ISSN 2664-3987 (Print) & ISSN 2664-6722 (Online)
South Asian Research Journal of Medical Sciences
Abbreviated Key Title: South Asian Res J Med Sci

| Volume-1 | Issue-1| Jun-Jul -2019 |

Original Research Article

The effect of surgical method on sperm parameters and pregnancy outcomes in primary infertile male patients who underwent varicocelectomy

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Article History
Received: 25.06.2019
Accepted: 14.07.2019
Published: 30.07.2019

Abstract: ***Background/aim:*** The purpose of the present study was to review the effect of varicocelectomy on semen parameters and spontaneous pregnancy in infertile men. ***Materials and methods:*** Data regarding 227 patients who underwent varicocelectomy were analyzed. Patients that was used a loop magnifier were labeled as group I(n=90), patients whom was used a microscope were labeled as group II(n=90) and patients who underwent open ligation were labeled as group III(n=47). Semen parameters and spontaneous pregnancy were compared between the groups. ***Results:*** The average age was 28.5 years. Preoperative azoospermia, oligospermia and normospermia were 13.3%, 52.2% and 34.4% in group I, 22.2%, 36.7% and 41.1% in group II, 6.4%, 48.9% and 44.7% in group III, respectively. Postoperative azoospermia, oligospermia and normospermia were 1.1%, 46.7% and 52.2% in group II, respectively($p<0.05$). Postoperatively, oligospermia and normospermia were 50% and 50% in group I, 42.6% and 57.4% in group III, respectivly($p<0.05$). Postoperative azoospermia were not observed in any of the patients in group I and grup III. Preoperative concentration was $12X10^6$/mL in group I, $12,9X10^6$/mL in group II, and $13X10^6$/mL in group III, postoperative concentration were $16,5X10^6$/mL, $27,5X10^6$/mL and $23X10^6$/mL in group I, group II and group III, respectively($p>0.05$). Preoperative morphology were 26.7% in group I, 33% in group II and 25.5% in group III, postoperative morphology were 58.9%, 75.6% and 76.6% in group I, group II and group III, respectively($p<0.05$). Preoperative sperm A was 19.9% in group I, 8.3% in group II, 21.3% in group III, postoperative sperm A was 32%, 21.1% and 33.7% in all groups, respectively($p<0.05$). Preoperative sperm A+B was 42.1% in group I, 14.2% in group II, 45.1% in group III, postoperative sperm A+B was 52.3%, 45.2% and 55.9% in all groups, respectively($p<0.05$). Spontaneous pregnancy was 37.8% in group I, 26.7% in group II and 38.3% in group III($p>0.05$). ***Conclusions:*** Improvement in semen parameters were found significant in microsurgery groups. While the concentration was insignificant in the open ligation group, spontaneous pregnancy was similar in groups.

Keywords: Male infertility, loupe magnifier, microscope, open ligation varicocelectomy

INTRODUCTION

The varicocele is defined as dilatation of the veins in the pampiniform plexus draining the testicles. Its prevalence is 15% in the general population and 40% in the infertile men [1]. The definitive treatment of varicocele is the surgical ligation of the veins. Currently, vein ligation involves laparoscopic, robotic, radiological and open surgical methods. Open surgical methods include high ligation (Palomo), macroscopic (Ivanissevich), subinguinal ligation (Marmar), non-microscopic subinguinal ligation (Marmar/modified Marmar), subinguinal loop varicocelectomy and microscopic varicocelectomy [2, 3]. Although the choice of a wide range of surgical options makes selection difficult, cost-efficiency, short recovery period, acceptable levels of complications, as well as advanced semen quality and spontaneous pregnancy rates are decisive. Microsurgical varicocelectomy procedure continues to be the gold standard with low complication rates, best results in postoperative semen parameters and high pregnancy rates. Surgical microscope and loupe magnifier are used as a magnifier in microsurgical varicocelectomy. Surgical microscope used in microscopic varicocelectomy has several disadvantages. These instruments are expensive, bulky and occupy too much space in the operating room, require experience and personal skills. On the other hand, loupe magnifier used in loop-assisted varicocelectomy is lightweight, can be used as eyeglasses, requires no training process and is cheaper. All these advantages make this device more attractive [4]. As a result, loupe magnifier can be an option in microsurgical varicocelectomy. In this study, we aimed to discuss the effect of open surgical

varicocelectomy, microscopic varicocelectomy and loop varicocelectomy on semen parameters and spontaneous pregnancy outcomes in the light of scientific data.

MATERIAL AND METHODS

The data of 601 patients who underwent varicocelectomy between 2009 and 2018 were analyzed retrospectively. Primary infertile 227 patients who had bilateral varicocelectomy and whose data were complete and who had informed consent were included in the study.

Enrollment criteria for the study included primary infertile patients (patients who had no children), patients with grade II and grade III varicocele on physical examination, patients with at least two semen analysis performed at 2-week intervals and with pathology in the semen parameters, patients with normal levels of serum FSH (1.7-12 ml/mL), LH (1.1-7 mlu/mL) and Testosterone (251-366 ng/dL), patients with normal physical examination findings and normal or near normal testicular size in scrotal color Doppler ultrasound. Varicocele was diagnosed by physical examination.Patients with chronic scrotal and testicular pain, patients with testicular mass, patients with recurrent varicocele and secondary infertile patients and subclinical varicoceles in scrotal color Doppler ultrasound were among the exclusion criteria.

Scrotal color Doppler ultrasound was used in patients who could not undergo an adequate physical examination due to obesity, short and/or hyperreflexic spermatic cord which becloud the diagnosis of varicocele.Physical examination was performed on the standing position and palpated veins without valsalva maneuver were classified as grade II varicocele and varicocele with visible venous sac was classified as grade III varicocele.

Semen analysis of the patients were repeated according to the latest World Health Organization (WHO) human semen analysis guidelines, two analysis results performed after 3-5 days of abstinence period at an interval of minimum 15 days were taken into consideration. After liquefaction, semen was analyzed for concentration, motility, and morphology. Makler chamber was used in assessment of the concentration and motility. Sperm concentration in semen analysis (values of 15 million/mL and above: normospermia; below 15 million/mL: oligospermia), sperm A (fast progressive motile [32% or more]) sperm A + B (fast progressive motile and nonprogressive motile [40% and above]) and morphology (4% and above) were analyzed [20].Surgical procedure was performed in patients who had an abnormality in at least one of the semen analysis parameters and who had bilateral varicocele.

Surgical procedures were performed under spinal or general anesthesia. Spermatic chord was reached with a subinguinal incision, using a loupe magnifier as a magnifying glass (42 cm / 1600; Keeler Ltd, West Berkshire, UK) and a microscope (VARIO 700; Carl Zeiss Meditec AG, Jena, Germany). Surgical procedures were performed at 3 X magnification with loupe magnifier and at 10 X magnification with microscope. In the open varicocelectomy method, the spermatic chord was reached with a subinguinal incision and the procedure was performed without the use of a magnifying glass.

Patients who underwent varicocelectomy in which a loupe magnifier was used during the surgical procedure were classified as Group I (n = 90); those who underwent varicocelectomy in which a microscope was used were classified as group II (n = 90), and patients who underwent open varicocelectomy were classified as group III (n = 47). Semen analysis results and spontaneous pregnancy rates were compared in the postoperative period with regard to semen analysis at 6th month and pregnancy status of the couples in the first year.

Statistical Analysis

Statistical analyzes were performed with MedCalc software (MedCalc Software, Broekstraat, Mariakerke, Belgium). The normal distribution of continuous variables was investigated by Kolmogorov-Smirnov test. Variables exhibiting Gaussian distribution were shown as mean ± SD and those showing non-Gaussian distribution were shown as median (25th percentile-75th percentile). Paired-samples t-test or Wilcoxonsigned-rank test was applied to compare the central tendency criteria of the variables between the two dependent groups. McNemar or marginal homogeneity test was used to compare the ratios of the dependent groups and Pearson's chi-square test was used to compare the ratios between the independent groups. Statistical significance was assessed at $p < 0.05$ (two-tailed).

RESULTS

The mean age of the patients was 28.5 (18-42) years. Postoperative azoospermia was not observed in any of the patients in Group I. In Group II, azoospermia was observed in 20 (22.2%) patients before surgery and in 1 (1.1%) patient after surgery. In Group III, the number of patients with preoperative azoospermia was 3 (6.4%) and azoospermia was not observed in any patient postoperatively ($p < 0.0001$). The number of oligospermic patients was 47 (52.2%) in Group I in the preoperative period and 45 (50%) in the postoperative period. In Group II, the number of patients with preoperative oligospermia was 33 (36.7%) and 42 (46.7%) postoperatively. In Group III, the number of patients with preoperative oligospermia was 23 (48.9%) and 20 (42.6%) postoperatively ($p < 0.0001$). The number of patients with normospermia was 31 (34.4%) in group I in the preoperative and 45 (50%) in the postoperative period. In Group II, the number of normospermic patients was 37 (41.1%) patients in the preoperative period and 47 (52.2%) in the

postoperative period. In Group III, these numbers were 21 (44.7%) and 27 (57.4%), respectively ($p < 0.0001$). Although the rates of improvement in azoospermic, oligospermic and normospermic patients were found to be statistically significant in all three groups, the improvement in group I and group II were higher than in group III patients.

Preoperative sperm concentration was 12.0 X 10^6/mL and 16.5 X 10^6/mL in postoperative period in group I ($p < 0.0001$). These values were 12.9 X 10^6/mL and 27.5 X 10^6/mL in group II ($p < 0.0001$). In group III, preoperative sperm concentration was 13 X 10^6/mL and 23.0 X 10^6/mL postoperatively ($p = 0.0623$). The number of patients with improvement in sperm concentration was significantly higher in group I and group II, but this improvement was not statistically significant in group III.
The number of patients with normal sperm morphology was 24 (26.7%) in Group I, 30 (33%) in Group II and 12 (25.5%) in Group III before surgery. The number of patients with normal sperm morphology in the postoperative period was 53 (58.9%), 68 (75.6%) and 36 (76.6%), respectively ($p < 0.0001$). The improvement in sperm morphology was statistically significant in all three groups.

Preoperative sperm A ratio was 19.9% in group I, 8.3% in group II, 21.3% in group III, while in the postoperative period, it was 32%, 21.1% and 33.7% respectively. Preoperative sperm A + B ratio was 42.1% in group I, 14.2% in group II and 45.1% in group III, while in the postoperative period, it was 52.3%, 45.2% and 55.9%, respectively ($p < 0.0001$). **(Table-1)** Sperm A and sperm A + B improvement rates were statistically significant in all three groups.

Spontaneous pregnancy occurred in 34 (37.8%) in group I, 24 (26.7%) in group II and 18 (38.3%) in group III ($p = 0,2111$). However, these results were not statistically significant in any of the groups. (**Table-2**)

Table-1: Changes in preoperative and postoperative semen parameters in the groups.

		Preoperative semen parameters	**Postoperative semen parameters**	**p**
Group I (n=90)	Azoospermia (n, %) Oligospermia (n, %) Normospermie (n, %)	12 (%13,3) 47 (%52,2) 31 (%34,4)	0 (%0) 45 (%50) 45 (%50)	**< 0,0001**[b]
	Concentration (10^6xmL)	12,0 (7,0-27,8)	16,5 (12,0-60,0)	**< 0,0001**[d]
	Morphology (n, %)	24 (%26,7)	53 (%58,9)	**< 0,0001**[a]
	Sperm A (%) Sperm A+B (%)	19,9±11,9 42,1±19,2	32,0±13,4 52,3±16,4	**< 0,0001**[c] **< 0,0001**[c]
Group II (n=90)	Azoospermia (n, %) Oligospermia (n, %) Normospermie (n, %)	20 (%22,2) 33 (%36,7) 37 (%41,1)	1 (%1,1) 42 (%46,7) 47 (%52,2)	**< 0,0001**[b]
	Concentration (10^6xmL)	12,9 (1,6-39,8)	27,5 (10,8-66,3)	**< 0,0001**[d]
	Morphology (n, %)	30 (%33)	68 (%75,6)	**< 0,0001**[a]
	Sperm A (%) Sperm A+B (%)	8,3±12,3 14,2±17,0	21,1±13,0 45,2±16,9	**< 0,0001**[c] **< 0,0001**[c]
Group III (n=47)	Azoospermia (n, %) Oligospermia (n, %) Normospermie (n, %)	3 (%6,4) 23 (%48,9) 21 (%44,7)	0 (%0) 20 (%42,6) 27 (%57,4)	**= 0,0290**[b]
	Concentration (10^6xmL)	13,0 (11,0-56,0)	23,0 (14,0-48,0)	= 0,0623[d]
	Morphology (n, %)	12 (%25,5)	36 (%76,6)	**< 0,0001**[a]
	Sperm A (%) Sperm A+B (%)	21,3±8,4 45,1±12,8	33,7±12,4 55,9±14,6	**< 0,0001**[c] **< 0,0001**[c]

*Morphology is defined according to the normal forms over 4% (Kruger's)
[a]The p value obtained by the McNemar test
[b]The p value obtained by marginal homogeneity test
[c]The p value obtained with T test paired-sample

Table-2: Postoperative pregnancy percentages of the groups

	Group I (n=90)	**Group II (n=90)**	**Group III (n=47)**	**p***
Spontaneous pregnancy (n, %)	34 (%37,8)	24 (%26,7)	18 (%38,3)	= 0,2111

*P value obtained by Pearson's chi-square test

DISCUSSION

Varicocele is an abnormal enlargement of the veins in the spermatic cord and the formation of a tortuous appearance [5]. Varicocelectomy is the only treatment for grade II and grade III varicocele. Laparoscopic, robotic, radiological methods, as well as high ligation (Palomo), macroscopic (Ivanissevich) ligation, subinguinal ligation (Marmar), microsurgical varicocelectomy methods, have taken place among the surgical options [6]. The choice of these methods is determined by the cost-effectiveness, low complication rates, short recovery period, maximum improvement in semen parameters and a significant increase in spontaneous pregnancy rates. Currently, varicocelectomy with open surgical method remains the gold standard in treatment [4, 6]. In many metaanalyses, microscopic varicocelectomy is the best method to improve semen parameters and spontaneous pregnancy rates [4, 7]. In a meta-analysis of Çayan *et al.* [8] comparing surgical methods and complications in varicocelectomy conducted in 2009, spontaneous pregnancy rates were higher in microsurgical varicocelectomy (41.9%) ($p = 0.001$). In the microsurgical subinguinal varicocelectomy technique performed in 2001, Testini *et al.* [9] found 80% improvement in semen quality and a spontaneous pregnancy rate of 46.3%. In their recent study, Chovelidze *et al.* [10] reported a 53% improvement in sperm concentration in subinguinal microsurgical varicocelectomy. Again, in a prospective, randomized, controlled study of Zucchi *et al*. [11] comparing open varicocelectomy and radiological sclerotherapy, an increase in progressive motile spermatozoa and a decrease in immotile spermatozoa ratios were found to be significant in the sclerotherapy group, however, the sperm concentration and morphology improvement rates were insignificant. In their most recent study, Al-Said *et al*. [12] compared open, laparoscopic and microsurgical varicocelectomy; the rates of improvement in sperm concentration, motility and morphology were found to be significant in all three groups, however, the improvement in sperm concentration and motility rates in the microsurgical varicocelectomy group were more significant. In their study comparing open, laparoscopic and microscopic varicocelectomy methods, Al-Kandari *et al*. [13] reported improvement in sperm motility and concentration in 65%, 67% and 76%, respectively. In the same study, the rate of pregnancy was 28% in the open varicocelectomy group, 30% in the laparoscopic group and 40% in the microscopic varicocelectomy group ($p < 0.05$).

Although the improvements in semen parameters and the increase in spontaneous pregnancy rates are significant advantages in microscopic varicocelectomy technique, its disadvantages include longer length of the operation time, high cost of the surgical microscope and requirement of the surgical skills and experience [14]. Up to now, studies on loupe-assisted varicocelectomy technique are limited. Hsieh *et al.* [15] reported that patients with subfertile varicocelectomy had a significant improvement in sperm motility and concentration and suggested that this technique can be used as a simple, easy to apply and effective method in clinics where a surgical microscope is not available. Again, Abdelrahman *et al.* [16] reported that they achieved more significant improvement in the concentration and motility with the loupe varicocelectomy compared to the non-microscopic varicocelectomy group. In another study, in which the results of loupe-assisted varicocelectomy were shared, the increase in motility was reported to be 46% and the mean sperm concentration was 17 X 10^6/mL (24 – 41 X 10^6/mL) [17]. In another study in which the results of microscopic varicocelectomy were reported, the rate of pregnancy was 55%, improvement in sperm concentration was 22%, motile A + B was 59%, and normal morphology ratio was 51% [18]. In their recent studies comparing the rates of loop varicocelectomy and microscopic varicocelectomy, Mohammad *et al*. [19] have emphasized that the complication rates were similar but the microscopic varicocelectomy technique was more expensive. In this study, we found a significant improvement in sperm A and sperm A + B parameters as well as in azoospermia, oligospermia, normospermia and normal morphology for all three groups. The improvement in concentration was 16.5 X 10^6/mL in the loupe-assisted varicocelectomy group, 27.5 X 10^6/mL in the microscopic varicocelectomy group and 23 X 10^6/mL in the open varicocelectomy group; however, the results were statistically insignificant in the open varicocelectomy group. Spontaneous pregnancy rates were 37.8% in the loupe-assisted varicocelectomy group, 26.7% in the microscopic varicocelectomy group, and 38.3% in the open varicocelectomy group ($p > 0.05$). The improvement in pregnancy rates was higher in the loupe-assisted varicocelectomy group.

CONCLUSION:

Loop magnifier-assisted varicocelectomy and microscopic varicocelectomy methods had a positive effect on semen parameters and spontaneous pregnancy results. The improvement in sperm concentration rates in the open varicocelectomy method was insignificant. Loupe magnifier-assisted varicocelectomy can be performed safely in clinics in which surgical microscopy is not available.

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