

## Determination of varicocele benefits, anthocyanin good effects on varicocele and relationship between remedial effects of varicocele and races

Sayed Alireza Mirsane <sup>1</sup>, Shima Shafagh <sup>2,\*</sup>

<sup>1</sup>Surgical Technology Student, School of Nursing and Midwifery, Kashan University of Medical Sciences, Kashan, I.R. IRAN

<sup>2</sup>General Surgery Specialist, Medical School, Kashan University of Medical Science, Kashan, I.R. IRAN

\*Corresponding author: Shima Shafagh, General Surgery Specialist, Medical School, Kashan University of Medical Science, Kashan, I.R. IRAN; Email: mirsane.oraei@gmail.com; Tel: +989398628850.

### Abstract

**Introduction:** A varicocele is defined as an abnormal venous dilatation and/or tortuosity of the pampiniform plexus in the scrotum. Varicocele is the major reversible cause of male infertility. It is observed in 35%–40% of all men with primary infertility.

**Objectives:** Our purposes were determination of varicocele benefits, anthocyanin effects on varicocele and also varicocele isn't contacted with races.

**Methods:** We did a review of 22 studies identified by searching Google scholar, PubMed, SID and Elsevier.

**Results:** All studies were based on the role of varicocele in improvement sperm and semen parameters as well as those were relied of the anthocyanin good effects for varicocele disease, also analysis of those showed varicocele isn't contacted with races.

**Conclusions:** We concluded that varicocele is a way for improvement sperm and semen parameters and it isn't contacted with races. Also anthocyanin has good effects for varicocele disease.

**Keywords:** Varicocele, Sperm and semen parameters, Races, Anthocyanin

### Introduction

A varicocele is defined as an abnormal venous dilatation and/or tortuosity of the pampiniform plexus in the scrotum (1). Varicocele is the major reversible cause of male infertility. It is observed in 35%–40% of all men with primary infertility and in up to 80% of those with secondary infertility (2). The higher incidence of varicocele in men with secondary infertility suggests its progressive nature, which might be explained by a progressive testicular dysfunction involving both spermatogenesis and steroidogenesis. The negative impact of varicocele on spermatogenesis has been documented by a progressive reduction in the size of testicle ipsilateral to the varicoceles (3). The effect of varicocele repair on male fertility remains debatable (4). Although the majority of studies report that varicocele repair results in improved semen parameters, not all reports support this finding (5,6). The impact on natural pregnancy rates is even more controversial (4). Purposes of this study is determination of varicocele benefits, anthocyanin good effects on varicocele and relationship between remedial effects of varicocele and races.

### Methods

We review 22 studies identified by searching Google scholar, PubMed, SID and Elsevier.

#### Review of Literature

These studies are in the following:

#### 1. Clinical Outcome of Microsurgical Varicocele in Infertile Men With Severe Oligozoospermia:

To evaluate the outcome of microsurgical varicocele in infertile men with severe oligozoospermia and to identify the predictive parameters associated with the efficacy of microsurgical varicocele in this cohort of patients. This study included 102 consecutive severe oligozoospermic patients who underwent microsurgical varicocele between 2000 and 2013. The significance of several parameters as predictors of response to microsurgical varicocele was evaluated using univariate and multivariate analyses. Responders were defined as those who fulfilled the following criteria: (1) sperm motility rate improved after surgery and (2) sperm

concentration increased from  $<1 \times 10^6$ /mL to  $\geq 5 \times 10^6$ /mL or from  $1-5 \times 10^6$ /mL to  $\geq 10 \times 10^6$ /mL. Univariate analysis identified preoperative sperm concentration ( $\geq 2.0$  vs  $< 2.0$  million/mL) and laterality of varicocele (bilateral vs unilateral) as significant predictors of response to varicocelectomy. Only preoperative sperm concentration appeared to be independently related to the efficacy of varicocelectomy in men with severe oligozoospermia on multivariate analysis. Varicocelectomy may improve the sperm quality and fertility potential in men with severe oligozoospermia, particularly for those with relatively high sperm concentration (7).

## **2. Predictors of success after microscopic subinguinal varicocelectomy:**

Varicocele is found in 35-40% of men with infertility. Although several meta-analyses have demonstrated that varicocelectomy improves semen parameters and pregnancy rates, it is still unclear as to which patients will benefit from this procedure. The aim of this study was to determine pre-operative clinical and laboratory predictors of success of microscopic subinguinal varicocelectomy as defined by a 50% improvement in sperm concentration. An Institutional Review Board retrospective study was conducted on all patients undergoing microscopic subinguinal varicocelectomy for infertility one year with abnormal semen parameters and palpable varicocele between 2005-2013. Demographic, clinical, and laboratory data was recorded. Microscopic subinguinal varicocelectomy results in improvement of multiple semen parameters with overall pregnancy rate of approximately 50%. The presence of grade 3 varicocele, irrespective of other pre-operative variables, predicts the most successful increase in sperm concentration (8).

## **3. Varicocelectomy is associated with increases in serum testosterone regardless of clinical grade:**

Men with clinically palpable varicoceles are at high risk for progressive decline in fertility, and more recent evidence suggests that these men are also at greater risk for androgen deficiency. Repair of a higher grade varicocele has been shown to result in greater improvement in sperm count and quality than repairing a lower grade varicocele. In this study we sought to determine whether grade is related to degree of improvement in serum testosterone levels

after varicocelectomy. We performed a retrospective review of men with total serum testosterone  $< 400$  ng/dl undergoing microsurgical subinguinal varicocelectomy for infertility and/or hypogonadism. All men had clinically palpable left varicoceles ( $\geq$  grade 1) and matching preoperative and postoperative serum total testosterone levels. For patients with bilateral varicoceles, the highest grade on either side was used to stratify patients. Patients with isolated left grade 1 varicoceles were not offered varicocelectomy for hypogonadism. Patients on medical treatment for hypogonadism were excluded. Changes in testosterone levels were evaluated with results expressed as mean  $\pm$  standard error.  $P < 0.05$  was considered significant. There were significant improvements in testosterone levels in all patients with bilateral varicoceles as well as patients who underwent repair for left grade 3 varicoceles. Microsurgical varicocelectomy results in significant increases in testosterone independent of varicocele grade. Microsurgical varicocelectomy should be offered to hypogonadal men regardless of varicocele grade (9).

## **4. Impact of the revised WHO semen analysis reference limits on selection criteria for microsurgical varicocelectomy:**

The AUA Best Practice Policy recommends varicocele repair in men with "abnormal" semen parameters, but reference limits for semen parameters have changed with publication of the 2009 WHO human semen reference ranges. The aim of this study was to evaluate the improvement in semen parameters and serum Testosterone (T) following varicocelectomy in those men considered abnormal by the 1999 WHO criteria but normal by the new 2010 criteria. A retrospective review of all men with clinical grade I-III varicoceles who underwent microsurgical varicocelectomy between 2000-2010 was performed. Inclusion criteria, based on semen parameters, were: sperm concentration 15-20 million/mL, motility 40-50%, or morphology 4-14%. Patients with a history of recurrent Vx, T supplementation, clomiphene citrate, or aromatase inhibitor use, were excluded. Data on demographics, varicocele characteristics, pre- and post-operative serum T and semen analyses, and pregnancy outcomes, where available, was abstracted for the selected patients. Paired t-test analysis was performed using SPSS software to evaluate differences in pre- and postoperative semen parameters and serum testosterone. A p-value  $< 0.05$

was considered significant. Microsurgical varicocelectomy in the subset of men considered to have normal semen parameters by the 2010 WHO reference ranges, but abnormal by 1999 references ranges, lead to a significant improvement in serum T, sperm concentration, and, in some cases, sperm motility. Varicocelectomy should be considered in this subset of men, as a means of improving fertility potential as well as T levels (10).

#### **5. Effects of anthocyanin extracted from black soybean seed coat on spermatogenesis in a rat varicocele-induced:**

Varicocele is the most common cause of primary male infertility and is associated with oxidative stress. The aim of the present study was to investigate the effects of anthocyanin on a rat model of varicocele. Twenty-four male rats were divided into four experimental groups: a normal control group, a varicocele-induced control group and two varicocele-induced groups treated with either 40 or 80 mg kg<sup>-1</sup>, p.o., anthocyanin for 4 weeks. Varicocele was induced by the partial obstruction of the left renal vein. After 8 weeks, the testes and epididymides from rats in all groups were removed, weighed and subjected to histological examination and semen analysis. Apoptosis in the testes was determined by terminal deoxyribonucleotidyl transferase-mediated dUTP-digoxigenin nick end-labelling (TUNEL) and oxidative stress was assessed by measuring 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels. Although no significant differences in sperm counts were observed among the groups, anthocyanin treatment of the varicocele-induced groups resulted in significantly increased testes weight, sperm motility and spermatogenic cell density ( $P < 0.05$ ). Anthocyanin treatment also significantly decreased apoptotic body count and 8-OHdG concentrations ( $P < 0.05$ ). We suggest that the antioxidant effect of anthocyanin prevented the damage caused by varicocele-induced reactive oxygen species (11).

#### **6. Decreased Sperm DNA Fragmentation After Surgical Varicocelectomy is Associated With Increased Pregnancy Rate:**

We prospectively evaluated changes in sperm chromatin structure in infertile patients before and after surgical repair of varicocele, and the impact on the pregnancy rate. Included in the study were 49 men with at least a 1-year history of infertility, a

palpable varicocele and oligospermia. World Health Organization semen analysis and sperm DNA damage expressed as the DNA fragmentation index using the sperm chromatin structure assay were assessed preoperatively and postoperatively. Pregnancy (spontaneous and after assisted reproductive technique) was recorded 2 years after surgery. Mean sperm count, sperm concentration and sperm progressive motility improved significantly after varicocelectomy from  $18.3 \times 10^6$  to  $44.4 \times 10^6$ ,  $4.8 \times 10^6/\text{ml}$  to  $14.3 \times 10^6/\text{ml}$  and 16.7% to 26.6%, respectively ( $p < 0.001$ ). The DNA fragmentation index decreased significantly after surgery from 35.2% to 30.2% ( $p = 0.019$ ). When the definition of greater than 50% improvement in sperm concentration after varicocelectomy was applied, 31 of 49 patients (63%) responded to varicocelectomy. After varicocelectomy 37% of the couples conceived spontaneously and 24% achieved pregnancy with assisted reproductive technique. The mean postoperative DNA fragmentation index was significantly higher in couples who did not conceive spontaneously or with assisted reproductive technique ( $p = 0.033$ ). After varicocelectomy sperm parameters significantly improved and sperm DNA fragmentation was significantly decreased. Low DNA fragmentation index values are associated with a higher pregnancy rate (12).

#### **7. Varicocelectomy: semen parameters and protamine deficiency:**

Different methods have been used to evaluate the beneficial effect of varicocelectomy; these include semen parameters and pregnancy rate. Because of high biological variability of semen parameters, sperm functional tests have been considered as an efficient end point in assessment of fertility. Therefore, the aim of this study was to evaluate the effect of varicocelectomy on semen parameters and sperm protamine deficiency in 192 patients. The results of the present study show that all the three semen parameters and percentage of sperms with normal protamine content have improved post-surgery. The cumulative pregnancy rate was 34.6%. Comparing the results of the semen parameters and protamine content between patients whose partner became pregnant to those who did not benefit from varicocelectomy before and 6 months after surgery show that patients may benefit from varicocelectomy that had higher initial semen density and better sperm morphology prior to surgery. Thus, it can be suggested that patients with

low initial sperm count may benefit more from assisted reproductive techniques or varicocelectomy followed by assisted reproduction (13).

#### **8. Effect of Subinguinal Varicocelectomy on Sperm Parameters and Pregnancy Rate: A Two-Group Study:**

To evaluate the changes in semen parameters and pregnancy rates after varicocelectomy. We evaluated the results of surgery in 146 men with primary infertility and palpable left varicoceles, compared with 62 men who refused surgery and were treated with tamoxiphene. Patients were selected with strict criteria in order to exclude any other infertility factor in the couple. They were followed up for at least 1 year after treatment. Statistical analyses were performed with the Wilcoxon signed rank test, Kolmogorov-Smirnov two-sample test and paired samples t test. After 1 year, the differences in the median values were significant for all parameters. The partners of 62 of the operated men (46.6%) and 8 of the nonoperated (12.9%) became pregnant within 1 year ( $p < 0.001$ ). Thus, the difference between the true 1-year pregnancy rates was 33.7%. Overall, 83.2% of the operated men improved their semen parameters compared to 32.3% of the nonoperated. Varicocelectomy improves all semen parameters and pregnancy rates significantly. Palpable varicoceles should be operated upon when found in infertile couples (14).

#### **9. Treatment of Varicocele for Male Infertility: A Comparative Study Evaluating Currently Used Approaches:**

To evaluate the results of four currently used approaches for the treatment of clinically diagnosed varicoceles, and compare their influence on semen parameters. In all groups statistically significant improvement as to the sperm concentration was found in both the 6- and 12-month follow-up. This significance was more prominent in group C followed by groups B and D, and finally by group A. As to sperm motility, in group C there was a statistical significance in both follow-up evaluations, and in group B statistical difference was reached only in the 12-month evaluation. Sperm morphology did not differ in any of the groups postoperatively compared to the preoperative values. The subinguinal approach disclosed a more prominent improvement in both semen concentration and

motility in the 6- and 12-month follow-up evaluation when compared to the other techniques. Furthermore, due to its simplicity and avoidance of opening the external oblique fascia, we believe it represents the more plausible approach when treating clinical varicocele (15).

#### **10. Microsurgical repair of the adolescent varicocele:**

Since clinically apparent varicoceles may affect testicular volume and sperm production, early repair has been advocated. The microsurgical technique has been successfully completed in a large series of adults with a dramatic reduction in complication and recurrence rates. We report our experience with the microsurgical technique in boys. The meticulous dissection necessary to preserve arterial and lymphatic supply, and to ligate all spermatic veins in the pediatric patient is readily accomplished using a microsurgical approach, and results in low recurrence and complication rates. Rapid catch-up growth of the affected testis after microsurgical varicocelectomy suggests that intervention during adolescence is effective and warranted (16).

#### **11. Effects of Varicocele Treatments in Adolescents: Changes of Semen Parameters after Early Varicocelectomy:**

The aim of this study was to evaluate the role of semen analysis in adolescent varicocele patients, and determine the deleterious effects of varicocele on spermatogenesis, as reflected by semen analysis, in adolescent boys compared to infertile adults. The seminal follow-up data of 47 adolescent patients (age range 16-20 years) and 68 adult patients (age range 29-50 years), who underwent a varicocelectomy for infertility, were compared. The results of the andrological and hormonal evaluations were also compared. The percentage of abnormal seminal parameters was lower in the adolescent group. Multiple seminal abnormalities were also less common in the adolescent group. Of the 18 adolescents who showed seminal abnormality, testicular volume discrepancy was demonstrated in only 5 (27.8%). The varicocelectomy significantly improved all the tested mean seminal parameters in both groups. However, the adolescent group showed earlier and more complete recovery than the infertile adult group. In a comparison of the patients with preoperative abnormal seminal parameters, only the adolescent group showed improvements in

the mean seminal parameters 3 month after the varicocelectomy. In late pubertal varicocele patients, semen analysis may be a useful tool in identifying those at risk of future subfertility (17).

### **12. Changes in the seminal plasma proteome of adolescents before and after varicocelectomy:**

To compare seminal plasma protein profiles before and after varicocele repair to assess whether surgical intervention alters the protein profile. Two semen samples were collected before bilateral subinguinal microsurgical varicocelectomy, and two semen samples were collected 3 months after surgery. Seminal plasma protein profiles were determined with the use of two-dimensional gel electrophoresis. Proteins were separated in 18-cm 3–10 pH races and 10%–17.5% gradient gels. Gels were stained, scanned, and compared with the use of Imagemaster 2D platinum 7.0. Spots of interest were removed from gels, and protein digestion was performed with the use of trypsin. Digests were identified with the use of electrospray ionization-quadrupole/time-of-flight tandem mass spectrometry (ESI-QTOF MS/MS), and spectra were analyzed with the use of the Mascot software. Proteins uniquely or overexpressed in each period (before or after varicocelectomy). Nineteen spots were differentially expressed between pre- and postsurgery samples. Identified proteins were albumin, proteasome subunit alpha type 6, alpha-1-antitrypsin, fibronectin, CD177, prostatic acid phosphatase, specific prostatic antigen, alpha-2-antiplasmin, vitamin D-binding protein, gastricsin, clusterin, semenogelin-1, semenogelin-2, superoxide dismutase, protein-glutamine gamma glutamyltransferase-4, and prolactin-inducing protein. Varicocelectomy is associated with changes in the seminal plasma protein profile. Understanding specific pathways leading to male infertility may further assist physicians in demonstrating deviation from homeostasis in male infertility. In addition, it may be possible to observe if surgical intervention does indeed revert altered pathways toward a homeostatic state (18).

### **13. Efficacy of Varicocelectomy in Improving Semen Parameters: New Meta-analytical Approach:**

To determine the efficacy of varicocelectomy in improving semen parameters. A meta-analysis was performed to evaluate both randomized controlled trials and observational studies using a new scoring

system. This scoring system was developed to adjust and quantify for various potential sources of bias, including selection bias, follow-up bias, confounding bias, information or detection bias, and other types of bias, such as misclassification. The combined analysis demonstrated that the sperm concentration increased by  $9.71 \times 10^6/\text{mL}$  (95% confidence interval [CI] 7.34 to 12.08,  $P < 0.00001$ ) and motility increased by 9.92% (95% CI 4.90 to 14.95,  $P = 0.0001$ ) after microsurgical varicocelectomy. Similarly, the sperm concentration increased by  $12.03 \times 10^6/\text{mL}$  (95% CI 5.71 to 18.35,  $P = 0.0002$ ) and motility increased by 11.72% (95% CI 4.33 to 19.12,  $P = 0.002$ ) after high ligation varicocelectomy. The improvement in World Health Organization sperm morphology was 3.16% (95% CI 0.72 to 5.60,  $P = 0.01$ ) after both microsurgery and high ligation varicocelectomy. Surgical varicocelectomy significantly improves semen parameters in infertile men with palpable varicocele and abnormal semen parameters (19).

### **14. Effect of Varicocelectomy on Male Infertility:**

Varicocele is the most common cause of male infertility and is generally correctable or at least improvable by various surgical and radiologic techniques. Therefore, it seems simple and reasonable that varicocele should be treated in infertile men with varicocele. However, the role of varicocele repair for the treatment of subfertile men has been questioned during the past decades. Although varicocele repair can induce improvement of semen quality, the obvious benefit of spontaneous pregnancy has not been shown through several meta-analyses. Recently, a well-designed randomized clinical trial was introduced, and, subsequently, a novel meta-analysis was published. The results of these studies advocate that varicocele repair be regarded as a standard treatment modality in infertile men with clinical varicocele and abnormal semen parameters, which is also supported by current clinical guidelines. Microsurgical varicocelectomy has been regarded as the gold standard compared to other surgical techniques and radiological management in terms of the recurrence rate and the pregnancy rate (20).

### **15. Varicocele and male infertility:**

Varicoceles are the most frequent physical findings in infertile men. Although the varicocele is generally regarded to be the most common correctable cause of male infertility, whether varicocelectomy is an

effective treatment for male factor infertility has been the focus of intense debate. A great deal of evidence indicates that varicocelectomy is clearly associated with a significant improvement in semen parameters (concentration, motility, and morphology). Varicocelectomy also appears to reduce seminal oxidative stress and sperm DNA damage. In contrast, the positive effect of varicocelectomy on improving natural pregnancy rates is less clear based on a few randomized controlled trials. Therefore, the need persists for well-designed, properly conducted randomized controlled trials to address this issue. Considering the beneficial effects of varicocelectomy on semen parameters, varicocelectomy should be considered in men with palpable lesions, at least one abnormal semen parameter and otherwise unexplained infertility (21).

#### **16. Factors Related to Improvement or Normalization of Semen Parameters after Microsurgical Subinguinal Varicocelectomy:**

To determine factors related to improvement or normalization of semen parameters after varicocelectomy, we retrospectively analyzed patients who underwent semen evaluation before and after varicocelectomy. Absence of testicular size discrepancy and preoperative sperm concentration were independent predictive factors for normalization of the sperm concentration. For improvement of sperm motility, a significant correlation was found with grade of varicocele. Meanwhile, for normalization of sperm motility, significant correlations were found with age and preoperative sperm motility. Substantial improvement and normalization in each semen parameter was observed after microsurgical subinguinal varicocelectomy. There were different independent predictive factors for improvement or normalization of each semen parameter (22).

#### **17. The effect of magnified bilateral varicocele ligation on semen quality and the natural paternity rate in subfertile men, based on the sum of varicocele grading:**

To evaluate the effect of magnified bilateral varicocele ligation on the semen quality and natural paternity rate in subfertile men, based on the sum of varicocele grading. In a prospective longitudinal study, 78 patients (mean age 36.5 years, range 21–56) with a total of 156 varicoceles underwent

bilateral varicocele ligation. Patients included had bilateral, primary and clinically palpable varicoceles, with a normal hormonal profile and abnormal semen; patients excluded had unilateral varicocele, or were recurrent cases, had infraclinical varicocele or had a genetic abnormality. Data were analyzed statistically using a paired t-test to compare the mean sperm variables before and after surgery, with  $P < 0.05$  considered to indicate significant differences. Overall, the mean sperm density, total sperm motility and sperm morphology increased from 13.44 to 26.48  $\times 10^6$ /mL, 27.4% to 53% and 41.4% to 65.0%, respectively; the differences were statistically significant for all variables ( $P < 0.001$ ). For each group separately there were significant improvements for both sperm density and motility, but for sperm morphology there were significant improvements in all groups except E, where the improvement was not correlated with those in the other groups. The paternity rate (by natural pregnancy) at 2 years was 26.9%, and this increased to 41% within 3 years. Magnified bilateral varicocele ligation based on the sum of varicocele grading significantly improved semen quality and the natural paternity rate in subfertile men (23).

#### **18. Antioxidant effects of anthocyanin on spermatogenesis in rat varicocele-induced model:**

Varicocele is one of the most common causes of primary male infertility and known as a disease associated with oxidative stress. This study was designed to investigate the effects of anthocyanin extracted from black soybeans in a rat model of varicocele. In comparison with that in the varicocele-induced group, administration of anthocyanin led to significantly increased testis weight and spermatogenic cell density ( $P < 0.05$ ). Also, it led to decreased apoptotic body counts and 8-hydroxy-2-deoxyguanosine (8-OHdG) concentrations significantly ( $P < 0.05$ ). The antioxidant effect of anthocyanin prevents the oxidative damage caused by varicocele-induced reactive oxygen species. Administration of anthocyanin may be effective for making healthy sperm in patients with varicocele (24).

#### **19. Effect of varicocelectomy on patients with unobstructive azoospermia and severe oligospermia:**

To assess the treatment outcome and benefits after varicocelectomy in men with unobstructive

azoospermia (UOA) and severe oligospermia (SO), the records were retrospectively evaluated for six patients with UOA and 54 with SO who had microsurgical inguinal varicocele ligation (mean age 33.3 years, SD 5.3). Fifty-one (85%) had a unilateral left-sided procedure (five of six with UOA, 46 of 54 with SO), and nine (15%) had a bilateral procedure. After ligation, spermatogenesis was induced in two of the six men with UOA; the mean (SD) sperm concentration increased from 2.3 (1.6) to 9.2 (12.6) million/mL ( $P < 0.001$ ), but the sperm motility did not change significantly. Four (7%) of the 54 men with SO achieved paternity, with unassisted pregnancies. Varicolectomy resulted in the induction or enhancement of spermatogenesis for several men with UOA or SO; it seems to be a reasonable option in selected patients with UOA or SO (25).

#### **20. Varicolectomy for Male Infertility: A Comparative Study of Open, Laparoscopic and Microsurgical Approaches:**

We compared the outcomes of 3 techniques of varicolectomy in infertile patients with varicocele. Compared to preoperative values in the 3 groups (microsurgical, open and laparoscopy groups) postoperative semen parameters showed significant improvement in sperm concentration, motility and morphology. The incidence of patients with improved sperm count and motility was significantly higher in the microsurgical group. The pregnancy rate at 1 year was not significantly different among the 3 groups. Compared with open and laparoscopic varicocele treatment microsurgical varicolectomy has the advantages of no hydrocele formation, a lower incidence of recurrent varicocele, and better improvement in sperm count and motility (26).

#### **21. Semen Parameters and Chromatin Packaging in Microsurgical Varicolectomy Patients:**

Varicolectomy is considered as standard treatment for male infertility for clinical varicocele. The aim of this study is to address the effects of varicolectomy on semen parameters, chromatin packaging, and pregnancy outcome. Both sperm parameters improved and the percentage of sperm protamine deficiency decreased significantly after varicolectomy. These results confirm that varicolectomy improves sperm parameters and chromatin packaging, thereby improving the chance of pregnancy. Positive aspects of this study include

the large number of patients studied, duration of follow up, one surgeon who performed all of the surgeries, and type of surgery (microsurgery). The spontaneous pregnancy results also suggest that if pregnancy is not achieved within twelve months post-surgery, an alternative approach such as assisted reproductive technology (ART) treatment should be considered (27).

#### **22. Changes in seminal quality following varicolectomy in infertile Nigerian males:**

Semen analysis in 116 subfertile and infertile patients with varicocele revealed oligospermia (counts less than 20 million/ml) in 66% of patients, asthenospermia (motility of less than 50%) in 59% of patients; and teratospermia (abnormal sperm morphology of greater than 50%) in 65% of patients. The sperm motility and morphology deteriorated with decrease in sperm concentration. After varicolectomy 53% of all patients showed improvement in the overall semen quality. The best post-operative results were noted in patients who had pre-operative counts over 20 million/ml. Deterioration in semen quality was observed in 6% of all patients. Factors which possibly played a role in the response to varicolectomy in our environment are discussed (28).

### **Results**

Findings from this review are:

- ✓ Results suggest that the antioxidant effect of anthocyanin prevented the damage caused by varicocele-induced reactive oxygen species.
- ✓ After varicolectomy sperm parameters significantly improved and sperm DNA fragmentation was significantly decreased. Low DNA fragmentation index values are associated with a higher pregnancy rate. Also varicolectomy is associated with changes in the seminal plasma protein profile.
- ✓ Varicolectomy leads to a significant improvement in serum testosterone, sperm concentration, and, in some cases, sperm motility.

- ✓ Varicocelelectomy should be considered in subset of men, as a means of improving fertility potential.
- ✓ Varicocelelectomy results in improvement of multiple semen parameters with overall pregnancy rate of approximately 50%.
- ✓ Varicocelelectomy improves all semen parameters and pregnancy rates significantly.
- ✓ Considering the beneficial effects of varicocelelectomy on semen parameters, varicocelelectomy should be considered in men with palpable lesions, at least one abnormal semen parameter and otherwise unexplained infertility.
- ✓ The adolescent group showed earlier and more complete recovery than the infertile adult group after varicocelelectomy.
- ✓ Varicocelelectomy resulted in the induction or enhancement of spermatogenesis for several men with unobstructive azoospermia (UOA) and severe oligospermia (SO); it seems to be a reasonable option in selected patients with UOA or SO.
- ✓ Varicocele improvement isn't contacted with races because analysis was based on the role of varicocelelectomy in improvement and treatment for all men in around the world, because these researches were belonged to different countries in worldwide. Also, in different pathways of varicocelelectomy, all results are significant.

good results in different surgical pathways, also beneficial effects of varicocelelectomy don't related to age range, but this is suitable for adolescent. Also anthocyanin has desirable effect on varicocele.

### Acknowledgement

This study is supported by professors of Khansar education office, Sayed Mojtaba Mirsane and Nasrin Oraei. We thanked them very much.

### Conflicts of interest

Authors declare no conflict of interests.

### Conclusions

Finally, we concluding varicocelelectomy is way for improvement reproduction system functioning also it can treat infertility and it isn't contacted with races. It should be noted that varicocelelectomy have

## References

1. Abdulmaaboud MR, Shokeir AA, Farage Y, Abd El-Rahman A, El-Rakhawy MM, et al. Treatment of varicocele: a comparative study of conventional open surgery, percutaneous retrograde sclerotherapy, and laparoscopy. *Urology*. 1998;52:294–300.
2. Gorelick JI, Goldstein M. Loss of fertility in men with varicocele. *Fertil Steril*. 1993;59:613–6.
3. Lipshultz LI, Corriere JN., Jr Progressive testicular atrophy in the varicocele patient. *J Urol*. 1977;117:175–6.
4. Baazeem A, Belzile E, Ciampi A, Dohle G, Jarvi K, et al. Varicocele and male factor infertility treatment: a new meta-analysis and review of the role of varicocele repair. *Eur Urol*. 2011;60:796–808.
5. Redmon JB, Carey P, Pryor JL. Varicocele – the most common cause of male factor infertility? *Hum Reprod Update*. 2002;8:53–8.
6. Will MA, Swain J, Fode M, Sonksen J, Christman GM, et al. The great debate: varicocele treatment and impact on fertility. *Fertil Steril*. 2011;95:841–52.
7. Enatsu N, amaguchiKY, Chiba K, Miyake H, Fujisawa M -Clinical Outcome of Microsurgical Varicocelectomy in Infertile Men With Severe Oligozoospermia - *Urology*, May 2014-Volume 83, Issue 5, Pages 1071–1074.
8. Johnson D, Harnisch B , Zganjar A, Sandlow J - PREDICTORS OF SUCCESS AFTER MICROSCOPIC SUBINGUINAL VARICOCELECTOMY- *The Journal of Urology*, Vol. 193, Issue 4, e944.
9. Hsiao W, Rosoff J, Pale J, Powell J, Goldstein M ;VARICOCELECTOMY IS ASSOCIATED WITH INCREASES IN SERUM TESTOSTERONE- *The Journal of Urology*, Vol. 185, Issue 4, e914.
10. Mehta A , Najari BB., Rosoff JS., Goldstein M - IMPACT OF THE REVISED WHO SEMEN ANALYSIS REFERENCE LIMITS ON SELECTION CRITERIA FOR MICROSURGICAL VARICOCELECTOMY- *The Journal of Urology*, Vol. 187, Issue 4, e921–e922.
11. Jang H, Kim S J, Yuk S M, Han D S, Ha U.-S, Hong S H and et al-Effects of anthocyanin extracted from black soybean seed coat on spermatogenesis in a rat varicocele-induced model - *Reproduction, Fertility and Development* ;15 April 2013-26(3) 485-490.
12. Smit M, Romijn J C, Wildhagen M F, Veldhoven J L.M, Weber R F.A, Dohle G R - Decreased Sperm DNA Fragmentation After Surgical Varicocelectomy is Associated With Increased Pregnancy Rate -*The Journal of Urology*, January 2010-Volume 183, Issue 1, Pages 270–274.
13. Nasr-Esfahani M. H, Abasi H, Razavi S, Ashrafi S and Tavalae M -Varicocelectomy: semen parameters and protamine deficiency- *International Journal of Andrology*, April 2009-Volume 32, Issue 2, pages 115–122.
14. Perimenis P, Markou S, Gyftopoulos K, Athanasopoulos A, Barbaliás G -Effect of Subinguinal Varicocelectomy on Sperm Parameters and Pregnancy Rate: A Two-Group Study, 2001- *European Urology*-Vol. 39, No. 3.
15. Barbaliás G.A, Liatsikos E.N, Nikiforidis G, Siablis D. Treatment of Varicocele for Male Infertility: A Comparative Study Evaluating Currently Used Approaches- *European Urology*, 1998-Vol. 34, No. 5.
16. Lemack GE, Uzzo RG, Schlegel PN, Goldstein M; Microsurgical repair of the adolescent varicocele; *J Urol*. 1998 Jul;160(1):179-81.
17. Shin JW, Kim SW, Paick JS.Effects of Varicocele Treatments in Adolescents: Changes of Semen Parameters after Early Varicocelectomy- *Korean J Urol*. 2005 May;46(5):481-486. Korean
18. Del Giudice P T, da Silva B F, Lo Turco E G, D.V.M - Changes in the seminal plasma proteome of adolescents before and after varicocelectomy, September 2013 - Volume 100, Issue 3, Pages 667–672.
19. Agarwala A, Deepinder F - Efficacy of Varicocelectomy in Improving Semen Parameters: New Meta-analytical Approach , September 2007- *Urology*-Volume 70, Issue 3, Pages 532–538.
20. Cho KS, Seo JT- Effect of Varicocelectomy on Male Infertility- *Korean J Urol*. 2014 Nov;55(11):703-709 .
21. Kim SW. Varicocele and male infertility- *J Korean Med Assoc*. 2012 Jan;55(1):37-46
22. Choi WS, Kim TB, Paick JS, Kim SW. Factors Related to Improvement or Normalization of Semen Parameters after Microsurgical Subinguinal Varicocelectomy- *Korean J Urol*. 2009 Jan;50(1):39-45.
23. Abdel-Hamid Mohamid M - The effect of magnified bilateral varicocele ligation on semen quality and the natural paternity rate in subfertile men, based on the sum of varicocele grading- *Arab Journal of Urology*, December 2012-Volume 10, Issue 4, Pages 434–439.
24. Bae WJ, Choi YS , Kim SJ, Cho HJ, Hong SH , lee JY ; MR O1. Antioxidant effects of anthocyanin on spermatogenesis in rat varicocele-induced model- *Translational Andrology and Urology*;(March 2012) Vol 1, Supplement 1 .
25. Ishikawa T, Kondo Y, Yamaguchi K, Sakamoto Y , Fujisawa M - Effect of varicocelectomy on patients with unobstructive azoospermia and severe oligospermia- *BJU International*, January 2008-Volume 101, Issue 2, pages 216–218.
26. Al-Said S, Al-Naimi A, Al-Ansari A, Younis N, Shamsodini A, A-sadiq K and et al- Varicocelectomy for Male Infertility: A Comparative Study of Open, Laparoscopic and Microsurgical Approaches- *The Journal of Urology*, July 2008-Volume 180, Issue 1, Pages 266–270.
27. Tavalae M, Abbasi H, Deemeh M R, Fotohi F, Sadoughi Gilani M A, Nasr Esfahani M H - Semen Parameters and Chromatin Packaging in Microsurgical Varicocelectomy Patients- *Int J Fertil Steril*. 2012 Oct-Dec; 6(3): 165–174.
28. Senbanjo RO, Lawani J, Nkposong EO- Changes in seminal quality following varicocelectomy in infertile Nigerian males-*African Journal of Medicine and Medical Sciences* 1986, 15(3-4):63-71 .