Late Hormonal Levels, Semen Parameters, and Presence of Antisperm Antibodies in Patients Treated for Testicular Torsion

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ABSTRACT: In spite of prompt diagnosis and either orchiectomy or preservation of the affected testis, infertility remains a significant sequel to testicular torsion. The objective of this study was to evaluate the late endocrine profile, seminal parameters, and antisperm antibody levels after testicular torsion. We also analyzed the impact of orchiectomy or detorsion on the organ fate. Of 24 patients evaluated after testicular torsion, 15 were treated with orchiectomy (group 1) and 9 were treated with orchiopexy (group 2). All subjects were assessed by semen analysis, endocrine profile (levels of follicle-stimulating hormone, luteinizing hormone, and testosterone), and seminal antisperm antibody levels. A group of 20 proven fertile men was used as the control. Median ischemia time in group 1 (48 hours) was significantly higher than in group 2 (7 hours). Both groups demonstrated decreases in sperm count and morphology compared with controls. Group 1 showed a significantly higher motility than group 2 ($P = .02$). Group 1 also showed a significantly better morphology by World Health Organization and Kruger criteria than group 2 ($P = .01$). All patients presented endocrine profiles within the normal range, and no significant differences in antisperm antibody levels were detected between the groups. However, a trend for higher levels was found in patients treated for testicular torsion, regardless of the fate of the testis. Moreover, no significant correlation was found between antisperm antibody levels and age at torsion, ischemia time, seminal parameters, or treatment applied. In conclusion, we found that after torsion patients maintain late hormonal levels within the normal range. Testicular fate did not have any correlation with the formation of antisperm antibodies. Although sperm quality was preserved in most of the patients with the exception of sperm morphology, patients treated with orchiectomy presented better motility and morphology compared with the detorsion group. Further studies may clarify whether maintenance of a severely ischemic testicle may impair testicular function.

Key words: Infertility, function, testis.

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Testicular torsion occurs in approximately 1 out of every 4000 men before the age of 25 years (Williamson, 1976). It demands immediate surgical exploration, and the risks of nonoperative management are well documented (Watkin et al, 1996). A better salvage rate is usually achieved if surgical exploration is performed within 6 hours after the onset of symptoms. In addition to duration, other factors such as the degree of rotation have been involved with testicular salvage (Heindel et al, 1990; Arap et al, 2000).

Endocrine testicular function is expected to be normal in the event of a lost gonad. On the other hand, the exocrine testicular function (spermatogenesis) may be compromised (Cosentino et al, 1985; Lievano et al, 1999). Patients with testicular torsion seem to have bilateral abnormalities that result in decreased spermatogenesis (Krarup, 1978). It is unclear whether these abnormalities are due to an autoimmune process that occurs after the rupture of the hematotesticular barrier leading to formation of antisperm antibodies or as a result of reperfusion-induced injury to the testis (Becker et al, 1997; Lievano et al, 1999).

To date, there has been substantial difficulty in evaluating whether or not exocrine testicular function correlates with the formation of antisperm antibodies. We analyzed late hormonal levels, semen parameters, and the presence of antisperm antibodies in patients with surgical diagnoses of testicular torsion to 1) address the correlation of testicular fate and the autoimmune process, 2) evaluate late seminal parameters among patients treated with orchiopexy and orchiectomy, and 3) compare endocrine testicular function between the groups.

Methods

The University of São Paulo Institutional Review Board approved this study. All of the men provided informed consent prior to their first appointments.

The records of 64 patients who underwent surgical treatment for testicular torsion between 1989 and 2002 were analyzed. Of these, 48 were eligible to enter the study (age >16 years and no history of sexually transmitted or neurologic disease), and 24 agreed to participate in the protocol. They were thoroughly counseled about the study details and provided signed informed consent. Patients were further classified into two groups according to surgical procedure. Group 1 was composed of patients treated with orchiectomy and contralateral orchidopexy (n = 15), and group 2 was composed of patients treated with detorsion and bilateral orchidopexy (n = 9). All patients were submitted to the same evaluation, consisting of past and recent medical and urologic history and complete physical examination. Twenty voluntary men requesting vasectomy with no previous history of endocrinopathy, sexually transmitted disease, or neuropathy were included as controls. All patients and controls were evaluated according to the same protocol, including hormonal profile, routine seminal parameters, and the presence of seminal antisperm antibodies.

For the hormonal profile, blood was collected between 8 and 9 AM. Follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone concentrations were measured by standard radioimmunoassay in our in-house laboratory. The normal range established in our laboratory for each hormonal level is 200 to 950 ng/dL for testosterone, 2.6 to 7.8 UI/L for FSH, and 1.4 to 9.2 UI/L for LH. Semen was collected in the hospital by masturbation after 2 to 4 days of sexual abstinence, and seminal parameters were analyzed within 1 hour of ejaculation. All semen samples were evaluated by the same biologist for ejaculated volume, sperm concentration, morphology, motility, and forward progression. Motility and concentration were determined according to World Health Organization (WHO) criteria and morphology according to WHO and Kruger strict criteria (Kruger et al, 1988; WHO, 1992). antisperm antibodies were analyzed by an Immunobeads assay (Bio-Rad, Richmond, Calif).

All data were compared between the groups, and statistical significance of the differences was analyzed for all criteria with 2-tailed nonparametric tests (Student's *t* test). Correlations between variables were calculated using Spearman's nonparametric method. All analyses were calculated with MINITAB 14.2 (Six Sigma, Austin, Tex) and SPSS 14.0 (SPSS Inc, Chicago, Ill). $P < .05$ was considered statistically significant.

Results

Demographic Data

All patients had normal libido, potency, and virilization. Patients from groups 1 and 2 were subjected to contralateral orchiopexy in the same manner, regardless of the primary diagnosis. The median patient age at surgery was 15 years (interquartile range [ICR], 13–17) for group 1 and 15 years (ICR, 13–24) for group 2. The median follow-up (from the day of surgery until the last follow-up visit) was 6 years (ICR, 5–7) for group 1 and 10 years (ICR, 5–12) for group 2.

The left testis was affected in 73% of patients in group 1 and 55.5% in group 2. The median ischemia time (estimated from the beginning of pain to surgical treatment) was significantly higher in group 1 (48 hours [ICR, 48–120]) compared with group 2 (7 hours [ICR, 3–21]) ($P = .0015$)(Table 1).

Hormonal Levels

The mean FSH concentration was statistically higher in group 1 compared with group 2. Although statistically nonsignificant, the mean FSH level in group 2 was higher than in the controls. LH levels in patients from group 1 were significantly higher than those in controls. No significant differences were observed between groups 1 and 2 and between group 2 and the control. Mean testosterone levels were significantly higher in both groups 1 and 2 compared with the controls. No significant difference was observed between groups 1 and 2 concerning mean testosterone levels (Table 2).

Seminal Parameters

Mean sperm count was normal for all groups, and no statistical difference was observed when groups 1 and 2 were compared with the controls or each other. Three

Table 1. *Demographic data of patients submitted to orchiectomy (group 1) or orchiopexy (group 2)**

Parameters	Group 1 (n = 15) Orchiectomy	Group 2 (n = 9) Orchiopexy	P
Average age at torsion, y (ICR)	15.0 (13, 17)	15 (13, 24)	.4
Follow-up, y (ICR)	6 (5, 7)	10 (5, 12)	.14
Ischemia, h (ICR)	48 (48, 120)	7 (3, 21)	.0015

* Values are medians and interquartile ranges (ICRs; 25%, 75%). Wilcoxon rank sum test was used for the analysis and $P < .05$ was considered statistically significant.

Table 2. *Seminal profiles and hormonal levels of patients subjected to orchiectomy (group 1) or orchiopexy (group 2) and the control group**

Parameters	Group 1 (n = 15) Orchiectomy	Group 2 (n = 9) Orchiopexy	Control Group (n = 20)	P1†	P2†	P3†
Sperm count (x $10^{6)}$	38.3 (27, 128)	47 (11, 102)	99.3 (83, 166)	.65	.46	.10
Motility (%)	77 (66, 85)	54 (45, 74)	64 (59, 73)	.028	.05	.31
Kruger (%)	4 (2, 6)	1 (0, 2)	8 (4, 11)	.01	.01	<.001
WHO† (%)	18 (11, 20)	7 (4, 12)	28 (20, 31)	.01	.006	<.001
Antibodies (%)	21 (8, 29)	20 (12, 30)	14.5 (10, 21)	.861	.073	.17
FSH† (UI/L)	7.6 (5, 9)	5.6 (4, 6)	4 (3, 5)	.046	<.001	.10
LH† (UI/L)	4.3 (3 ,5)	2.6 (2, 4)	3.4 (2, 4)	.057	.01	.91
Testosterone (ng/dL)	701 (606, 870)	641 (598, 703)	440 (338, 568)	.23	<.001	.017

* Values are medians and interquartile ranges (25%, 75%). Wilcoxon rank sum test was used for the analysis and *$P < .05$ was considered statistically significant.

† FSH indicates follicle-stimulating hormone; LH, luteinizing hormone; *P*1, *P* between groups 1 and 2; *P*2, *P* between groups 1 and controls; *P*3, *P* between groups 2 and controls; and WHO, World Health Organization.

patients (21%) from group 1 and 3 patients (33%) from group 2 presented with oligospermia (Table 2). The average sperm motility was normal for groups 1 and 2. However, patients subjected to orchiectomy showed better sperm motility than those subjected to detorsion and orchiopexy. No significant difference was found when groups 1 and 2 were compared with the controls. According to Kruger criteria, mean sperm morphology was abnormal in all groups, including the controls. Moreover, patients submitted to orchiopexy had the lowest mean Kruger score (Kruger et al, 1988). Patients treated by orchiectomy had an mean Kruger score between controls and those subjected to bilateral orchiopexy (Kruger et al, 1988). According to WHO criteria, mean sperm morphology was abnormal in all groups, and again a significant difference was observed

for groups 1 and 2 compared with the controls and compared with each other (Table 2).

Antisperm Antibodies

Mean seminal antisperm antibody levels were normal for the control group and abnormal for both groups 1 and 2. However, no significant difference was observed when groups 1 and 2 were compared with the control and when compared with each other (Table 2). In addition, no significant correlation was found between antisperm antibody levels and age at torsion, ischemia time, seminal parameters, or treatment applied (Table 3).

Discussion

Testicular torsion accounts for one fourth to one third of pediatric patients presenting with acute scrotal pain (Sessions et al, 2003). To avoid testicular loss and eventual impaired fertility, prompt diagnosis and immediate surgery are the most important issues for the treatment of these patients. In our study, mean ischemia time was significantly longer for patients submitted to orchiectomy (group 1), confirming the importance of immediate diagnosis and surgical exploration for testicular torsion. Impaired spermatogenesis has been reported in animals and humans after testicular torsion (Krarup, 1978; Mastrogiacomo et al, 1982; Choi et al, 1993; Kosar et al, 1999). The three main hypotheses to explain these findings are 1) primary impaired spermatogenesis concomitant with anomalous development of the processus vaginalis in a testis prone to torsion (Anderson and Williamson, 1990), 2) an autoimmune response triggered by the rupture of the hematotesticular barrier leading to antisperm antibody formation (Mastrogiacomo et al, 1982; Choi et al, 1993;

Table 3. *Correlation of antisperm antibody levels with age at torsion, ischemia time, and sperm parameters in patients treated for testicular torsion*

Variable	Anti-Sperm Antibody Levels	
	r	*P**
Age at torsion	.36	.08
Ischemia time	−.31	.15
Sperm concentration	.14	.51
Sperm motility	.03	.87
WHO† morphology	−.26	.22
Kruger morphology	−.15	.47
FSH†	.01	.96
LH†	−.22	.33
Testosterone	.07	.75
Surgical treatment applied (orchiectomy or detorsion)	−.08	.71

* $P < .05$ was considered statistically significant (Spearman's ρ test).

† FSH indicates follicle-stimulating hormone; LH, luteinizing hormone; and WHO, World Health Organization.

Kosar et al, 1999), and 3) the result of a reperfusion-induced injury to the testis that may be related to significant increases in germ cell apoptosis due to high testicular oxidative stress following the reperfusion (Becker et al, 1997; Lievano et al, 1999; Turner et al, 2004).

Average patient age in our study was comparable to that in other series (Krarup, 1978; Anderson et al, 1992; Kosar et al, 1999). Hormonal alterations following testicular torsion have been previously described in human as well as experimental studies (Bartsch et al, 1980; Fisch et al, 1988; Turner et al, 2005). The increase in gonadotropins, mainly FSH, may be due to tubular destruction related to testicular ischemia, ultimately leading to a diminished sperm concentration. Another possible explanation is a previously undetected deficient spermatogenesis (Anderson et al, 1986). Indeed, patients who underwent orchiectomy had higher levels of FSH when compared with those submitted to detorsion and orchiopexy. In addition, this difference was even higher when they were compared with the controls. Mean LH levels were also higher in patients submitted to orchiectomy than in controls, confirming previous studies (Bartsch et al, 1980; Fisch et al, 1988). Interestingly, although there was a difference in baseline hormone levels between the two groups, all values were within the normal range. In addition, mean testosterone levels were higher for both groups 1 and 2 compared with controls. These findings suggest that endocrine testicular function is preserved in patients treated for testicular torsion, probably due to an increase in LH levels.

Several groups have reported abnormal sperm concentration and motility after testicular torsion (Bartsch et al, 1980; Mastrogiacomo et al, 1982; Anderson and Williamson, 1990). In our series, the mean sperm concentration was normal for all groups and we did not identify significant differences among them. However, there was significantly better sperm motility in patients who underwent orchiectomy compared with patients whose gonad was preserved. This could be related to the release of abnormal sperm cells by the previously ischemic testis or to the rupture of the hematotesticular barrier and subsequent formation of antibodies against sperm cells (Mastrogiacomo et al, 1982).

To compare sperm morphology, we used Kruger strict criteria and WHO morphology (WHO, 1992). All patients, including the controls, had abnormal Kruger strict criteria (Kruger et al, 1988). When the WHO criteria was used, all but one patient from group 1 and 6 patients from the control group had abnormal morphology (WHO, 1992). We found a significant difference for groups 1 and 2 when compared with controls for both morphology criteria (Kruger et al, 1988; WHO,

1992). This was particularly evident for patients from group 2 (orchiopexy), who presented with the worst morphology. Again, this may result from abnormal sperm cells derived from the preserved testis. It is of note that our results may indicate a need to re-evaluate the established normal criteria, at least in our population, as the great majority of patients from the control group also presented with abnormal sperm morphology. According to other studies, the cut-off values for morphology normality are substantially lower than those proposed by the WHO manuals (Ombelet et al, 1997; Menkveld et al, 2001). There is a strong recommendation from WHO to individualize the references for normality of semen parameters in each laboratory. Decreased morphology has been reported by other investigators following testicular torsion (Bartsch et al, 1980; Schutte et al, 1986); however, Anderson et al (1992) did not observe significant differences among patients submitted to orchiectomy or orchiopexy in regard to sperm motility or morphology.

Mastrogiacomo et al (1982) identified antisperm antibodies in the semen of patients with testicular torsion and correlated antibody levels with sterility and particularly with motility alterations. On the other hand, Fraser et al (1985) followed 47 patients from 2 to 10 years after torsion and found gonadal dysfunction but no correlation to autoimmune response. More evidence against autoimmune reaction is found in the article of Anderson et al (1992), who verified pre-existing contralateral testis abnormalities in biopsies at the time of surgery and did not detect any cases of antisperm antibodies after testicular torsion. We believe that the qualitative sperm findings in our study were not related to autoimmune responses, as we did not find significant differences regarding antibodies between groups 1 and 2.

Animal models usually show histologic lesions occurring in the contralateral testis and abnormal levels of antisperm antibodies after experimental testicular torsion (Harrison et al, 1981; Cosentino et al, 1985; Kosar et al, 1997; Kosar et al, 1999). Given these results, it has been suggested that the best procedure is to remove the affected testis (Kosar et al, 1997). However, animal models for testicular torsion do not reproduce the conditions found in humans, such as the anatomy of the testis, known to be abnormally loose inside the vaginal layer (Anderson and Williamson, 1990). We did not verify significant differences in antisperm antibody levels among any of the groups. However, there was a tendency for both groups 1 and 2 to have higher antibody values compared with the controls (Table 2). Therefore, we believe that antibody formation is not related to the maintenance or removal of the affected

testicle but possibly to an irreversible autoimmune response triggered at the moment of torsion.

The limited number of patients and cross-sectional design are the drawbacks of this study. However, the data were collected prospectively and all patients were treated with a careful follow-up and pre-established protocol; comprising the strengths of this study.

In conclusion, we presented evidence that patients treated for testicular torsion show mainly morphologic semen abnormalities and endocrine profiles within the normal range, despite the subclinical increases in FSH levels. Testicular fate did not have any correlation with the formation of antisperm antibodies. Patients subjected to orchiectomy presented with better motility and morphology compared with the detorsion group. Although these findings suggest that the maintenance of a severely ischemic testicle may impair seminal parameters, further studies may clarify whether maintenance of a severely ischemic testicle impacts testicular function.

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