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ORIGINAL ARTICLE

The influence of antisperm antibodies, intratesticular haemodynamics and the surgical approach to varicocelectomy on seminal variables

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KEYWORDS

Varicocele;
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Intratesticular haemodynamics;
Spermatogenesis

ABBREVIATIONS

ASAs, anti-sperm antibodies;
BTB, blood–testis barrier;
PSV, peak systolic velocity;
EDV, end diastolic velocity;
RI, resistive index;
PI, pulsatility index;

Abstract ***Objective:*** To evaluate the effect of antisperm antibodies (ASAs), hormonal levels, intratesticular haemodynamics and the surgical approach on the outcomes of varicocelectomy in infertile men, as assessed by seminal variables.

Patients and methods: In a prospective case-series study, 82 infertile men with varicocele (35 left and 47 bilateral) were evaluated. The preoperative assessment included a physical examination, semen analysis, assessment of ASAs in seminal plasma, hormonal levels (follicle-stimulating hormone (FSH), luteinising hormone and testosterone), and scrotal colour Doppler ultrasonography (CDUS) to measure the peak systolic velocity (PSV), end diastolic velocity (EDV), resistive index (RI) and pulsatility index. Patients were scheduled for varicocelectomy, with high ligation (Palomo) used in 40 patients (18, 45%, with left and 22, 55%, with bilateral varicocele), or an inguinal approach (Ivanissivich) with loupe magnification used in 42 (17, 40%, with left and 25, 60%, with bilateral varicocele). The men were reassessed at $\geqslant$3 months after surgery and according to the improvement in seminal variables (expressed as a $\geqslant$50% increase in total motile sperm count, TMSC), patients were further categorised into 'improved' or 'unimproved'. Binary logistic regression analysis was used to investigate the predictors of improvement.

Results: Before surgery the ASAs were positive in 17 men (21%). There was no significant difference between the right and left sides in intratesticular

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BTV, bilateral testicular volume;
CDUS, colour Doppler ultrasonography;
TMSC, total motile sperm count;
LH, luteinising hormone

haemodynamics. The TMSC was improved in 52 (63%) patients who had a significant improvement in the haemodynamic variables. Intratesticular haemodynamics, serum FSH and testosterone levels differed significantly between the improved and unimproved patients. Positivity for ASAs, the surgical approach and laterality of the varicocele were not significantly different, although the ASA-positive cases were characterised by a significant decrease in motility. Logistic regression analysis showed that the EDV, PSV, FSH, testosterone level and bilateral testicular volume (BTV) were significant predictors of improvement.

Conclusion: Positivity for ASAs is not a predictor of the outcome after varicocelectomy but affects only the motile fraction in positive cases, despite the improvement in other seminal variables and testicular haemodynamics, and regardless of the surgical approach. The EDV, PSV, FSH, testosterone and BTV were significant predictors of a successful outcome.

Introduction

A varicocele is the pathological dilatation of spermatic veins and is found in ≈15% of all adult males [1], in 11.7% of men with a normal semen analysis and in 25.4% of men with abnormal semen values [2], and it is considered to be the most frequent correctable cause in 14.8% of infertile men [3]. Surgical ligation of the spermatic vein is the generally accepted treatment, when semen quality usually improves afterwards, as shown in a recent meta-analysis [4], and with reversal of any DNA damage [5]. Varicocele has been associated with testicular dysfunction through several mechanisms, such as the retrograde flow of toxic metabolites from the adrenal glands or kidney, venous stasis with germinal epithelial hypoxia, alterations in the hypothalamic-pituitary-gonadal axis, and increases in testicular temperature [6]. Anti-sperm antibodies (ASAs) are an important cause of infertility, found in 8–21% of infertile men [7] and adversely affecting fertility in patients with varicocele, with a small but significant decrease in both sperm concentration and motility [8]. Sperm-bound immunoglobulins are present in a greater percentage of infertile men with varicocele than in infertile men with no varicocele [9]. The testis needs a good blood supply to maintain its function. As postulated in experimental studies [10,11], with varicocele-impaired venous drainage and an increased venous pressure, the blood supply and microperfusion of the testes can be decreased by down-regulating arterial inflow to maintain the homeostasis of the intratesticular vascular pressure. The peak systolic velocity (PSV) and resistive index (RI) were found by some authors [12] to be higher in patients with varicocele (fertile or not) than in fertile control men, and an increased RI might be suggestive of a pathological sperm count [13]. Recent opinion suggests that varicocele is a cofactor associated with other genetic and molecular factors resulting in infertility [14]. In previous studies investigating the predictors of improvement after varicocelectomy, some authors [15] highlighted the role of ASAs while others [12,13] investigated the role of intratesticular haemodynamics. Hormonal levels, testicular volume and varicocele grade were also investigated [16] as predictors of improvement. With these perspectives, the aim of the present study was to assess the probable role of the combined variables of ASAs, hormonal levels, ultrasonographically estimated testicular volume and intratesticular haemodynamics on the outcome of varicocelectomy in infertile men, as expressed by improvements in seminal variables. In addition, the intratesticular haemodynamic changes in infertile patients with varicocele were assessed and compared according to the surgical approach of varicocelectomy.

Patients and methods

Between August 2011 and May 2013, 82 infertile men with abnormal seminal values associated with a clinical varicocele were referred for varicocelectomy and evaluated in a prospective, open-label observational study. Patients with documented primary (60) or secondary (22) infertility for >1 year, with unilateral or bilateral varicocele and abnormal seminal variables were included in the study. Patients with azoospermia and marked oligozoospermia (sperm count $<$ 5 million/mL), recurrent varicocele, cryptorchidism, a history of exposure to gonadotoxins, or known genetic abnormalities and infectious inflammatory processes of the ancillary genital glands (leucocyte count $>$ 1 million/mL) were excluded. Those with a history of testicular trauma, epididymitis, orchitis or a previous surgical intervention of the scrotum were also excluded. The study was approved by the ethics committee of the Benha Faculty of Medicine. Informed consent for participation was obtained from all patients, and the procedure and possible risks explained thoroughly, according to Declaration of Helsinki. In all, 82