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Progressive Sperm Motility, Sperm Condensation and Spontaneous Pregnancy Rate in Infertile Varicocele Patients at 3-12 Months after Varicocelectomy

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Abstract: To evaluate the effect of varicocele repair on sperm motility, sperm condensation and pregnancy rate in varicocele patients who referred to Department of Urology of Golestan and Apadana hospitals. The records were retrospectively evaluated for infertile patients with palpable varicocele who underwent varicocelectomy at Department of Urology of Golestan and Apadana Hospitals, Ahwaz, Iran from December 1990 to September 2008. The semen analysis of patient at pre-operatives and 3, 6 and 12 months post-operative and also pregnancy rate was calculated at 3, 6 and 12 months of follow-up. Before operation, no significant differences were seen among patients with right and left varicocele in sperm motility and condensation ($p>0.05$). Significant differences were seen in sperm motility and condensation of patients with bilateral varicocele compared to another patients ($p<0.05$). After surgery in three groups of patients with varicocele, the sperm motility and condensation significantly increased ($p<0.05$). Percentage of spontaneous pregnancy in 1 year after varicocele treatment is 31 to 40% of cases. The results of present study have shown that repair of varicocele by surgery significantly improved sperm motility, condensation and also 31-40% of infertile patients achieved pregnancy spontaneously.

Key words: Varicocelectomy, fertilization, sperm analysis, repair, Apadana hospital

INTRODUCTION

Varicocele is a dilation of internal spermatic veins that drain the testicle (Kadyrov *et al*., 2007). It is very common condition present in 15% of the general male population and 40% of men evaluated for infertility (Naughton *et al*., 2001). A varicocele develops because of defective valves that normally allow for blood to flow away from the testicle toward the abdomen (Ahlberg *et al*., 1996). Testicular injury occurs due to abnormal back flow of blood from the abdomen into the scrotom and this create a hostile environment for sperm development (Sepal *et al*., 1981). A unilateral varicocele may affect both testicles (Jarow, 2001). The most probable explanation for the more frequent development of a varicocele on the left side alone is because the left spermatic vein is longer than the right (Gray, 2005). The left vein enter the left renal vein at a right angle near a site of compression by the mesenteric artery while the right spermatic vein drains at a softer angle into the vena cava. These anatomical factors promote back flow of blood in the left spermatic vein, resulting in pooling of blood and increased temperature and congestion in the testicle (Tam, 2004; Sigman and Jarow, 1997). The diagnosis of varicocele can usually be made on physical examination of the scrotom while the patient is standing. The varicocele feels like a bag of worms and disappears or becomes significantly reduced when the patient lies down (Hargreave *et al*., 1991). Repair of the varicocele is indicated when the couple has documented infertility with normal or potentially normal female partner but a male with one or more abnormal semen parameters and the presence of varicocele on physical exam and also when a varicocele causes testicular pain or discomfort or there is a significant discrepancy between the sizes of two testicles (Ishikawa and Fujisawa, 2005). The important sperm functions are impaired in patients with varicocele (El-Segini *et al*., 2002).

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The improvement of seminal parameters after varicocele correction has been reported by several investigators in clinical series (Libman *et al*., 2006; Pasqualotto *et al*., 2005; Gat *et al*., 2005; Grober *et al*., 2004). Furthermore some researches suggest that varicocelectomy can improve human sperm DNA integrity in infertile men with varicocele (Niederberger, 2005; Zini *et al*., 2005). Non randomized comparative studies (Reichart *et al*., 2000; Perimenis *et al*., 2001; Onozawa *et al*., 2002) and randomized clinical trials (Madgar *et al*., 1995; Nieschlag *et al*., 1998). More controversies exist concerning the role of varicocele treatment to obtain pregnancy in infertile couples (Evers *et al*., 2004; Ficarra *et al*., 2006). The aim of this study was to evaluate the effect of varicocelectomy on sperm motility, sperm condensation and pregnancy rate.

MATERIALS AND METHODS

This retrospective cross-sectional study included infertile patients with palpable varicocele who underwent varicocelectomy at Department of Urology of Golestan and Apadana Hospitals, Ahwaz, Iran from December 1990 to September 2008. This study was reviewed and approved by the Institutional Ethics Committee of Ahwaz Jondishapour University of Medical Sciences. All patients provided informed consent. The Mean±SD patients age was 30.4±6.9 years (rang 16-40 years). Pre-operative evaluations included a complete history, physical examination and semen analysis. The presence of varicocele was diagnosed on the basis of venous diameter of greater than 3 mm, with increasing diameter during Valsalva maneuvers or when changing from supine to upright with scrotal gray-scale ultrasonography (McClure *et al*., 1991). Increased venous retrograde flow in the pampiniform plexus in the upright position, or during the Valsalva maneuver was used as a supporting sign of the presence of varicocele (Petros *et al*., 1991). The varicocele diagnosis was assigned according to World Health Organization (World Health Organization, 1993). Varicocele was graded as:

- **Grade I:** A distinct dilation of the internal spermatic veins palpable during a Valsalva maneuver when upright
- **Grade II:** A palpable vein when upright with no Valsalva maneuver or
- **Grade III:** A vein both palpable and visible through the scrotal skin when upright with no Valsalva maneuver

We excluded patient who were <16 or >40 years old, single patients, patients with sub-clinical and grade one varicocele, patients with normal semen analysis and patients with further pathologies that were associated to varicocele and potentially were responsible for an alteration of semen analysis. In all patients, pre-operative semen analysis were performed using two different semen specimens (the higher value was adopted), each obtained by masturbation and at least 3 weeks pre-operatively and 3,6 and 12 months after varicocele treatment according to the World Health Organization recommendation (1992a). Specifically, the abstinence period was 2-3 days in all cases. Preoperative evaluation included the execution of two semen analysis. The interval between the two sample collections had to be >7 days or <3 weeks. The spontaneous pregnancy rate was calculated at 3, 6 and 12 months after varicocelectomy.

Statistical analysis: The Chi-square and ANOVA were used as appreciated for comparisons sperm motility and sperm count before and after treatment of varicocele. The p-value less that 0.05 considered as significant difference. All computations were performed using the Statistical Package for the Social Sciences (SPSS-PC1for Windows; SPSS; Chicago, IL).

RESULTS

During this study the records of 1290 infertile men with varicocele who referred to Urology Department of Golestan and Apadana hospitals in Ahwaz, Iran were evaluated. The median age of patients was 30.4±6.9 years (rang 16-40 years). The varicocele was located on the right side in 144 (11.16%) cases, on the left side in 1083 (83.95%) and bilaterally in 63 (4.88%). The median value of the percentage of progressive motile sperm was 30.12, 28.83 and 19.53 in patient with varicocele located in right, left and bilateral side respectively (Table 1). Statistical analysis show that the progress sperm motility difference in patient with unilateral varicocele was not significant ($p>0.05$) but difference between patient with bilaterally varicocele and patients with unilateral varicocele was significant ($p<0.05$). Median sperm condensation as 16.15, 13.63 and 9.52 in patient with varicocele located in right, left and bilateral side, respectively. Statistical analysis show that sperm condensation in patient with bilateral

Table 1: Progressive sperm motility in varicocele patients

Varicocele side	No. of patients	Progressive motile sperm (%)	Sperm condensation (10^6 mL^{-1})
Right	144.0(11.16%)	30.12±1.65	16.15±3.25
Left	1083.0(83.95%)	28.83±1.32	13.63±1.25
Bilateral	63.0(4.88%)	19.53±1.01	9.52±2.12
Total	1290.0	27.49±1.32	13.07±2.20

Data are expressed as Mean±SD

Table 2: Sperm motility after 3-12 months after varicocelectomy

Varicocele side	No. of patients	Months 3	6	12
Right	105 (9.09%)	45.11±1.99	56.16±1.01	55.33±1.69
Left	998 (86.40%)	40.16±3.12	47.17±1.09	51.31±0.09
Bilateral	52 (4.50%)	25.03±1.66	29.09±1.36	47.12±2.08
Total	1155	36.76±2.25	44.14±1.15	51.25±1.28

Data are expressed as Median±SD

Table 3: Sperm condensation 3-12 months after varicocelectomy

Varicocele side	No. of patients	Months (10^6 mL^{-1}) 3	6	12
Right	105 (9.09%)	20.75±3.25	28.03±1.99	40.13±1.96
Left	998 (86.40%)	15.33±3.17	25.96±3.12	30.63±1.69
Bilateral	52 (4.50%)	12.13±2.08	13.46±0.81	16.12±3.99
Total	1155	22. 73±2.83	22.48±1.97	28.96±2.54

Data are expressed as Mean±SD

varicocele significantly low in compare with another patients ($p<0.05$). The sperm condensation in two groups of patients with varicocele in left and right was not difference ($p>0.05$).

As shown in Table 2 and 3; 39,105 and 11 patients were excluded from patients with right, left and bilateral varicocele group, respectively. The remaining 105 (9.09%) patients with right side varicocele, 998 (86.04%) patient with left side varicocele and 52 (4.50%) patients with bilateral varicocele met the study inclusion criteria.

The median value of the percentage of progressive motile sperm in patients with right side varicocele was 45.11, 56.16 and 55.33, respectively in 3, 6 and 12 months after varicocelectomy. This data show that after varicocelectomy the percentage of progressive motile sperm improved after repair of varicocele. Significant differences were seen in 6 and 12 months compared to 3 months after varicocelectomy ($p<0.05$). The difference between 6 and 12 months after surgery was not significant ($p>0.05$). Sperm condensation in patients with right side of varicocele at 3, 6 and 12 months after surgery was 20.75, 28.03 and 40.13 million mL^{-1}, respectively and improved sperm concentration was seen after surgery. The sperm condensation at 12 months after repair of varicocele was significantly high ($p<0.05$). The median value of the percentage of progressive motile sperm and sperm condensation in patients with left side varicocele significantly improved after varicocelectomy and at 12 months after varicocelectomy were significantly high ($p<0.05$) as same as in patient with bilateral varicocele highest sperm motility and condensation achieved at 12 months after surgery.

In this study 17, 105 and 17 patients were excluded from patients with right, left and bilateral varicocele group, respectively. The remaining 88 (9.60%) patients with right side varicocele, 793 (86.57%) patient with left side varicocele and 17 (3.82%) patients with bilateral varicocele met the study inclusion criteria. The fertilization rate in patient with varicocele at 3-12 months after repair of surgery was 40.90, 40.85 and 31.42%, respectively (Table 4). The difference between different type of varicocele was not significant ($p>0.05$).

Table 4: Percentage of spontaneous pregnancies 3-12 months after varicocelectomy

Varicocele side	No. of patients	Months 3	6	12	Total
Right	88 (9.60%)	8 (9.09%)	13 (14.77%)	15 (17.04%)	36(40.90%)
Left	793 (86.57%)	88(11.09%)	126(15.88%)	110(13.87%)	324(40.85%)
Bilateral	35 (3.82%)	2(5.71%)	4(11.42%)	5(14.28%)	11(31.42%)
Total	916	98 (8.41%)	143(15.61%)	130(14.19%)	371(40.50%)

DISCUSSION

Varicocele affects fertility and is the most common known cause of infertility (Konodo *et al*., 2009). Various mechanisms have been suggested to account for the testicular dysfunction associated with varicoceles, including retrograde flow of toxic metabolites from the adrenal gland or kidney, venous stasis with germinal epithelial hypoxia, alteration in the hypothalamic-pituitary-gonadal axis and increases in testicular temperature (Takihara *et al*., 1991). In addition, deregulations of nitric oxide (Miropoulos *et al*., 1996), reactive oxygen species (Sharma and Agarwal, 1996) and regulators of apoptosis (Fazilioglu *et al*., 2008) have been implicated in the pathophysiology of varicoceles. The results of the present study demonstrate that the repair of varicocele by surgery cause highly significant improvement of progressive motility in sperm and as same as condensation. Nasr-Esfahani *et al*. (2007) in a study show that all the three semen parameters and percentage of sperms with normal protamine content have improved post-surgery so that they suggested that patients with low initial sperm count may benefit more from assisted reproductive techniques or varicocelectomy followed by assisted reproduction. The vast majority of physicians who manage male infertility patients believed that varicoceles are a major cause of male infertility and that repair of varicocele will improve fertility (World Health Organization, 1992b). Some controversial researches are whether or not varicoceles should be repaired prophylactically to prevent future infertility and whether varicocele size has prognostic significance. Interestingly, the results of this research show that the choice of varicocele to improve the fertility and pregnancy may be better. The latter issue has a major impact upon deciding whether or not sub-clinical (non-palpable) varicoceles should be diagnosed and

repaired. However, there are many clinicians who are not convinced that varicocele repair improves male fertility (Kamischke and Nieschlag, 1999). Evers *et al.* (2009) claimed that no evidence that treatment of varicoceles in men from couples with otherwise unexplained subfertility improves the couple's chance of conception, interestingly the data of this study show that in patients with varicocele 1 year after varicocele treatment, the percentage of spontaneous pregnancies accounts for 31-40% of cases. This data is similar to earlier study by Schlegel (1997). This study has documented reduced sperm motility and condensation in men with bilateral varicoceles as compared with unilateral varicocele men.

In conclusion based upon the current data available several conclusions maybe reached. First, there is very strong evidence to support the fact that, as observed for centuries, varicoceles exert a deleterious effect upon the sperm motility and condensation. This effect appears to be bilateral, even in men with unilateral Varicoceles. Second, repair of varicocele improved the sperm motility and condensation. Third, 31-40% of infertile patients one year after varicocele treatment achieved pregnancy. Finally, the varicocele surgery may be the correct choice to enhance the chance of the fertility and pregnancy.

REFERENCES

Ahlberg, N.E., O. Bartley and N. Chidekel, 1996. Right and left gonadal veins: An anatomic and statistical study. Acta. Radiol. Diagn. (Stokh), 4: 593-601.

El-Segini, Y., W.B. Schill, F.M. Köhn, S.A. Zeid, A.A. Kamshushy and S. Marzouk, 2002. Assessment of sperm functions in infertile patients with varicoceles. Andrologia, 34: 291-295.

Evers, J.L.H., J.A. Collins and P. Andekerckhove, 2004. Surgery of embolization for varicocele in subfertile men. Cochrane Database Syst. Rev., 3: CD000479-CD000479.

Evers, J.H., J. Collins and J. Clarke, 2009. Surgery or embolization for varicoceles in subfertile men. Cochrane Database Syst. Rev., 21: CD000479-CD000479.

Fazilioglu, A., I. Yilmaz, O. Mete, F. Kurtulus, O. Parlakkilic, O. Guctas and M. Cek, 2008. The effect of varicocele repair on experimental varicocele induced testicular germ cell apoptosis. J. Androl., 29: 29-34.

Ficarra, V., M.A. Cerruto, G. Liguori, G. Mazzoni, S. Minucci and A. Tracia, 2006. Treatment of varicocele in subfertile men: The cochrane review a contrary opinion. Eur. Urol., 49: 258-263.

Gat, Y., G.N. Bachar, K. Everaert, U. Levinger and M. Gornish, 2005. Induction of spermatogenesis in azoospermic men after internal spermatic vein embolization for the treatment of varicocele. Hum. Reprod., 20: 1013-1017.

Gray, H., 2005. Gray's Anatomy. 39th Edn., Churchill Livingstone, Edinburgh, ISBN: 0-443-06676-0.

Grober, E.D., J. O'brien, K.A. Jarvi and A. Zini, 2004. Preservation of testicular arteries during subinguinal microsurgical varicocelectomy: Clinical considerations. J. Androl., 25: 740-743.

Hargreave, T.B. and J. Liakatas, 1991. Physical examination for varicocele. Br. J. Urol., 67: 328-328.

Ishikawa, T. and M. Fujisawa, 2005. Effect of age and grade on surgery for patients with varicocele. Urology, 65: 768-772.

Jarow, J.P., 2001. Effect of varicocele on male fertility. Hum. Reprod. Update, 7: 59-64.

Kadyrov, Z.A., K.S. Ishonakov, N.A. Svitskii, O.O. Zokirov and N.O. Muminov, 2007. Videoendoscopic ligation of the internal seminal veins in bilateral varicocele. Urologiia, 4: 54-59.

Kamischke, A. and E. Nieschlag, 1999. Analysis of medical treatment of male infertility. Hum Reprod., 14: 1-32.

Konodo, Y., T. Ishikawa, K. Yanagimashi and M. Fujisawa, 2009. Predictors of impair seminal characteristics by varicocele repair. Andrologia, 41: 20-23.

Libman, J., K. Jarvi, K. Lo and A. Zini, 2006. Beneficial effect of microsurgical varicocelectomy is superior for men with bilateral versus unilateral repair. J. Urol., 176: 2602-2605.

Madgar, I., R. Weissenberg, B. Lunenfeld, A. Karasik and B. Goldwasser, 1995. Controlled trial of high spermatic vein ligation for varicocele in infertile men. Fertil. Steril., 63: 120-124.

McClure, R.D., D. Khoo and K. Jarvi, 1991. Subclinical varicocele: The effectiveness of varicocelectomy. Urology, 145: 789-791.

Miropoulos, D., G. Deliconstntinos and A. Zervas, 1996. Nitric oxide synthase and xanthine oxidase activities in the spermatic vein of patients with varicocele: A potential role for nitric oxide and peroxinitric in sperm dysfunction. J. Urol., 156: 1952-1958.

Nasr-Esfahani, M.H., H. Abasi, S. Razavi, S. Ashrafi and M. Tavalaee, 2009. Varicocelectomy: Semen parameters and protamine deficiency. Int. J. Androl., 32: 115-122.

Naughton, C.K., A.K. Nangia and A. Agarwal, 2001. Pathophysiology of varicoceles in male infertility. Hum. Reprod. Update, 7: 473-481.

Niederberger, C., 2005. Beneficial effect of microsurgical varicocelectomy on human sperm DNA integrity. J. Urol., 174: 1943-1943.

Nieschlag, E., L. Hertle, A. Fischedick, K. Abshagen and H.M. Behre, 1988. Update on treatment of varicocele: Counseling as effective as occlusion of the vena spermatica. Hum. Reprod., 13: 2147-2150.

Onozawa, M., F. Endo, T. Suetomi, H. Takeshima and H. Akaza, 2002. Clinical study of varicocele: Statistical analysis and the results of long-term follow-up. Int. J. Urol., 9: 455-461.

Pasqualotto, F.F., A.M. Lucon, P.M. de Goes, J. Hallak, B. Sobreiro and E.B. Pasqualotto, 2005. Testicular growth, sperm concentration, percent motility and pregnancy outcome after varicocelectomy based on testicular histology. Fertil. Steril., 83: 362-366.

Perimenis, P., S. Markou, K. Gyftopoulos, A. Athanasopoulos and G. Barbalias, 2001. Effect of subinguinal varicocelectomy on sperm parameters and pregnancy rate: A two-group study. Eur. Urol., 39: 322-325.

Petros, J.A., G.L. Andriole and W.D. Middleton, 1991. Correlation of testicular color doppler ultrasonography, physical examination and venography in the detection of left varicoceles in men with infertility. J. Urol., 145: 785-788.

Reichart, M., F. Eltes, Y. Soffer, E. Zigenreich, L. Yogeva and B. Bartoov, 2000. Sperm ultramorphology as a pathophysiological indicator of spermatogenesis in males suffering from varicocele. Andrologia, 32: 139-145.

Schlegel, P.N., 1997. Is assisted reproduction the optimal treatment for varicocele-associated male infertility? A cost-effectiveness analysis. Urology, 49: 83-90.

Sepal, D.C., S.S. Howards, T.T. Turner and E.D. Miller, 1981. Influence of surgical induced varicocele on testicular blood flow, temperature and histology in adult rats and dogs. J. Clin. Invest., 68: 39-45.

Sharma, R.K. and A. Agarwal, 1996. Role of reactive oxygen species in male infertility. Urology, 48: 835-850.

Sigman, M. and J.P. Jarow, 1997. Ipsilateral testicular hypotrophy is associated with decreased sperm counts in infertile men with varicoceles. J. Urol., 158: 605-607.

Takihara, H., J. Sakatoku and A.T.K. Cockett, 1991. The pathophysiology of varicocele in male infertility. Fertil. Steril., 55: 861-868.

Tam, P.C., 2004. Varicocele: Current controversies in pathophysiology and treatment. Ann. Coll. Surg., 4: 90-97.

World Health Organization, 1992a. WHO Laboratory Manual for Examination of Human Semen and Sperm-Cervical Mucus Interaction. 3rd Edn., Cambridge University Press, Cambridge, ISBN: 0-323-03577-3.

World Health Organization, 1992b. The influence of varicocele on parameters of fertility in a large group of men presenting to infertility clinics. Fertil. Steril., 57: 1289-1293.

World Health Organization, 1993. WHO Manual for the Standardized Investigation and Diagnosis of Infertile Couple. 1st Edn., Cambridge University Press, Cambridge, ISBN: 0-456-03649-0.

Zini, A., A. Blumenfeld, J. Libman and J. Willis, 2005. Beneficial effect of microsurgical varicocelectomy on human sperm DNA integrity. Hum. Reprod., 20: 1018-1021.