Relationship between the number of veins ligated in a varicocelectomy with testicular volume, hormonal levels and semen parameters outcome

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Purpose: Correlate semen analysis, hormones, and testicular volume with the number of veins ligated.

Methods: Patients were divided into three groups: Group 1 (≤ 5 veins), Group 2 (6–10 veins), and Group 3 (> 10 veins). We evaluated testicular volume, hormonal levels, sperm concentration, and motility before and after the surgical procedure.

Results: In Group 1, even though there was an improvement in both testicular volume and sperm concentration; testosterone levels and sperm motility did not improve with surgery. In Group 2, no changes were detected in the both testicular volumes, in sperm concentration, motility, and testosterone levels. In Group 3, an improvement was seen in the right testicle volume, testosterone levels, and sperm concentration. Follicle-stimulating hormone levels decreased following the surgical procedure in all groups.

Conclusion: Patients with more than 10 ligated veins have better chances to improve sperm concentration. FSH levels decreased in all groups of patients.

KEY WORDS: Hormone; semen; spermatozoa; testicle; veins.

INTRODUCTION

A clinical varicocele is observed in 10–20% of the general population, in 35–40% of men with primary infertility and in up to 80% of men with secondary infertility (1–4). The effects of the varicocele vary but may often result in a generalized impairment of sperm production, characterized by abnormal semen quality, ranging from oligospermia to complete azoospermia (5). A few reports have independently found that varicocele repair in men with azoospermia and severe oligoasthenozoospermia resulted in

the induction or enhancement of spermatogenesis in 40–60% of the patients, thus demonstrating the benefit of performing a varicocele repair in men with azoospermia (5–9).

The exact mechanism by which an incidental varicocele becomes pathological remains unclear. Varicoceles may produce a gradual temporal loss of normal spermatogenesis over time as a result of raised intratesticular temperatures and subsequent progressive germ cell injury or loss (10,11). Recently, studies have demonstrated the role of oxidative stress in men with varicocele and infertility (11–13).

Many reports have correlated hormonal levels, testicular volume, specific biochemical parameters, and preoperative clinical grade with the improvement following a varicocele surgical repair (14–16). In addition, even though studies have shown that semen parameters are poorer preoperatively in men with large varicoceles and their response to operations

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are more dramatic, there are no correlation between the semen parameters outcome following varicocelectomy and the number of veins ligated during the surgical procedure. For instance, only one study has correlated the preoperative clinical grade of a varicocele with the number of veins discovered and ligated during a microsurgical subinguinal repair (17). Belani and Naughton (2002) showed that lower grade varicoceles tend to have a greater number of small veins and total veins compared to higher grade varicoceles, which tend to have more medium and large size veins at surgery (17). Unfortunately, this study did not correlate the number of veins ligated and the semen quality afterwards. Even though little difficulty is encountered in the identification of large or moderate-sized varicoceles, discordance between investigators may occur. For instance, a grade II varicocele for one investigator may be classified as grade III for another one. Therefore, criteria such as the number of veins ligated may be more reliable for comparisons than grade of varicocele.

The goal of our study was to correlate semen analysis, hormonal levels, and testicular volume before and after varicocele repair procedures with the number of veins ligated in an attempt to determine how the number of dilated veins influence the outcome following the surgical correction.

MATERIAL AND METHODS

This study was approved by the University of São Paulo review board and all patients granted informed consent. From September 2000 to December 2001, 61 varicocelectomies were performed for fertility purposes and the number of veins ligated counted in a prospective way. All these men had primary infertility. The mean age of the wife at presentation was 29.8 ± 6.96 years. All women were normal based on history, hormonal levels, and hysterosalpingogram. The minimum duration of infertility required was defined as a failure to establish a pregnancy within 1 year with unprotected intercourse. A basic infertility evaluation including a detailed history and a complete physical examination was undertaken. Only varicoceles identified on physical examination were included. Patients who were taking antioxidants like vitamin C and E were excluded from the study.

The testicular size was evaluated in all patients with a caliper or by scrotal ultrasound. Mean preoperative right testicular volume was 18.77 ± 8.37 cc

and left testicular volume was 18 ± 10.49 cc. Mean preoperative follicle-stimulating hormone levels were 7.09 ± 6.38 mIU/mL, and total testosterone levels were 619.65 ± 203.23 ng/dL.

All patients had at least two semen analyses obtained by masturbation after 2–5 days of abstinence before the surgery. Three patients with pyospermia were treated before varicocele repair. A microsurgical sub-inguinal approach was performed in 38 patients and conventional inguinal technique in 23 patients. Of the 61 varicocelectomies, 29 were unilateral (3 grade I, 6 Grade II, and 20 grade III) and 32 bilateral (2 were bilateral grade I, 14 had a left grade II, and right grade I/II; and 16 had a left grade III varicocele and grade I/II/ right varicocele. Two new semen analyses were performed on each patient at 6 and 12 months postoperatively. In the tables, we report the last semen analysis obtained for comparisons between before and after surgery.

Patients were divided into three groups according to the number of vein ligated during the procedure: Group 1 (≤ 5 veins; $n = 28$), Group 2 (6–10 veins; $n = 21$), and Group 3 (>10 veins; $n = 12$). We evaluated in each group right and left testicular size, follicle-stimulating hormone (FSH) and total testosterone levels, sperm concentration and motility before and after the surgical procedure.

Statistical Analysis

Values are presented as the mean $\pm$ SD, with Student's *t*-test and the Wilcoxon paired test used for statistical evaluation. A value of $p < 0.05$ was considered statistically significant. Statistical calculations were performed with computer software (Statistical Package for Social Sciences, version 10.0—SPSS inc., Chicago, IL, USA).

RESULTS

In Group 1, even though there was an improvement in left (16.47 ± 3.4 to 20.61 ± 2.6) and right testicular volume (17.0 ± 3.5 to 20.4 ± 2.9) ($p < 0.05$), and a decrease in FSH levels (9.5 ± 2.4 to 6.1 ± 2.6 ; $p = 0.04$), and sperm concentration (38.87 ± 13.2 million/mL to 22.09 ± 8.5 million/mL; $p = 0.03$); testosterone levels (600.3 ± 73.2 to 609.9 ± 93.1) and sperm motility did not change with the surgical procedure ($45.9 \pm 22.3\%$ to $42.8 \pm 21.3\%$) (Table I).

In Group 2, no changes were seen in the left (19.42 ± 3.2 to 17.54 ± 2.6) and right testicular

Table I. Variables Assessed in Group 1 (≤ 5 Veins Ligated)

Variables	Before surgery	After surgery	<i>p</i>
FSH	9.5 $\pm$ 2.4	6.1 $\pm$ 2.6	0.04
Total testosterone	600.3 $\pm$ 73.2	609.9 $\pm$ 93.1	0.09
Left testicle (mL)	16.47 $\pm$ 3.4	20.61 $\pm$ 2.6	0.04
Right testicle (mL)	17.0 $\pm$ 3.5	20.4 $\pm$ 2.9	0.04
Sperm concentration ($\times 10^6$ /mL)	38.87 $\pm$ 13.2	22.09 $\pm$ 8.5	0.03
Sperm motility (%)	45.9 $\pm$ 22.3	42.8 $\pm$ 21.3	0.09

Note. Comparisons were made before and after surgery.
 $p < 0.05$ was considered significant.

volume (20.3 $\pm$ 2.8 to 21.6 $\pm$ 4.1), sperm concentration (13.4 $\pm$ 4.6 million/mL to 12.9 $\pm$ 5.9 million/mL), sperm motility (35.4 $\pm$ 14.6% to 43.7 $\pm$ 18.3%) and testosterone levels (654.1 $\pm$ 89.2 to 719.9 $\pm$ 102.1). However, FSH levels decreased (9.1 $\pm$ 2.7 to 5.7 $\pm$ 3.2; $p = 0.04$) in Group 2 (Table II).

In addition, in Group 3, an improvement was seen in the right testicular volume (23.5 $\pm$ 2.9 to 27.2 $\pm$ 4.9; $p = 0.04$), left testicular volume (17.49 $\pm$ 25.28 $\pm$ 4.7; $p = 0.04$), testosterone levels (628.4 $\pm$ 89.4 to 727.3 $\pm$ 101.4; $p < 0.05$), and sperm concentration (13.28 $\pm$ 7.2 million/mL to 37.45 $\pm$ 13.2 million/mL; $p = 0.04$). Also, FSH levels decreased following the surgical procedure (8.17 $\pm$ 2.4 to 6.1 $\pm$ 2.1) and sperm motility did not change after the varicocelectomy (39.7 $\pm$ 14.3%–41.55 $\pm$ 15.7%) (Table III).

DISCUSSION

Left idiopathic varicocele has been shown to induce infertility in the male population and its surgical correction can improve the prospect of eventual fertility in the future (3,18,19). In current medical practice, a decrease in sperm count, sperm motility and morphologically normal spermatozoa with an increase in head abnormalities suggests that

Table II. Variables Assessed in Group 2 (6–10 veins ligated)

Variables	Before surgery	After surgery	<i>p</i>
FSH	9.1 $\pm$ 2.7	5.7 $\pm$ 3.2	0.04
Total testosterone	654.1 $\pm$ 89.2	719.9 $\pm$ 102.1	0.08
Left testicle (mL)	19.42 $\pm$ 3.2	17.54 $\pm$ 2.6	0.07
Right testicle (mL)	20.3 $\pm$ 2.8	21.6 $\pm$ 4.1	0.08
Sperm concentration ($\times 10^6$ /mL)	13.4 $\pm$ 4.6	12.9 $\pm$ 5.9	0.09
Sperm motility (%)	35.4 $\pm$ 14.6	43.7 $\pm$ 18.3	0.09

Note. Comparisons were made before and after surgery.
 $p < 0.05$ was considered significant.

Table III. Variables Assessed in Group 3 (> 10 Veins Ligated)

Variables	Before surgery	After surgery	<i>p</i>
FSH	8.17 $\pm$ 2.4	6.1 $\pm$ 2.1	0.04
Total testosterone	628.4 $\pm$ 89.4	727.3 $\pm$ 101.4	0.03
Left testicle (mL)	17.49 $\pm$ 3.4	25.28 $\pm$ 4.7	0.04
Right testicle (mL)	23.5 $\pm$ 2.9	27.2 $\pm$ 4.9	0.04
Sperm concentration ($\times 10^6$ /mL)	13.28 $\pm$ 7.2	37.45 $\pm$ 13.2	0.04
Sperm motility (%)	39.7 $\pm$ 14.3	41.55 $\pm$ 15.7	0.09

Note. Comparisons were made before and after surgery.
 $p < 0.05$ was considered significant.

a varicocele may be present (3). In addition, improvement in semen parameters has been significant following varicocelectomy and related to varicocele size (14,15).

The apparent predisposition for the development of varicoceles on the left side may be explained by the anatomy of the internal spermatic system (4,11). The left internal spermatic vein drains perpendicularly into the left renal vein, taking a course longer than the right internal spermatic vein, which inserts into the vena cava at an oblique angle (20,21). Increased hydrostatic pressure within the left internal spermatic vein may result from the angle of insertion into the left renal vein and from compression of the left renal vein between the superior mesenteric artery and aorta. The absence of valves within the left internal spermatic vein in cadavers with varicoceles and the presence of numerous valves within the internal spermatic vein in cadavers without varicoceles may contribute to the pathology associated with varicocele. Besides, the absence of valves was less common in the right internal spermatic vein (20,21).

There is growing evidence that patients with varicocele-induced oligoasthenoazoospermia and even azoospermia may benefit from varicocele repair (5–9). It should be noted that once sperm is detected in the semen analysis after the varicocelectomy, patients need to be warned of the possibility of relapse and offered the option of sperm cryopreservation (5).

Sofikitis and Miyagawa observed that the surgical repair of an experimental varicocele in the rabbit can significantly improve the parameters indicating the harmful effects of the varicocele on the testicles (22). In addition, while studying animal models researchers had observed that the surgical repair of the secondary right varicocele improved all semen parameters indicating the harmful consequences

of the primary induced left varicocele on the right testis (23). Therefore, it appears that the primary left varicocele leads to a development of a secondary right varicocele due to activation of a tension reception within the wall of the left testicular vein.

Men with large varicoceles have poorer preoperative semen quality but demonstrate greater postoperative improvement compared to those with small or medium varicoceles. Then the take home message is that, bilateral surgical repair is indicated for bilateral large varicoceles. However, Scherr and Goldstein recently demonstrated that bilateral varicocelectomy resulted in significantly greater improvement in postoperative seminal parameters than unilateral repair in patients with grade II to III left varicocele associated with grade I right varicocele (24). The authors concluded that even a small, unrepaired palpable right varicocele continued to have a detrimental effect on bilateral testis function. Therefore, men with palpable varicoceles require bilateral repair.

A recent study showed that in infertile couples undergoing intrauterine insemination, where the female evaluation is normal and the male has a varicocele, pregnancy and live birth rates are significantly higher if the man has varicocele treatment (25). The authors conclude that men should be screened for varicocele before intrauterine insemination is initiated for male factor infertility. It seems that a functional factor not measured in routine semen analysis may affect pregnancy rates.

According to Shiraishi, although the diameter of the spermatic veins measured directly during operation correlated well with clinical grade, it is the diameter of veins and patient's age at operation, and not clinical stage, that determine the reversibility of testicular injury following varicocelectomy (26). Recently, Belani and Naughton showed that lower grade varicoceles tend to have a greater number of small veins and total veins compared to higher grade varicoceles, which tend to have more medium and large size veins at surgery (17). This is an important observation but, at the same time, obvious. If a clinician is able to detect a grade III varicocele in the physical examination, more visible dilated veins are present and the probability to have larger veins is higher compared to patients with only grade I varicocele. In addition, the authors did not evaluate the semen quality outcome following the varicocelectomy based on the diameter of the ligated veins and/or number of ligated veins.

The focus of our study differed from others. In fact, we were interested in evaluating semen quality after

varicocelectomy according to the number of ligated veins and not to the grade of varicocele. In our series of patients, sperm concentration increased only in patients with more than 10 veins ligated. The reason why sperm concentration decreased in patients with less than five ligated veins is unknown. One of the possible reasons could be the low grade (mainly grade I) of varicoceles in this group (data not shown). Another reason could be that, in this particular group of patients, the varicocele was not the reason for male infertility and another cause for semen quality impairment could be present.

Interestingly, testicular volume increased in patients with five or less veins and more than 10 ligated veins, proving that varicocelectomy may improve testicular volume. However, the reason why in patients with 6–10 veins ligated, did not increase their testicular volume is unknown.

In our study, FSH levels decreased in all groups of patients, showing that, irrespective of the number of veins ligated in the varicocele repair, testicular function may improve after treatment. However, testosterone levels increased solely in patients with more than 10 ligated veins. Probably, the damage caused by varicocele in testosterone levels may be reversed only when there is an important amount of dilated veins causing pathophysiological effects of the varicocele on testicular and/or hormonal functions.

Most of the studies in the literature show that improvement in sperm motility may occur following a varicocele repair. However, this was not the case in our series of patients. The reason why sperm motility did not change across the different groups after surgery is not known.

In conclusion, patients with more than 10 ligated veins during the surgical procedure have better chances to improve sperm concentration compared to patients with less veins to be ligated. Irrespective of the number of veins ligated, FSH levels decreased in all groups of patients. The decrease in sperm concentration following the varicocelectomy seen in Group 1 may only represent that the varicocele is not the reason for the male infertility in this group of patients.

CONCLUSIONS

In conclusion, patients with more than 10 ligated veins during the surgical procedure have better chances to improve sperm concentration compared to patients with less veins to be ligated. Irrespective

of the number of veins ligated, FSH levels decreased in all groups of patients. The decrease in sperm concentration following the varicocelectomy seen in Group 1 may only represent that the varicocele is not the reason for the male infertility in this group of patients.

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