

Original research

The Effect of Varicocele on Semen Analysis and Serum Levels of Inhibin B

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Abstract:

Background: Varicocele means dilation and torsion of spermatic veins. About 15%-40% of infertile men suffer from Varicocele. It seems that 70% of secondary infertility in men occurs due to Varicocele. Varicocele is the most common surgical cause for male infertility. Varicocele is considered as the best treatment method for patients with Varicocele that increases 30%-50% of the postoperative fertility rate. The purpose of this study was to investigate the effect of Varicocele on inhibin B and use this marker to predict infertility in men.

Methods: In this study, all infertile patients in any age that were candidate for Varicocele and hospitalized in Imam Hospital in Urmia were included. Exclusion criteria were defined as orchitis, trauma, diabetes, radiotherapy, chemotherapy and coitus complications. Sperm analysis (SA) was conducted three times for patients and then serum levels of FSH, LH, T, inhibin B, SA were measured before surgery and also six months after surgery. Furthermore, during the hospitalization and infertility period, testes were examined before surgery in terms of consistency and size.

Results: The mean \pm SEM (standard error median) age of 40 patients was 28.4 ± 5.14 (range: 18-40) years old. Mean size of the testes and mean sperm density and serum levels of LH, FSH remained the same. However, mean sperm motility, serum levels of T and inhibin B were statistically significant after the Varicocele (p-value=0.005). A significant relationship was found between serum levels of inhibin B and infertility; however, there was no significant relationship between sperm count and serum levels of LH, FSH and T. Varicocele can improve sperm motility and increase Inhibin B in patients and so improves spermatogenesis parameters and it may be one of the causes of fertility in patients.

Conclusion: The results of this study indicate that sperm motility and increase in inhibin B after Varicocele can improve spermatogenesis parameters. Serum levels of FSH, T, LH and sperm morphology and also grade of Varicocele, patient age, and testis size have no effect on spermatogenesis and fertility after Varicocele.

Keyword: Inhibin B; Varicocele; Follicle Stimulating Hormone; Luteinizing hormone; Testosterone.

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1. Introduction

Varicocele means dilatation and torsion of spermatic veins. About 15%-40% of men suffer from Varicocele-related infertility and it seems that 70% of secondary male infertility occurs due to Varicocele. Between 4% to 25% of men with semen abnormality suffer from Varicocele. Varicocele is the most common surgical cause for male infertility (1). The accurate mechanism of Varicocele-related infertility is unknown,

however, a combination of various factors lead to infertility in the Varicocele, including (1) increased testicular temperature, which makes spermatogenesis comes to a halt due to venous blood congestion, thereby reducing oxygen and epididymis activity through the intravenous backflow and resulting in testicular dysfunction; (2) Return of metabolites of renal tubule and its adjacency to the testis; (3) Reducing arterial blood flow in the testicular atrophy and thereby reducing spermatogenesis; (4) The effect of serotonin on the androgen synthesis and the contractile effect on testicular vessels, thereby increasing the number of premature spermatozooids in the semen; (5) Hormonal changes in the hypothalamus, pi-

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tuitary, gonadal; the use of drug therapy such as prostaglandins-including aspirin and indomethacin-increases the amount of spermatozooids and also the use of spermatogenesis drugs, including clomiphene is similarly considered as one of the treatments (1, 2). However, surgery is the main treatment for Varicocele. The inhibin B is a KD32 glycoprotein consisting of 2 chains (β - α), the β -chain has two subgroups (A, B) and can be detected by radioimmunoassay and Elisa (2, 3). Inhibin B is secreted by sertoli Cells in response to FSH, which controls gametogenesis with the effect of negative feedback on FSH secretion (4, 5).

Inhibin B is used as an endocrine marker for the normal activity of gonads in both sexes (3). It has recently been shown that inhibin B has a high sensitivity to testicular size and FSH level and testicular biopsy for the evaluation of men with oligozoospermia, so that there is a significant difference between the serum levels of inhibin B and the total amount of sperm and testicle size (6, 7). The best treatment for patients with Varicocele is Varicocelectomy surgery with 30-50% of postoperative pregnancy (8).

However, since the infertility pathophysiology and Varicocele is not clear, there are no precise predictor for examining and predicting the status of the patients before and after surgery. This study was designed to find a predictor of the outcome of the Varicocele surgery for finding the patients with little or no benefit from the operation. This study seeks to measure the level of inhibin B before and after Varicocele surgery to evaluate its effect on spermatogenesis.

2. Method

In this study was conducted in 2015-2017. All infertile patients in each age group who were candidates for Varicocelectomy and had referred to Imam Khomeini Hospital in Urmia were selected. Exclusion criteria were defined as a history of orchitis, trauma, diabetes, radiotherapy, chemotherapy, and coitus problems. Meanwhile, all Varicoceles were on the left side and testicles size did not change after the Varicocelectomy (conventional).

Three semen analyses were carried out for patients. Serum levels of LH, FSH, T, and Inhibin B were measured before surgery and six months later. In addition, SA was performed six months after surgery. And the effect of Varicocelectomy on laboratory parameters was investigated. During hospitalization and infertility period before Varicocelectomy, the patient's testicles were examined in terms of size and consistency. Besides, its effect on SA and hormonal parameters before and after surgery, as well as the changes in the size of the testicles after surgery was analyzed.

Data were analyzed using SPSS 21. Written consent form was obtained to use its information and the confidentiality of information was guaranteed by the main investigator. In order to compare the quantitative variables in more than two groups, ANOVA or Kruskal-Wallis nonparametric equivalents were used. Also, for comparing indices before and after treatment, paired t-test or non-parametric equivalent of Wilcoxon was used. Finally, the Mann-Whitney test was used to compare the quantitative variables in the two groups. Normality of data was investigated by Kolmogorov Smirnov test.

3. Result

The mean age of the patients was 28.40 ± 5.14 years old (minimum = 18 and maximum = 40, average = 29). The classification of age group was as follows: 7 patients (17.5%) in the age group of 18-22 years old, 4 (10%) in the age group of 22- 26 years old, 17 (42.5%) in the age group of 27-30 years old, 7 (17.5 %) in the age group of 30-34 years old, 3 (7.5%) in the age group 34-38 years old and finally, 2 (5%) in the age group of 38-42 years old.

From the 40 studied patients, 16 (40%) patients suffered from second grade Varicocele and 24 (60%) patients suffered from third grade Varicocele. Examination of the patients' semen parameters before and after the operation of Varicocelectomy has been mentioned in Table 1. According to kruskal wallis, the mean sperm count before (P-value = 0.593) and after surgery (P-value = 0.406) in all the age groups was not significantly different. Also, according to ANOVA, there was no significant difference in the mean of motility before (p-value = 0.834) and after surgery (p-value = 0.282) among different age groups.

Also, the serum levels of LH, T, FSH and Inhibin B before and six months after surgery was measured which the results are as shown as Table 2.

According to kruskal wallis test, the mean of LH, FSH and T in different age groups before (P-value = 0.618) and after surgery (p-value = 0.107) was not differ significantly among age groups. The mean of inhibin B before surgery was not significantly different between the age groups (P value = 0.338), but it was significantly different after surgery among various age groups (p-value = 0.043).

In this study, the factors were evaluated in terms of Varicocele grade. The Wilcoxon test showed that follow factors did not differ significantly in terms of Varicocele grade in patients before and after surgery : Mean sperm count (Before: p-value = 0.151) (After: p-value = 0.305), sperm motility (Before: p-value = 0.976) (After: p-value = 0.734) The mean of LH (Before: P value = 0.836) (After: P value = 0.345), mean FSH (Before: P-value =

Table 1: Comparison of average semen analysis (count and motility) before and after Varicocelectomy

Variable	Mean	Std. Deviation	P
Motility before surgery	29.5500	8.40924	0.005
Motility after surgery	32.4500	7.64585	
Count before surgery	56.3750	29.26947	0.332
Count after surgery	56.7000	28.82502	

Table 2: The results of Wilcoxon test for comparison of mean LH, FSH, T and Inhibin B before and after Varicocelectomy

Variable	Before surgery (Mean± Std. Deviation)	After surgery (Mean± Std. Deviation)	P
LH	3.53±1.96	3.68±1.80	0.40
FSH	4.60±2.54	6.08±5.68	0.97
T	11.46±6.20	7.82±5.49	0.001
Inhibin B	272.3±189.43	265.09±154.86	0.01

Table 3: Comparison of the mean of inhibin B before and after Varicocelectomy in terms of infertility and fertility in the subjects.

Variable	Before surgery (Mean± Std. Deviation)	After surgery (Mean± Std. Deviation)	P
Infertility	268.87±158.32	243.77±143.40	0.34
Fertility	249.95±150.87	206.17±141.76	0.005

0.392) (After: P-value = 0.500) and mean T (Before: P-value = 0.269) (After: P-value = 0.937), while the mean of inhibin B before (P-value = 0.018) and after surgery (P-value = 0.034) had a significant difference in terms of Varicocele grade in patients.

The size of the testes was measured by ultrasound (testis volume cut off point for atrophica in sonographic less than 20% opposite side testis). In the study of atrophic size of testes, the results showed that atrophy was observed in 7 (17.5%) out of 40 patients and it was not seen in 33 (82.5%) patients.

Wilcoxon test showed that the mean count of sperm (Before: p-value = 0.302) (After: p-value = 0.802), mean sperm motility (Before: p-value = 0.440) (After: p-value = 0.702), mean of LH (Before: p-value = 0.206) (After: p-value = 0.194), FSH (Before: p-value = 0.310) (After: p-value = 0.154), T (Before: p-value = 0.285) (After: p-value = 0.177) and Inhibin B (Before: p-value = 0.176) (After: p-value = 0.917) before and after surgery was not significantly different in the size of the testes in the subjects.

Furthermore, in this study, the duration of infertility and its effect on the parameters of the semen were studied. Mean sperm count (Before: p-value = 0.623) (After: p-value = 0.497), mean sperm motility (Before: p-value = 0.930) (After: p-value = 0.763), mean LH (Before: p-value = 0.362) (After: p-value = 0.580), FSH (Before: p-value = 0.640) (After: p-value = 0.644), T (Before: p-

value = 0.280) (After: p-value = 0.337) and finally the mean of Inhibin B (Before: p-value = 0.151) (After: p-value = 0.413) before and after surgery was not significantly different in terms of duration of infertility in the subjects.

The fertility of the patients was considered in this study, so that among 35 patients (19%) who referred one year later, 7 (20%) were fertile and 28 (80%) were not fertilized. In comparison with Inhibin B before and one year after the operation, the results of our study showed that the mean pre-operative inhibin B level in the seven patients who were fertilized was 141.76 ± 206.17 and one year after operation, the mean inhibin B level was 150.87 ± 249.95 , which according to Wilcoxon test, there was a significant difference between pre-operative and post-operative Inhibin B in patients who have been fertilized ($P = 0.005$) in the comparison with Inhibin B before and one year after the operation of Varicocelectomy in 28 non-fertile patients. Our study showed that the mean of Inhibin B before surgery was 143.40 ± 243.77 and one year after the operation, the mean inhibin B was 158.32 ± 268.87 . The paired sample t-test showed that there was no significant difference between pre-operative and post-operative Inhibin B in patients who did not have fertility ($0.34 = P$) (Table 3).

4. Discussion

In general, in patients with Varicocele, there is a possibility of fertility and improvement of testicular growth and hormonal parameters and semen analysis after Varicocelectomy. As shown in this study and previous studies (2), there are factors that affect Varicocele and Varicocelectomy surgery, including Varicocele grade, size of testes, the age and duration of infertility. In our study, the age of the patients had no effect on the results of semen analysis after Varicocelectomy, but the level of inhibin B increased after Varicocelectomy.

Romeo et al. showed that inhibin B levels were decreased in adolescent patients with Varicocele, which could be a marker for the effects of Varicocelectomy (2). The results of the present study showed that there was a relationship between Varicocele grade and serum levels of Inhibin B, which after Varicocele surgery, the amount of Inhibin B reduced in both Grade II and III groups, which could be due to the lack of correlation of Varicocele grade and spermatogenesis severity.

Romeo et al. (2007) demonstrated that patients with Varicocele had less testicular density and serum levels of inhibin B. Their results showed that a pronounced decrease in inhibin B that was related to testicular density (2), but the results of the present study is not consistent with their study.

Dadfar et al. in 2010 concluded that the size of the testes remained constant before and after surgery, which is consistent with the results of the present study (9).

In their study, the count, morphology and motility of the sperm had a postoperative recovery, but in our study there was no significant difference in the semen analysis. Moreover, inhibin B was not significantly different before and after surgery in terms of the size of the testes.

In this study, the duration of infertility had no effect on semen analysis and inhibin B. In none of the previous studies, the duration of infertility was not investigated. Finally, in this study, the improvement of sperm motility (as one of the semen analysis parameters) was consistent with the results of the study by Pierik and Dibiscyulie (8) Ozdeng (10), but was not consistent with the results of the study by Dadfar (9) and Turkicilmaz Z (11) in 2010 that stated Varicocelectomy had not an effect on sperm motility.

In this study, the serum levels of Inhibin B increased after Varicocelectomy that is consistent with the results of Pierik and Dibiscyulie (8) and Beesar (12), but was not consistent with the study by Fuji Sava et al. (6). The serum levels of T in this study was reduced after surgery, but in Pierik (8) and Nowroozi (13) Vernaev V (14) Balleca JL (15, 16), no changes in serum testosterone levels were observed after surgery.

Also, in this study, there was a significant increase in Inhibin B in patients who were infertile after surgery, which has not been studied in previous studies.

5. Conclusion:

The results of this study on 40 patients indicate that Varicocelectomy can improve sperm motility and increase inhibition B as a result of the improvement of spermatogenesis parameters. Also, the factors affecting Varicocelectomy are not limited to these causes, and other factors such as the size of the testes and Varicocele grade and other underlying and environmental diseases also play an important role in Varicocelectomy; complementary research by taking into account new factors can represent these effects.

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7. Conflict of interest

There is no conflict of interest in the current study.

8. Funding source

The authors declare that there are no sources of funding.

9. Author contribution

All the authors have the same contribution.

10. Reference

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