic abnormalities, immunological factors, 40% of male infertility is idiopathic (multiple factors) [17].

Varicocele is defined as an abnormal dilation of the spermatic veins within the pampiniform plexus of the spermatic cord. According to statistical data, varicocele is the most common cause of primary and secondary infertility. They occur in about 15-20% of the general male population and account for 35% of the primary and 81% of cases of the secondary cause of infertility. In the group of examined men treated for infertility with clinically present varicocele, semen analysis outcomes were normal in 11%, however 25% had abnormal results. [4].

Varicocele, in 85-90%, occur on the left side, isolated varicose veins on the right side are rare [5,6]. It is dependent on the anatomical structure - left testicular vein joins left renal vein at a right angle, which contributes to the obstruction of blood and thereby increases the hydrostatic pressure. Right testicular vein however joins the inferior vena cava at an obtuse angle. In rare cases varicose veins may be caused by tumors located in the retroperitoneal space, which is worth remembering in everyday practice [7].

Failure or a lack of venous valves, a nutcracker syndrome, otherwise referred to as a syndrome of left renal vein compression through the aorta and upper mesenteric artery may cause reflux in the testicular vein. During the reversal flow, metabolites from kidneys and adrenal glands flow into the testicles causing arterial spasm, increase in hydrostatic pressure, hypoxia and oxidative stress [11,13].

Varicocele adversely affect function of the testicle. They account for elevated pressure, elevated temperature of the testis, hypoxia and oxidative stress, which may result in decrease of testosterone secretion by Leydig cells and limitation of secretory function of Sertoli cells [8,9,10].

Diagnosis of infertility should begin with a thoroughly conducted subjective examination. During an interview, one should take into account duration of infertility, the number of intercourses, the use of contraception, comorbidities in both male and female, childhood diseases, past surgeries, use of medications and stimulants.

During physical examination, one should pay attention to changes in the genital area. When examining scrotum, we determine the size of testes, epididymides; width of spermatic cord vessels; accurately describe deviations in form of bumps, cysts, varicocele, and underdevelopment of the vas deferens. During penile examination, attention should be paid to pathological changes occurring within the outer urethra, foreskin, glans and penile body. We also assess the body structure of patient, the degree of obesity and examine mammary glands.

The hormonal tests necessary during infertility diagnosis are FSH, LH, testosterone, prolactin, TSH and cortisol. Abnormal values of gonadotropins indicate pituitary or hypothalamic condition, high levels of FSH indicate primary spermatogenesis failure. The Leydig cell function is represented by testosterone level (8-12 nmol/L), values below the lower limit of norm indicate hypogonadism. Determination of levels of inhibin B and insulin-like growth factor facilitates diagnosis of infertility [14,15,16].

Semen analysis is one of the basic examinations in the process of diagnosis of infertility. It is performed according to the guidelines of the World Health Organization [Table 1].

Based on the parameters, we can determine the degree of spermatogenesis damage and the cause of infertility. The level of obstruction may be deduced from alpha-glucosidase (secreted by the epididymis), fructose (secreted in seminal vesicles), zinc (secreted in the prostate) [1].

Table. 1 WHO reference values for human semen (2010)	
Parameter	**Reference values**
Volume of ejaculate (ml)	≥ 1.5
Total number of sperm cells (10^6/ejaculate)	≥ 39
Sperm concentration (10^6/ml)	≥ 15
Total sperm motility(%)	≥ 40
Progressive motility of sperm (%)	≥ 32
Live sperm cells(%)	≥ 58
Spermatozoa with normal morphology ± (%)	≥ 4
Time of ejaculate liquefaction	up to 60 min
pH	≥ 7.2
Peroxidase-positive leukocytes (10^6 / ml)	<1
Round cells (10^6 / ml)	<5
Zinc (µmol / ejaculate)	≥ 2.4
Fructose (µmol / ejaculate)	≥ 20 micromoles per ejaculate
neutral α-glucosidase (mU / eaculate)	≥ 13

Ultrasonography is a basic examination of scrotum, that allows detection of abnormalities in form of microcalcifications, tumors, cysts and varicocele. During ultrasound examination we determine size of testes and epididymis, normal testicular volume is 12-15ml, the size of the epididymis head is about 7.5 mm. Varicose veins are presented as numerous anechoic turbulent structures with a tortuous shape, with width exceeding 2.45 mm during rest and 3 mm during the Valsalva maneuver. In order to improve the quality of ultrasound we can use the Doppler option, thanks to which during the Valsalva maneuver we can notice the reversal of blood flow and increased or decreased blood flow in testes and epididymis.

Some patients may present with varicocele caused by tumor located in the retroperitoneal space compressing testicular veins. This applies mainly to the right side, which is why we should perform additional ultrasound of the abdominal cavity in the risk group [12].

Errors while determining the size are up to 15%. Pathologies such as varicocele, microcalcifications, spermatocele and hydrocele within the scrotum are detected in 50% of infertile men.

European Society of Urology guidelines include recommendations of the operative treatment of varicocele. Firstly patients with clinically evident spermatic cord varicose veins, decreased sperm parameters and infertility lasting longer than 2 years were described. Secondly, treatment for inexplicable infertility in couples and for young men with varicocele, who have functional abnormalities and testicular damage was proposed [17].

The classical methods are carried out using the Palomo or Bernardi method. The cut is performed medially from the anterior superior iliac spine, about 5 cm above the deep inguinal ring. After reaching the retroperitoneal space, the vein and the testicular artery are dissected. The Palomo method involves simultaneous ligating and cutting the vein and the testicular artery. The modification of this technique is Bernardi's surgery, which involves saving the testicular artery.

Complications of varicocele surgery include hematoma, bleeding, wound infection and testicular hydrocele, that can occur in 3-5% of patients. Testicular atrophy occurs very rarely, which may be related to the lack of cremaster muscle artery or vas artery [17,18,19]. Presence of varicose veins after surgery or relapse occurs in about 7%.

The microsurgical method is recommended due to the high effectiveness and possibility of saving the artery and lymphatic vessels. The percentage of complications is lower. Relapse or sustaining of the disease

occurs in 0.8-4%, hydrocele in approximately 0.4% of patients. Few institutions perform this surgery in Poland [17,18,19,21] .

Laparoscopic method is performed from transperitoneal access. After formation of pneumoperitoneum and introduction of trocars, we cut the mesentery in the area of the inguinal canal. We dissect the venous vessels of the testis, attach two clips proximally and distally, and then cut. Operation using this method can be performed using one, two or three ports. The effectiveness of the method is approx. 33%, complications in the form of testicular hydrocele- 2.8%, recurrence was observed in approx. 3-7% [17,18,19,20,21,21].

Endovascular methods rely on embolization or sclerotherapy of a testicular vein. During these operations venography is performed to accurately assess the vessels. Procedure is minimally invasive, therefore some centers carry it out on an outpatient basis. Advantage of this method is a short convalescence period. Disadvantages include a high percentage of relapses, about 12%. The effectiveness of spontaneous pregnancies is 33% [17,18,19].

The scrotal access procedure is currently not performed due to the difficult assessment of the number of ligated venous vessels and due to the number of postoperative complications.

Material and methods:

During the period from November 2010 to December 2016, 120 patients underwent surgery in our department due to varicocele. A group of 60 patients was selected and qualified for varicocelectomy surgery due to infertility. A detailed interview was conducted with each patient, including primary disease, concomitant diseases, previous operations, family history and lifestyle.

The patients underwent a physical examination in which the structure of the body, including the genital organs, was assessed. Particular attention was paid to the degree of varicocele, size of testes, epididymis and Valsalva maneuver was performed. Each patient presented at least two results of semen analysis, hormonal and imaging tests.

The results of sperm analysis before and after surgery were compared, early and late postoperative complications were described, medical recommendations and treatment results (changes in semen parameters over time, number of pregnancies finished with birth and time from conception to delivery) were described. Data regarding patients were included in the research protocol, summarized in the form of a table, compared and conclusions were drawn. In addition, the latest publications on the treatment of varicocele of the spermatic cord were analyzed to compare with the results obtained in our department.

Results:

The analysis included data from 120 patients with varicocele, with 60 patients treated for infertility in this group. The average age of patients is 33 years (from 25 to 49 years). Patients were directed for treatment by urologist or gynecologist from specialist outpatient clinics and additional tests and medical documentation were provided to the hospital.

They presented semen analyses, hormonal tests and scrotal ultrasound performed by a radiologist. Pain was reported by 7 out of 60 patients, three admitted, that they smoke cigarettes. Four patients were treated surgically for inguinal hernia, four underwent orchidopexy for cryptorchidism, one was diagnosed with a brain tumor. The average time of trying to conceive was 3 years. The paper does not take into account the female infertility factor due to the insufficient amount of data provided by couples regarding the health status of female partners.

The body structure of the patients did not deviate from the norm, the abdomen was soft, painless without pathological resistance, prostate in the transrectal examination without pathologies. In penile examination without deviations, scrotum with detectable varicocele on the left side, according to the Dubin and Amelar classification, stages II and III. The test was performed in a upright and horizontal position. Soft nodule within the epididymis was found in one of the patients. Valsalva test was positive in all patients.

In the laboratory results, deviations from the norm were not observed, genetic tests and venography were not performed. The scrotal ultrasound confirmed the presence of varicocele. The ultrasound examination was performed in a supine position, the pampiniform plexus of the spermatic cord vessel diameter was measured, the presence of reflux was confirmed (by means of a color Doppler). Then a Valsalva test was carried out, with the diameter measurement of plexus and regurgitation. The width of the pampiniform plexus of the spermatic cord during the study was in the range of 2.4 to 6 mm (average approx. 3.5 mm). In addition, the size of testes and epididymis were assessed. Presence of epididymal cysts was confirmed in one of the patients.

Each patient presented at least two semen analyzes that, in different degrees, deviated from the norm. The average concentration of semen during the first study was 3.7 million/ml, after three months 4.08 million/ml, and after 6 months 6.7 million / ml. The mean total sperm count before surgery was 6.4 million, in third month after surgery 9.1 million and in the sixth month 18.9 million. Sperm pH before surgery and after

surgery remained at a similar level, within 7.9-8.0. Change in morphology: before surgery 7.3%, after surgery in the 3rd month 9.47% and in the 6th month 9.8%. The average volume did not change significantly, before the operation 3.62 ml, in the third month after the operation 3.54 ml, and in the sixth month, 3.9 ml. Progressive motility before surgery was on average 15.7%, improved after surgery: 24.6% in the third month and 28.2% in the 6th month.
Patients underwent laparoscopic varicocelectomy. None of the performed procedures required conversion. Early complications observed in the first day after surgery include pain and bleeding from the wound. Each patient was discharged home after average of four days from admission, in good general condition with the recommendation of a daily wound toilette, dressing changes, removal of stitches after 7-10 days and control visit at the outpatient urological clinic. Semen tests were performed after 3, 6 and 12 months after surgery.

In the group of patients treated for infertility with clinically evident varicocele, there was a statistically significant improvement in the total sperm count, sperm concentration, morphology and sperm motility. There was no statistically significant change in semen volume and pH. In 4 patients, sperm parameters deteriorated. In 64% of patients, semen parameters improved in the third month, and in 70% in the 6th month. A spontaneous pregnancy took place in 30% of couples. Two pregnancies were aborted spontaneously, 16 children were born. The mean time and standard deviation from surgery to conception was equal 7.7 ± 7 months.

Discussion:

Varicocele have an unfavorable effect on the function of the testis, are responsible for elevated pressure, elevated testicular temperature, hypoxia, oxidative stress, which may result in decreased testosterone secretion by Leydig cells and limitation of the secretory function of Sertoli cells. They are the most common cause of primary and secondary infertility, occurring in about 15-20% of the general population. About 15% of sexually active couples are unable to conceive a child and require infertility treatment, while 1/8 couples have difficulties in conceiving the first child, and 1/6 couples in the conception of the second. In 50% of infertile couples, the male has deviated sperm parameters.

Proper diagnostic process is the basis for determining further actions. Doctor performs physical, physical and hormonal examination, at least two semen analyzes and scrotal imaging.

Guidelines of the European Society of Urology recommend the treatment for patients with clinically evident varicocele, decreased sperm parameters, infertility lasting longer than 2 years and infertility of couples inexplicable by other possible causes. The aim of the operation is to reverse the adverse effect of varicocele on the secretory and hormonal function of the testis.

Previous studies have shown, that improvement of semen may occur as early as 3 months after surgery, which corresponds to one spermatogenesis cycle lasting about 64 days. The American Association of Reproductive Medicine published a report showing the improvement of sperm parameters at 3 and 6 months after varicose veins surgery [41]. This is important, especially for older couples trying to conceive. Female factor plays here very important role, because in women over 30 years of age, a significant reduction in ovarian reserve is observed, thus reducing the chance of conception. Women aged 35-38 have a 30% risk that they will not conceive, while women aged 20-25 only 5%.

During the study, a group of 60 patients treated for infertility with clinically evident spermatic veins had an improvement in total sperm count, sperm concentration, sperm morphology and motility. No changes in semen volume and pH were observed. In 4 patients deterioration of sperm parameters was observed. In 64% of patients, semen parameters improved in third month, and in 70% in the 6th month after surgery. A spontaneous pregnancy took place in 30% of couples. Two pregnancies ended with spontaneous abortion, 16 children were born. The mean time and standard deviation from surgery to conception was 7.7 ± 7 months.
The results of our study show a positive effect of surgery on some sperm parameters and fertility of couples, in addition, the treatment increases the chances of conceiving a child. It is therefore a good information for couples struggling with infertility.

In 2011, Baazeem, et. al. published data from a meta-analysis of studies showing the impact of varicocele treatment on sperm parameters and fertility of couples. The results were based on 22, 17 and 5 prospective studies, including prospective randomized and non-randomized studies. A significant effect of treatment of varicoceles on sperm parameters, reduction of oxidative stress, reduction of DNA damage of sperms was noticed, there was no significant effect of treatment on fertility of couples [31].

A randomized trial including 145 patients was published by Abdel-Meguid et.al. in 2011. It shown satisfactory results, improvement in sperm parameters in the treated group and no improvement in the control group (18.1 ± 5.8 versus 32.2 ± 10.6 × 106 sperm / ml, 25.3 ± 12.8 versus 41.0 ± 10 %, and 31.2 ± 4.1 versus 39. ± 4.5% for sperm concentration, motility and morphology, respectively, all $P < 0.0001$) [43].

Another prospective study on a group of 416 men conducted by Karami H. et. al., published in 2016, presented, that in patients with varicocele in stage I and II, sperm concentration, motility and morphology significantly improved in the sixth month after surgery (P <0.05). In patients with stage III varicocele, only sperm concentration (P <0.05) improved, motility and morphology showed no significant changes a year after surgery [33]. [33].

The patient groups presented in the above mentioned studies are considerably heterogeneous. They present positive effect of treatment of varicocele on sperm parameters: concentration, total number and progressive motility. Effect on fertility is not clear, the analyses differ from each other, therefore there is a need for further randomized trials on larger groups of patients

Conclusions:

Varicocele may have an adverse effect on the hormonal and spermatogenic function of the testicles. They may cause decrease in sperm parameters, and thus may contribute to male infertility. Both the data contained in our study and the data presented in recent clinical trials and RTC mata-analysis demonstrate the beneficial effect of treatment of patients with clinically evident varicocele and decreased sperm parameters, bring hope to couples struggling with infertility and increase the likelihood of conceiving a child.

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