

EFFECTS OF VARICOCELECTOMY ON TESTIS VOLUME AND SEMEN PARAMETERS IN ADOLESCENTS: A RANDOMIZED PROSPECTIVE STUDY

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ABSTRACT

Because the treatment of a varicocele in adolescents remains controversial, we undertook a prospective study in 51 male adolescents, aged 15–21 years, who were referred for a varicocele. Twenty-nine patients were treated with high retroperitoneal ligation of the left spermatic vein, and 22 were untreated. Eighteen healthy adolescent volunteers without a varicocele were also assessed. Testicular volume was measured using an orchimeter, and semen analyses were carried out at referral and after 1 year of follow-up. In addition, serum luteinizing hormone (LH), follicle-stimulating hormone (FSH) and testosterone levels were estimated by radioimmunoassay. Both patient groups had significantly smaller testis volumes than the controls at the outset. In the follow-up, the treated patients had testis volumes similar to those of the controls. Both testes increased significantly in volume after treatment. Although semen parameters were comparable in all groups initially, sperm concentration increased significantly after treatment of the varicocele. We concluded that varicocele treatment in adolescents leads to increased testis volume and a higher sperm concentration; however, whether early treatment will improve testicular function remains to be elucidated.

Key words: Adolescents, Preventive treatment, Semen quality, Testis volumes

INTRODUCTION

Research on varicoceles in adolescents has received insufficient attention to date; consequently, the appropriate treatment in adolescents remains undefined. Clearly, further investigation and treatment in younger patients is critical if future fertility problems are to be prevented. Several surveys on varicoceles in adolescents report an incidence ranging from 12.4% to 25.8%,^{1–6)} with a peak incidence at around 14 to 15 years of age.⁵⁾ In Oster's survey of 1072 school boys in Denmark, no varicoceles were found in 188 boys, 6 to 9 years of age.²⁾ Lyon et al. claimed an 8-year-old to be the youngest reported patient with a varicocele,⁷⁾ but Sawczuk et al. reported a varicocele in a 1.5-year-old.⁸⁾

Varicocele-associated testicular growth failure has been reported in adolescents.^{3,7,9,10)} In addition, histologic abnormalities, similar to those found in adults, have been found in testicular biopsies taken from adolescents with a varicocele.^{11–13)} The loss of testicular mass and the abnormal histologic findings in adolescents with varicoceles cannot definitely be attributed to varicoceles, and its link to future fertility problems is unknown.⁶⁾

In 1988, a Japanese group compared testicular volumes and semen parameters in a healthy group of adolescents (control) with two varicocele-treated groups of adolescents; one group by

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varicocelectomy, and the other by conservative medical treatment.¹⁴⁾ A reversal of testicular growth failure and an increase in semen quality in the surgically corrected group was reported. Although their studies suggest some beneficial effects of a varicocelectomy, these conclusions are based only on information about testis volumes and semen quality before therapy and during the follow-up in treated, untreated and healthy individuals. To gain reliable information about testicular function in young adolescents, an age-matched control group should be conducted simultaneously.

The aim of the present study was to compare testis volumes and semen qualities at intake and after 1 year of follow-up in adolescents in the control, the treated and the non-treated varicocele group.

MATERIALS AND METHODS

Patients

Fifty-seven male varicocele patients, (ages: 15 to 21 years), were evaluated at the Department of Urologys' Andrology Clinic. A group of 18 healthy male adolescents without a varicocele (ages: 14 to 20 years) served as a control group.

A medical history was obtained from all participants, and both groups underwent a physical examination. None of the participants reported previous episodes of cryptorchidism, hydrocele, testicular trauma, or underwent surgery of the urogenital tract. Varicoceles were graded according to Dubin and Amelar¹⁵⁾ into small (grade I, only palpated during Valsalva's maneuver), moderate (grade II, easily palpated without Valsalva's maneuver), or large (grade III, causing visible bulging of the scrotal skin). Testicular volumes were measured using an orchimeter according to Takihara *et al.*¹⁶⁾ The orchimeter was fitted over the stretched anterior scrotal skin excluding the head and the body of the epididymis, while the volume was measured.

Adolescents with a varicocele were assigned into two groups, untreated (Group 1) and treated (Group 2), using a random number table. Varicocele repair was undertaken using a high retroperitoneal ligation of the internal spermatic vein. All participants of the untreated and treated groups, as well as the adolescents without a varicocele (the control group), had the same pretreatment and follow-up examinations including semen analysis. All patients were informed of the nature of the study and were provided with a written description of the protocol.

Semen Analysis

Semen samples were collected after a 5-day period of sexual abstinence. Semen was obtained by masturbation during intake and the follow-up. Semen analysis was performed immediately after the ejaculated semen had been liquefied according to standard World Health Organization procedures.¹⁷⁾ During the investigation, the same laboratory and personnel were used to analyze all semen samples, and the personnel were not informed of the group to which the participants were allocated.

Hormone Measurements

Hormone measurements were performed at intake and after 1 year of follow-up. Serum luteinizing hormone (LH), follicle-stimulating hormone (FSH) and testosterone (T) levels were determined in serum samples taken between 8.00 a.m. and 9.00 a.m. Serum LH, FSH and T were measured using a commercially available double-antibody radioimmunoassay (RIA) technique. Normal range for LH, FSH and T were 1.8–5.2 IU/L, 2.9–8.2 IU/L and 270–1070 ng/dL, respectively.

Statistical Analysis

To test whether data were normally distributed, the Kolmogorov-Smirnov test was used. If a normal distribution was present, parametric tests were used; otherwise nonparametric tests were used. Analysis of variance (ANOVA) was used to compare the means of the three different groups at intake and after 1 year of follow-up with regard to testis volumes and semen parameters. The resulting P value, if significant, was further scrutinized using Duncan's multiple range test to determine which groups were significantly different from each other. The Wilcoxon signed rank test was used to compare testis volumes and semen parameters at intake and after 1 year of follow-up within each of the consecutive groups. Statistical significance was considered to be present when the P value was <0.05 . All values were expressed as mean \pm SD. Statistical analysis was performed using a commercially available software package (Systat Inc., Chicago, IL U.S.A.).

RESULTS

Testis Volume

Initially, 57 adolescents with a varicocele were randomly assigned to either the untreated group (n=28) or to the treated group (n=29). The 18 healthy volunteers were assigned to the control group. In the untreated group, 6 participants were excluded in the follow-up. Thus, the final number in the untreated group was 22. The age ranges for the untreated, the treated, and the control group were 15 to 19 (18.4 ± 0.5), 17 to 21 (18.6 ± 1.5), and 14 to 20 years (18.2 ± 1.5), respectively; the ages were not significantly different. In the untreated group, 8 of 22 (36%) had a grade I, 13 (58%) had a grade II and one (4.5%) had a grade III varicocele. In the treated group, these percentages were (12/29) 42%, (16/29) 55% and (1/29) 3.4%, respectively. The results of the testis volume measurements are summarized in Table 1. The mean left testis volume at intake was significantly smaller in adolescents with a varicocele as compared with the control group ($p < 0.03$). Although the right testis volume was also smaller in adolescents with a varicocele, this difference was not statistically significant. After the varicocele group had been treated, left testis volumes increased significantly toward volumes comparable with those found in the control group ($p < 0.002$). Although to a lesser extent, the increase in right testis volume within the treated group was also statistically significant ($p < 0.05$). The left and right testis volumes did not differ significantly at intake and after 1 year of follow-up within the untreated and control groups. After 1 year of follow-up, however, the left testis volume of the treated and control groups were significantly larger than those in the untreated group ($p < 0.03$). Right testis volumes, although smaller in the untreated group, were not significantly different after 1 year of follow-up between the three groups.

Table 1. Testis Volume of Adolescents With and Without Varicocele.

Group	Untreated (n=22)		Treated (n=29)		Controls (n=18)	
	Intake	Follow-up	Intake	Follow-up	Intake	Follow-up
Left Testis (ml)	21.0 \pm 5.2	21.5 \pm 3.8	21.0 \pm 5.2	25.2 \pm 4.8*	24.6 \pm 4.2	24.9 \pm 3.9
Right Testis (ml)	22.5 \pm 5.6	23.1 \pm 4.2	22.8 \pm 4.9	24.8 \pm 4.9#	25.2 \pm 5.9	25.6 \pm 3.6

* $p < 0.002$, # $p < 0.05$

Semen Analysis

Statistical analysis was performed on the data of the first semen sample collected during intake as well as during the follow-up period. The results of the semen analysis are summarized in Table 2. No statistically significant differences were observed between the three groups in the initially collected samples. In the treated group, a significant increase in the sperm concentration was observed ($p < 0.002$). After 1 year of follow-up, the sperm concentration in the treated group was significantly higher than that in the untreated and control groups ($p < 0.002$). All other semen parameters did not differ significantly either within or between groups at intake or during the follow-up period.

Table 2. Semen Parameters in Adolescents With and Without Varicocele.

Group	Untreated (n=22)		Treated (n=29)		Controls (n=18)	
	Intake	Follow-up	Intake	Follow-up	Intake	Follow-up
Conc.*	49.2 ± 32.1	46.3 ± 28.1	50.5 ± 28.1	73.9 ± 31.2 [#]	50.2 ± 15.6	53.1 ± 28.2
Motile Sperm (%)	53.1 ± 15.2	54.5 ± 16.2	52.1 ± 16.8	57.3 ± 18.2	53.5 ± 14.2	54.5 ± 15.8
Normal Sperm (%)	60.1 ± 13.8	61.2 ± 14.2	60.1 ± 14.2	58.2 ± 15.6	59.1 ± 15.8	58.9 ± 18.2

*Sperm concentration ($\times 10^6/\text{ml}$)

[#] $p < 0.002$

Hormone Measurement

All serum hormone levels of LH, FSH and T measured at intake and after 1 year of follow-up were within the normal range in both adolescents with and without a varicocele.

DISCUSSION

In the present prospective randomized study, a significant left testicular growth failure was found in adolescents demonstrating a left-sided varicocele as compared with an age-matched group of healthy adolescents without a varicocele. Although to a lesser extent, a similar growth retardation of the right testis was observed. Similar testicular growth failure has been reported by several authors.⁷⁻⁹⁾

Within 1 year after treatment, the left testis volume significantly increased to an extent comparable with the value found in the healthy volunteers without a varicocele. Although not significant, a similar tendency in the right testis volume could be observed in treated adolescents. Testis volumes of untreated varicocele patients remained at the same level during the 1 year of follow-up.

Though previously unappreciated, it is clear that a varicocele in adolescents is not a rare entity; therefore, it is imperative to establish its physiologic significance. Lipshultz and Corriere indicated that the presence of the varicocele was associated with a loss of testicular mass, which appeared progressive with age.¹⁸⁾ Their report first raised the question whether earlier ligation would arrest this process. Lyon and his associates also reported progressive testicular volume loss in adolescents with a varicocele.⁷⁾

VARICOCELE TREATMENT IN ADOLESCENTS

Testicular biopsies in peripubertal children with a varicocele have demonstrated similar damage, as seen in adults. Heinz et al. indicated that testicular histology was already abnormal in 12-year-old boys; more severe histologic abnormalities were seen in older adolescents.¹¹⁾ Pozza and associates examined adolescents with varicoceles, and reported a 74% incidence of testicular atrophy and a 90% incidence of abnormal histology.¹⁹⁾ Thus, histologic damage occurs early in pubertal development and appears to be progressive with time.

Most authors discuss testicular atrophy secondary to a varicocele; however, some have suggested that the varicocele-associated testicle seen in pubescence may be suffering from growth retardation.^{7,9)} This concept was suggested by Kass and Belman, who demonstrated a significant increase in testicular volume after a varicocelectomy in adolescents (ages: 11–19), which they referred to as “catch-up” growth.⁹⁾ Although no assessment of spermatogenesis was undertaken in their study, the reversal in growth retardation would indicate that the removal of a noxious stimulus results in improved testicular development. “Catch-up” growth of testes after varicocele treatment has been described by other authors.^{7,12)}

Sperm concentration did not change in the untreated and control subjects, but significantly increased in the treated group in our present study. The other sperm parameters did not change in the treated, the untreated, or the control groups. If the increase in either testis volume or sperm concentration is to be explained by late pubertal changes in testicular function, similar tendencies should be observed in the untreated and control subjects. Both the increase of testis volume and sperm concentration after treatment cannot be explained by developmental changes in testicular function; apparently, they are a real phenomena caused by varicocele treatment. It is speculated that a varicocele initially has a negative influence on the differentiation of the spermatogenic epithelium not yet accompanied by testicular growth failure. Later on, the proliferation of the spermatogenic epithelium is also compromised, resulting in left testicular growth failure. Varicocele treatment reverses this proliferation and results in catch-up growth. Subsequently, spermatogenic differentiation improves and sperm output increases. Our findings indicate that a varicocelectomy results in either the cessation of a progressive effect or the reversal of an established effect. Our controlled study appears to be constant with findings of others who have reported progressive deterioration of semen parameters in patients with untreated varicoceles.^{20,21)}

The ultimate goal of treatment of the pediatric varicocele is preservation of fertility. Existing studies do not enable us to predict which boys with varicoceles and loss of testicular volume will have impaired spermatogenesis and, ultimately, infertility. It is important to recognize that most men with varicoceles have normal fertility; only 13% of men with varicoceles will be infertile.⁶⁾ The uncertainty about the benefits in terms of future fertility and risk of recurrence or surgical complications has led most surgeons to adopt the position that the pediatric varicocele should be left untreated unless there is significant testicular asymmetry (the left testis smaller than the right by 5 mm or more) or retarded testicular growth documented on serial examination.⁹⁾ Testicular growth retardation indicating a potentially significant physiologic lesion is the only objective parameter available in this population. An additional indication for surgical intervention is a massive varicocele that is either symptomatic or disfiguring. It is less clear whether repair is indicated for an asymptomatic grade 2 or 3 varicocele with no reduction in testicular mass.

In conclusion, treatment of a varicocele in adolescents leads to increased testis volume and a higher sperm concentration; however, whether early treatment will improve testicular function remains to be elucidated. Analysis of results after a longer period of follow-up might eventually allow us to draw more definite conclusions regarding this issue.

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