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Original Article

Semen analysis in patients treated for varicocele in pediatric age: are surgical outcomes enough to preserve the fertility potential?

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Abstract: Preserving the fertility potential of adolescent patients with varicocele is still the main outcome of pediatric and adolescent urologysts; the aim of this study is to assess the fertility potential of patients treated for varicocele with testicular hypotrophy in absence of post-operative complications, with complete ipsilateral testicular catch-up growth and normal hormonal values. Methods: The Authors collected data from adolescents with varicocele aged between 10 and 16 years treated at their Institution between September 2010 and September 2015. Inclusion and exclusion criteria were created; all patients were followed clinically and with hormonal tests before and after surgery and then re-evaluated after semen analysis. Semen quality was correlated with hormonal status, surgical complications and testicular volume. Results: 133 subjects without recurrences and with testicular catch-up growth were enrolled; at surgery 52 patients had grade III varicocele, 80 had grade II varicocele and 1 patient had grade I varicocele. Surgical complications at 18 months were 6 hydroceles (2 in grade III and 4 in grade II varicocele). Semen analysis was performed on 41 patients: 75% had a good semen quality, 9.7% fairly good semen quality and 14.6% poor semen quality. Considering grade III patients (12 subjects), 7 (58%) had good quality, 3 (25%) fairly good quality and the remaining 2 (16.6%) poor semen quality. In grade II patients, 23 (79.3%) had good quality, 4 (13.7%) fairly good quality and 2 (6.8%) had poor quality (P>0.05). There was no correlation between semen quality, hormonal status and pre-operative grade of varicocele and post-operative testicular volume. Conclusions: The results demonstrate that varicocelectomy alone in well-studied and fully treated pediatric patients does not wholly preserve their fertility potential.

Keywords: Varicocele, pediatric age, semen analysis

Introduction

Idiopathic varicocele is the most frequently diagnosed peripubertal andrologic disease and the most commonly treatable cause of male-related impaired fertility potential [1].

It is now accepted that the treatment of varicocele in pediatric age should be concomitant with the onset of ipsilateral testicular hypotrophy (or testicular growth arrest) and when varicocele is accompanied by pain. Obviously, changes in semen quality are not considered as a parameter for surgery in paediatric patients, while they remain the first indication for surgery in adult patients, or as soon as patients are old enough for semen analysis [2].

The main outcome of varicocelectomy is to avoid testicular damage with secondary abnormal semen analysis; it is clear that, based on recent research about the sperm DNA damage, varicocelectomy alone cannot resolve the problem of male fertility potential [3].

Based on our recent data base, the aim of this study is to report the fertility potential status of the patients treated in the pediatric-adolescent age for varicocele, focusing on the post-operative evaluation of the semen.

Materials and methods

The data about adolescents with varicocele aged between 10 and 16 years treated at the Authors' Institution was investigated; all the patients treated between September 2010 and September 2015 were included. Oral and written consent was given by the parents and by the patients when >18 years of age. The study

was approved by the IRB of the pediatric fertility lab group (no.018).

All patients underwent surgery for ipsilateral testicular hypotrophy. Varicocele was classified as follows: grade I-palpable varicocele only with Valsalva; grade II-palpable varicocele without Valsalva; grade III-visible varicocele. Testicular hypotrophy was defined as a testicular volume loss >20% with respect to the contralateral testis, assessed using Siemens Sonoline Elegra Ultrasound Imaging System (Siemens AG, Munich, Germany) with a 7.5 MHz probe. Testicular length, width, and height were measured by electronic calipers. Testicular volume was estimated with the formula for a prolate ellipsoid: [Vol (ml) = 523 x *L* x *W* x *H*] [4].

The inclusion criteria for this study were the following: subjects with normal body mass index (BMI) and non-smokers with regular sports activity; left varicocele; testicular hypotrophy at Ultrasound (US); no previous infections of the urinary system; no previous testicular traumas nor previous inguinal or scrotal surgeries; no other metabolic disease; completed follow-up (3, 6 and 18 months after surgery).

Other parameters considered were: mean testicular volume before and after surgery for both sides, catch-up growth after surgery, hormonal value before and after surgery, surgical complications (hydrocele and recurrence). Patients with recurrences were excluded from The final analysis to avoid bias.

All patients were treated with standard "3 5-mm ports" laparoscopic approach using clips without cutting the spermatic vessels and with artery and lymphatic sparing technique.

The long-term fertility potential was assessed recording the semen quality for all the patients. The evaluation criteria for semen quality followed the indications issued by the World Health Organization (WHO; 2010). Sperm results were divided into 3 subgroups: "gGood", if the results met all the evaluation criteria, "Fairly Good" with 2 abnormal parameters and "Poor" in the remaining cases. Two semen samples, collected 3 weeks apart after 4 days of abstinence, were collected immediately after masturbation in clean plastic containers supplied by the laboratory and analyzed within 1 hour of collection. All sperm sampless were analyzed by the same laboratory. The analysis focused specifically on sperm motility, sperm concentration and count, sperm form and vitality [4].

Semen analysis

Semen specimens were collected and then immediately transferred immediately to the diagnostic semen laboratory, where they were kept at 37uC until liquefied. Sperm concentration was determined by counting 2 sides of a hemocytometer. Semen volume was measured by drawing up the entire sample into a graduated pipette. Motility was defined as the proportion of sperm that was progressively motile at 37uC measured with a Makler chamber. Sperm morphology was evaluated by a single examiner using strict criteria [5].

Hormonal assessment

Hormonal assessment (FSH: U/L range 1-14; LH U/L range 2-10; TT ng/dL range 240-950) was done before and after surgery (at the time of semen analysis).

Statistical analysis was performed using the student t-test, chi-square and Fischer exact tests. Significance value was set at $P<0.05$. The analysis was conducted with the Statistical Package for Social Sciences (SPSS) software version 15 for Windows SPSS Inc, Chicago, USA.

Results

During the study period, 133 subjects without recurrence and with testicular catch-up growth were enrolled; 52 patients had grade III varicocele, 80 had grade II varicocele and 1 patient had grade I varicocele. Surgical complications at 18 months were 6 hydroceles (2 in grade III and 4 in grade II varicocele).

Data analysis did not show statistically significant differences between pre- and post-operative hormonal values for FSH, LH and Testosterone ($P>0.05$).

None of the patients is currently showing hypogonadism nor testicular dysfunction.

In grade III patients the mean pre-operative left testicular volume was 8 ml (± 2.2 ml), while the mean right testicular volume was 10 ml (± 1.8 ml). After surgery (18 months) the mean left

testicular volume was 10 ml (± 1.5 ml), while the mean right testicular volume was 11.5 ml (± 2 ml). In grade II the mean pre-operative left testicular volume was 8 ml (± 1.7 ml), while the mean right testicular volume was 11 ml (± 2 ml). After surgery (18 months) the mean left testicular volume was 9.2 ml (± 0.7 ml), while the mean right testicular volume was 10.8 ml (± 2.1 ml). There were no statistical differences between catch-up growth after surgery, no correlation between grade of varicocele before surgery and the associated catch-up growth (P>0.05).

At 18-months follow-up, all patients had a preserved testicular artery detected on Doppler velocimetry; as described in a previous study, the semen quality of these patients is better than in those without artery sparing techniques [4].

Semen analysis was performed and recorded for 41 (31%) patients; 12 with grade III varicocele and 29 with grade II varicocele. All other patients were under 18 years of age at the last follow-up visit.

Of these 41 patients, 75% had good semen quality, 9.7% had fairly good semen quality and 14.6% had poor semen quality. In the grade III group (12 patients), 7 (58%) had good quality, 3 (25%) fairly good quality and 2 (16.6%) poor quality. In grade II patients, 23 (79.3%) had good quality, 4 (13.7%) fairly good quality and 2 (6.8%) patients had poor quality (P>0.05).

In these patients there was not a correlation between semen quality and grade of varicocele at surgery, or differences between quality distribution per group.

In the group of patients with post-operative hydrocele, 5 had good semen quality while 1 patient was classified as having fairly good quality. This means that post-operative hydrocele did not affect semen quality (P>0.05).

Motility and form were the parameters that were mainly affected in the groups with fairly good semen quality. There were not statistical differences between the groups in terms of sperm concentration or vitality (P>0.05).

Discussion

Testicular hypotrophy still remains the main clinical indication for varicocelectomy in pediatric age [6-10]. The main outcomes of varicocelectomy is to achieve normal ipsilateral testicular size, and to preserve the fertility potential. Based on different studies, the techniques preserving the testicular artery, offer a better semen quality [4].

Recent studies regarding male infertility reported that infertile men are at risk for hypogonadism, have more comorbidities as well as increased mortality. Poor semen quality is associated with body weight and metaboilic derangements; infertile men with poor semen quality seem to be at risk for metabolic syndrome, osteoporosis, higher rate of hospitalization especially for cardiovascular diseases and diabetes mellitus [11-13].

Two longitudinal studies suggested that infertile males have higher long-term morbidity; although there is no evidence of such a correlation in younger men with an impaired fertility potential. It was reported that 30% of infertile men had varicocele and that 30-35% of these patients had an abnormal semen analysis. With a range between 25 and 40% of cases, varicocele was associated with abnormal semen analysis, including Azoospermia, Isolated astheno, Isolated terato and Astheno-terato and Oligospermia. Men with low sperm count (SC) (<39 million/ejaculate) had a 12-fold increased risk of developing hypogonadism. The highest risk was observed in men with Total SC <10 million, genetic causes, history of cryptorchidism and idiopathic forms. Men with low sperm count had higher BMI, waist circumference, systolic pressure, LDL-cholesterol, triglycerides, and lower HDL-cholesterol, and higher prevalence of metabolic syndrome. The worst data were recorded from patients with low testosterone levels; somewhat better, but still worrying, were the data from men with isolated high LH values. Low Total sperm count *per sée* was associated with poor metabolic values [13, 14].

This study suggests that low sperm count is associated with poorer metabolic, cardiovascular and bone health. Hypogonadism is mainly involved in this association, but low sperm count itself is a marker for a patient's general health status. Infertile patients have the great opportunity to benefit from the accurate Identification of specific diagnostic and prognostic markers, and clinically important comorbidities and risk factors.

If varicocele is still the main cause of male infertility, all clinicians have to treat varicocele, when indicated, to preserve the fertility potential. Long-term results, as reported in this study, demonstrate that even when all the clinical parameters of an successful surgery are present (testicular catch-up growth and no recurrences), 14.6% of patients still have an impaired fertility potential. This finding is especially important for adults because many infertile males treated for varicocele still show abnormal semen analysis, which could not be simply related to varicocele. 75% of young males having good semen analysis, means that the treatment alone is not satisfactory and that these patients have to be followed till adulthood.

Another interesting finding regards the presence of post-operative hydrocele, which did not affect semen quality. This means that in cases with small or mild post-operative hydrocele, without symptoms, probably the patients should not be treated surgically. Further studies are necessary to confirm this view.

According to the data collected during this study, it is possible to point out as follows: 1) Although 75% of cases with testicular catch-up have good semen quality, many cases still show poor semen quality; 2) In adolescents there is not a correlation between normal or abnormal semen quality and hormonal values, suggesting that those cases with poor semen quality are not affected by hypogonadism; 3) An important finding of the study is that testicular catch-up growth and semen quality are independent variables. As many other studies have shown, testicular hypotrophy is not always correlated with alterations of semen quality; consequently, it seems correct to suppose that also testicular catch-up growth is not correlated with semen quality [15, 16].

What can be done for those having poor semen quality? For sure these patients need to be followed till adulthood; probably, they will require additional genetic tests to identify some genes deficit; however, generally, more than 15-20% of males are infertile without any specific cause.

In conclusion, the study results demonstrate that varicocelectomy alone in well studied [17] and fully treated pediatric patients does not completely preserves the fertility potential, although research in on the right path.

Disclosure of conflict of interest

None.

Abbreviations

US, Ultrasound; BMI, Body mass index; FSH, Follicle stimulating hormone; LH, Lutenizing hormone; TT, Testosterone; SC, Sperm count.

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References

[1] Zampieri N, Corroppolo M, Zuin V, Cervellione RM, Ottolenghi A, Camoglio FS. Longitudinal study of semen quality in adolescents with varicocele: to treat or not? Urology 2007; 70: 989-993.

[2] Sakamoto H, Ogawa Y, Yoshida H. Relationship between testicular volume and varicocele in patients with infertility. Urology 2008; 71; 104-109.

[3] Agarwal A, Cho CL, Majzoub A, Esteves SC. The society for translational medicine: clinical practice guidelines for sperm DNA fragmentation testing in male infertility. Transl Androl Urol 2017; 6 Suppl: S720-733.

[4] Zampieri N, Zuin V, Corroppolo M, Chironi C, Cervellione RM, Camoglio FS. Varicocele and adolescents: semen quality after 2 different laparoscopic procedures. J Androl 2007; 28: 727-733.

[5] Menkveld R, Stander FS, Kotze TJ, Kruger TF, van Zyl JA. The evaluation of morphological characteristics of human spermatozoa according to stricter criteria. Hum Reprod 1990; 5: 586-92.

[6] Sakamoto H, Saito K, Ogawa Y, Yoshida H. Effects of varicocele repair in adults on ultrasonographically determined testicular volume and on semen profile. Urology 2008; 71: 485-489.

[7] Kass EJ, Belman AB. Reversal of testicular growth failure by varicocele ligation. J Urol 1987; 137: 475-476.

[8] Atassi O, Kass EJ, Steinert BW. Testicular growth after successful varicocele correction in adolescents: comparison of artery sparing tecniques with the Palomo procedures. J Urol 1995; 153: 482-483.

[9] Kass EJ, Stork BR, Steinert BW. Varicocele in adolescence induces left and right testicular volume loss. BJU Int 2001; 87: 400-501.

[10] Pasqualotto FF, Lucon AM, de Goes PM, Hallak J, Sobreiro B, Pasqualotto EB, Arap S. Testicular growth, sperm concentration, percent motility, and pregnancy outcome after varicocelectomy based on testicular histology. Fertil Steril 2005; 83: 362-366.

[11] Latif T, Kold Jensen T, Mehlsen J, Holmboe SA, Brinth L, Pors K, Skouby SO, Jørgensen N, Lindahl-Jacobsen R. Semen quality as a predictor of subsequent morbidity: a danish cohort study of 4,712 men with long-term follow-up. Am J Epidemiol 2017; 186: 910-917.

[12] Eisenberg ML, Li S, Behr B, Cullen MR, Galusha D, Lamb DJ, Lipshultz LI. Semen quality, infertility and mortality in the USA. Hum Reprod 2014; 29: 1567-1574.

[13] Salonia A, Matloob R, Gallina A, Abdollah F, Saccà A, Briganti A, Suardi N, Colombo R, Rocchini L, Guazzoni G, Rigatti P, Montorsi F. Are infertile men less healthy than fertile men? Results of a prospective case-control survey. Eur Urol 2009; 56: 1025-1031.

[14] Ventimiglia E, Capogrosso P, Boeri L, Serino A, Colicchia M, Ippolito S, Scano R, Papaleo E, Damiano R, Montorsi F, Salonia A. Infertility as a proxy of general male health: results of a cross-sectional survey. Fertil Steril 2015; 104: 48-55.

[15] Zucchi A, Mearini L, Mearini E, Fioretti F, Bini V, Porena M. Varicocele and fertility: relationship between testicular volume and seminal parameters before and after treatment. J Androl 2006; 27: 548-551.

[16] Wu AK, Walsh TJ, Phonsombat S, Croughan MS, Turek PJ. Bilateral but not unilateral testicular hypotrophy predicts for severe impairment of semen quality in men with varicocele undergoing infertility evaluation. J Urol 2008; 71: 1114-1118.

[17] Vitku J, Kolatorova L, Hampl R. Occurence and reproductive roles of hormones in seminal plasma. Basic Clin Androl 2017; 27: 19-31.