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Research Paper

The Effect of Varicocelectomy on Sex Hormone Levels and Semen Parameters

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ABSTRACT

Objectives: Varicocelectomy is a surgical intervention to treat varicocele. It may recover fertility in men by improving semen parameters and sex hormones. This research studied the role of varicocelectomy, focusing on semen properties and sex hormones.

Methods: In this cross-sectional study, the data were collected from 45 patients with different varicocele grades who underwent varicocelectomy. The data were collected and compared before and after clinical examination.

Results: After varicocelectomy, a significant improvement was observed in certain semen parameters, such as motility and concentration. However, among sex hormones, only testosterone increased after the surgical intervention (P=0.007).

Discussion: To our knowledge, varicocele treatment may almost improve male fertility. Accordingly, varicocelectomy positively affects parameters such as testosterone and serum FSH levels and sperm count and motility. As such, varicocelectomy emerges as a practical approach to improve male fertility and sex disorders.

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Introduction

Male infertility is a highly prevalent disorder, with several factors involved, the most important of which is varicocele. It can be considered an essential factor in causing the early testicular disorder, marked by an obstruction in the genital tract [1]. Varicocele is a complication caused by the anomalies of veins inside the testicles, resulting in the blockage of blood and subsequent swelling [2]. An overall prevalence of varicocele varies between 15% and 45% in men, with clinical manifestation typically appearing at puberty. The prevalence is estimated to be about 1% before adolescence, increasing to 2% to 16% in adolescence and peaking at 20% by age 15 [3]. Several underlying factors have been reported, including oxidative stress, hypoxia, and hormone imbalance. The primary mechanism responsible for varicocele-induced damage is attributed to DNA injury in the sperm head due to oxidative stress (with high levels of active oxygen species) or reduction of the total antioxidant capacity [4].

Moreover, varicocele progression during adolescence may harm the male reproductive system. Varicocele may increase or decrease in testis size [5]. Once varicocele occurs, prominent features, such as reduced sperm count, decreased testosterone levels, and diminished size (in the same area), are often observed [6]. Varicocele can be associated with a distinct or obscure pain in the testicles or the groin [7]. Other symptoms include a heavy testicular sensation, testicular atrophy, benign prostatic hyperplasia, and other urinary problems [8].

The underlying factors for varicocele are not fully known. Suggested contributors include hyperthermia, testicular blood flow, intravenous pressure, hormonal disorders, renal reflux, autoimmune disorders, and oxidative stress [9]. Hormonal disorders, such as testosterone hormone fluctuations, have been reported in varicocele [10]. Surgical treatment through varicocelectomy can affect serum testosterone levels in the affected cases.

Besides, affected men are at a risk of androgen deficiency [11]. Several studies have shown that varicocelectomy can significantly correct sperm parameters and sex hormones, including the serum testosterone level [12]. Varicocelectomy is a surgical procedure to improve fertility in men. This surgical procedure aims to treat varicocele by preventing the intravenous drainage of the reflux into the testicle and maintaining arterial flow and lymph drainage [13]. Evidence shows that varicocelectomy can improve postoperative testosterone levels, with a concomitant facilitative (and somewhat satisfactory) impact on sperm parameters [14]. We aimed to investigate the effect of microsurgical varicocelectomy on sex hormones in affected men. This study assessed the role of varicocelectomy, focusing on semen properties and sex hormones.

Materials and Methods

The present cross-sectional study was conducted in Bandar Abbas City, Iran, from December 17 to March 15, 2019. The study included male patients aged between 22-40 years. A total of 45 patients with varicocele Grade 2 or above, presenting at the Infertility and Urology Center with complaints of infertility or genital pain, underwent examination by a urologist. After diagnosis, patients with a complete medical history, physical examinations, and hormonal profiles were included in the study. After signing an informed consent letter, a demographic profile and clinical data were collected for each patient. The exclusion criteria were affliction with conditions such as testicular atrophy, genitourinary infection, cryptorchidism, testicular trauma, post-genital surgery, hyperprolactinemia, testosterone replacement therapy or antiestrogen, aromatase inhibitors, uncontrolled diabetes, and hypertension. The varicocele grade was determined based on Dubin and Amelar's system.

In grade 1, or low intensity, varicocele is not palpable while examining the testicles but becomes palpable after the Valsalva maneuver. In grade 2 or moderate intensity, varicocele is not visible but is palpable without a Valsalva maneuver, and in grade 3, it is visible through the scrotum without a Valsalva maneuver [15].

Microsurgical varicocelectomy was performed by the method described by Zini et al. [16]. The internal and external spermic vessels were blocked while keeping the elliptic and lymphatic arteries open. Sperm samples were collected through self-stimulation after 3 days of abstinence. Semen analysis assessed parameters such as concentration, viability, motility percentage, sperm shape, and morphology based on World Health Organization (WHO) criteria.

An endocrinologic evaluation was done for serum testosterone levels, FSH, and LH evaluation, followed by electrochemiluminescence. The spermogram data and preoperative sexual hormone values were compared with the data 6 months after varicocelectomy. The data were analyzed in SPSS software, version 16 through paired-sample t-test and Wilcoxon test. $P<0.05$ were considered the significant data interpretation level.

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Results

In this study, 45 male participants with varicocele were included. Their mean age was 29.5±5.7 years. The demographic data showed that 26.7% of patients had a smoking history, and 22.2% reported consanguinity with their spouses (Table 1).

The results showed that most participants (86.7%) had varicocele grade 2, with only 13.3% presenting with varicocele Grade 3 (Table 2).

According to the results, the mean follicle stimulating hormone (FSH) level before and after the intervention was 9.83±11.75 IU/L and 8.72±10.04 IU/L, respectively (Table 3). The Wilcoxon test results showed no statistically significant difference between these two phases (P=0.069). Similarly, the mean luteinizing hormone (LH) levels before and after the intervention were 6.55±4.25 and 7.07±6.20 IU/L, respectively, with no statistically significant difference observed (P=0.820). Additionally, the mean prolactin levels before and after the intervention were 373.70±180.08 and 342.43±284.25 µIU/mL, respectively, without statistically significant difference (P=0.670).

The results showed that the mean testosterone levels were 3.02±1.33 and 4.06±1.51 ng/mL before and after the intervention, respectively, presenting a statistically significant difference (P=0.007).

The results showed that the mean volumes of semen, before and after the intervention, were 2.32±1.32 and 3.15±1.22 mL, respectively. The difference between the pre-test and post-test was not statistically significant (P=0.054). Also, the pH value remained constant at 7.8 before and after the intervention.

Based on the results, the mean progressive motility was 33.87%±23.34% before the intervention and 40.95%±21.31% after the intervention, with no statistically significant difference between these two phases (P=0.136). According to the findings, the mean sperm motility index was 108.53±104.66 before the intervention, changing to 104.40±72.56 after the intervention. The difference between the pre- and post-test was not statistically significant (P=0.053).

Table 1. Distribution of demographic data

Personal Data		Mean±SD/No. (%)
Age (y)		29.5±5.7
Consanguinity	Yes	10(22.2)
	No	35(77.8)
Family history of infertility	Yes	6(13.3)
	No	39(86.7)
Smoking	Yes	12(26.7)
	No	33(73.3)
Addiction	Yes	6(13.3)
	No	39(86.7)

Table 2. Distribution of varicocele status

Varicose Status		No. (%)
Grade	2	39(86.7)
	3	6(13.3)
Position	Left	39(86.7)
	Bilateral	6(13.3)

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Table 3. Sex hormone profile before and after intervention

Hormones	Mean±SD			P
	Before	After	Difference	
FSH (IU/L)	9.83±11.75	8.72±10.04	1.11±3.99	0.069
LH (IU/L)	6.55±4.25	7.07±6.20	0.52±3.71	0.820
Prolactin (µIU/mL)	373.70±180.08	342.43±284.25	31.27±278.47	0.670
Testosterone (ng/mL)	3.02±1.33	4.06±1.51	-1.04±1.29	0.007*

FSH: Follicle stimulating hormone; LH: Luteinizing hormone.

*P<0.05.

Furthermore, the mean total sperm motility was 58.77±70.13 million before the intervention. However, it increased to 64.68±74.08 after the intervention (P=0.001). The results also showed that the mean total functional sperm concentrations before and after the intervention were 40.09±50.39 and 42.06±51.26 million, respectively (Table 4), showing a statistically significant difference (P=0.003).

Discussion

Varicocele can adversely affect spermatogenesis by increasing testicular temperature and refluxing toxic metabolites [17]. Varicocelectomy is a surgical intervention for treating male infertility in male adults and adolescents. Moreover, it treats testicular hemorrhage and hypogonadism and improves sex hormones such as testosterone [18]. The present study demonstrated that varicocelectomy may have therapeutic effects on infertile patients. Our finding showed that testosterone level was 3.01 ng/mL before surgery, but after surgery, a significant elevation of up to 4.06 ng/mL was observed (P=0.007). Several studies reported that men with total testosterone below 400 ng/dL (4 ng/mL) exhibited higher serum testosterone levels than those with normal total testosterone [19]. However, other studies showed no significant increase in testosterone levels after varicocelectomy [20].

Table 4. Semen parameters before and after the intervention

Variables	Mean±SD			P
	Before	After	Difference	
Semen volume (mL)	2.32±1.32	3.15±1.22	0.83±1.53	0.054
pH	7.80±0.00	7.80±0.00	0.00±0.00	---
Total alive concentration (10^6/mL)	39.39±43.67	33.54±29.65	5.85±43.86	0.613
Progressive motility (%)	33.87±23.34	40.95±21.31	-7.08±17.32	0.136
Normal morphology (%)	26.27±13.92	30.07±12.98	-3.80±11.78	0.232
Motile sperm concentration (10^6/mL)	21.93±31.01	24.00±31.49	-2.07±1.48	0.001*
Functional sperm concentration (10^6/mL)	18.72±24.07	20.55±25.55	-1.83±1.65	0.001*
Sperm motility index	108.53±104.66	104.40±72.56	4.13±57.20	0.053
All sperm (million)	100.97±117.05	110.38±121.93	-9.41±13.47	0.001*
Total motile sperm (million)	58.77±70.13	64.68±74.08	-5.91±5.55	0.001*
Total functional sperm concentration (million)	40.09±50.39	42.06±51.26	-1.97±2.08	0.003*

*P<0.05.

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In addition, similar results have been obtained in other studies [21, 22]. Resorlu et al. did not report any change in serum total testosterone levels in infertile patients after surgery. This finding was consistent with the study by Such et al. Consequently, this surgery may decrease the odds of abnormalities in the Leydig cells. These researchers showed that age is not a significant contributor to varicocelectomy surgery and the high success rate across different ages [23]. However, varicocelectomy in older patients with hypogonadism has been ended with more satisfactory results [19].

In another study by Ishikawa et al., it was noted that the serum testosterone levels are insufficient to estimate elliptic androgens' production. While the serum testosterone level was normal in patients with varicocele, the production of elliptic testosterone decreased in patients with varicocele. In this study, the increased serum-free testosterone levels after varicocelectomy could increase sperm concentration and motility [24]. There is no significant relationship between the mechanism showing how varicocele affects testosterone synthesis. However, the mechanisms that might underlie the reduced activity of 17 and 20 desmolase and 17 a-hydroxylase and disrupted enzymes could increase the testicular temperature and disorder the Leydig cell response to defective gonadotropin stimulation [25].

Also, the varicocelectomy and its effect on sperm parameters were evaluated in this study. Three studies identified a significant correlation between the correction of some sperm parameters after varicocelectomy. For instance, in the total motility parameter, the amount of movement before the intervention was 58.77 million, and after the intervention, 64.68 million (P=0.001). The total functional sperm concentration (P=0.003) was 40.09 before the intervention and increased to 42.06 after the intervention. In this study, the total concentration of sperm movement before was 21.93 and reached 24.00 after the intervention. The difference was statistically significant. Varicocelectomy can play a corrective role in the performance of sperm parameters. Several studies showed that sperm motility can be significantly increased compared to preoperative surgery. At the same time, the correction of morphology and count did not reveal any statistically significant differences [26].

In another study by Chu et al., varicocelectomy affected several sperm parameters. In this study, the total motile count was significantly increased and improved. The count was 2.8 million before the surgery, reaching 18.2 million after the varicocelectomy [27]. Shabana et al. also reported that varicocelectomy could significantly change and increase the density and progression of sperm motility [28].

In contrast, the FSH and LH hormones did not change significantly, and the observed alterations in these hormones were minimal. Furthermore, the upward trend of testosterone was also effectively increased [28]. Other studies have shown that FSH and LH were significantly reduced in patients with hypogonadism, which may be due to an increase in total testosterone levels due to the improved function of Leydig cells in the follow-up. Previous studies did not show a specific effect of varicocelectomy on serum LH, even when the mean serum total testosterone improved [21]. Leydig cell disorder leads to an increase in FSH and LH in infertile men with varicocele. Fujisawa et al. (2006) maintained that patients undergo varicocelectomy with decreased FSH and LH levels [29].

In our study, the level of FSH and LH before and after varicocelectomy also changed. However, the difference was not statistically significant, and the level of FSH before and after surgery was 9.83 and 8.72 IU/L, respectively, similar to other studies. However, the LH levels before and after the surgery were 6.55 and 7.07 IU/L, respectively, which is not consistent with previous studies. Chen et al. showed that the essential factor to ascertain the success of varicocelectomy is the low serum FSH concentration [30].

On the contrary, Chen et al. showed no significant difference in FSH levels and fertility rates after varicocelectomy [30]. Fuping Li reported that the mean serum testosterone level increased after varicocelectomy surgery, accompanied by a decrease in the level of FSH and LH after surgery. This pattern aligns with the negative feedback mechanism of the hypothalamic-pituitary-gland axis [31]. Kaneko et al. showed that after varicocelectomy, sperm volume increased in adolescents and adults. In patients with improved sperm volume, FSH level was significantly reduced. The serum FSH levels may play a predictive role in post-surgery testicular function [32]. Su et al. reported that although varicocelectomy improved serum testosterone, no difference was seen between serum FSH and LH levels or the relationship between varicocele grade and serum testosterone levels. Also, in terms of semen parameters, sperm motility was significantly increased compared to the sperm count after surgery, which can be explained by the recovery of testosterone synthesis needed for epididymis function [33].

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In another study, Fujisawa showed that the quality of sperm increased in varicocele patients after varicocelectomy, but no significant difference was found in testosterone levels [34]. In a study by Plymate et al. on patients with varicocele, a significant increase was seen in serum FSH before surgery, and the quality of semen was impaired, too. When the serum FSH levels decreased, the function of Sertoli cells could be improved, which results from surgery [35].

A proposed hypothesis regarding the effective role of varicocelectomy suggests a post-surgical improvement of testicular environmental temperature [36]. Increasing the testicular scrotum temperature decreases the concentration of 5αreductase, associated with converting testosterone to 5α-dihydrotestosterone, potentially causing complications for varicocele in patients. Varicocelectomy corrects this problem [37]. The Leydig cell function is to produce testosterone under the control of LH. FSH initially develops testosterone production. This process protects LH, and this function requires the regular operation of the hypothalamic-pituitary-gland axis [38].

In our study, it has been shown that varicocelectomy, as in most previous studies, has a statistically significant positive effect on testosterone. Moreover, our study results were consistent with most other results regarding the FSH hormone, although this observation was not significant. In the sperm parameter analysis, our study showed a significant positive effect on sperm motility after the surgery.

It should be noted that the present research faced several limitations, such as the lack of cooperation by some patients, the need to substitute them with other cooperative patients, and the time-consuming and exhaustive duration of research. To obtain more comprehensive information, it is recommended to conduct cohort studies.

Conclusion

In light of the present findings, varicocelectomy positively affected parameters such as serum testosterone, FSH levels, sperm count, and motility. Varicocelectomy is an effective intervention to improve fertility and sexual dysfunction in infertile men.

Ethical Considerations

Compliance with ethical guidelines

The present study was approved by the Ethics and Human Rights Committee of Hormozgan University of Medical Sciences (Code: IR.HUMS.REC.1394.193).

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Authors' contributions

Study design and administration: Soghra Fallahi; Data collection, manuscript draft preparation: Ali Mohammad Falahati; Data collection: Mohammad Mohajer-Bastami and Elahe Taqvaee; Clinical examination: Mohammad Natami; Experiments: Alireza Sobhani; Resources, review and editing: Masoomeh Latifi.

Conflict of interest

The authors declared no conflict of interest.

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