Vasectomy Reversal Outcomes in Men Previously on Testosterone Supplementation Therapy

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OBJECTIVE To report considerations for preoperative management and outcomes of vasectomy reversal (VR) in men with a history of testosterone supplementation therapy (TST).

METHODS A retrospective review of men on TST before VR from 2010 to 2013 was performed. For inclusion, patients were required to have baseline and follow-up hormone levels as well as postoperative semen analyses. Preoperative use of medical testicular salvage therapy and testicular sperm aspiration (TESA), intraoperative findings, and pregnancies were also analyzed.

RESULTS Six of 265 men who underwent VR had prior TST and met inclusion criteria. Median age was 39 years with a median obstructive interval of 7.5 years. Median duration of TST was 9 months before discontinuation and transition to testicular salvage therapy with clomiphene citrate with or without human chorionic gonadotropin for a median of 2.8 months. At baseline, decreased luteinizing hormone (median, 2 mIU/mL), follicle stimulating hormone (median, 5 mIU/mL), and total testosterone (median, 249 ng/dL) were observed. Two men (33%) with uncertain recovery of spermatogenesis based on physical examination and hormone response underwent preoperative testicular sperm aspiration confirming the presence of sperm. Nine vasovasostomies and 3 epididymovasostomies were performed. Patency was 83% after a median follow-up of 6.4 months and was 100% in men undergoing at least 1 vasovasostomy. Spontaneous pregnancy was achieved by 50% during the follow-up period.

CONCLUSION Testicular salvage medical therapy may play a role in the preoperative management of VR in men with prior TST. VR after TST can have outcomes comparable to those in the general population. UROLOGY 84: 1335–1341, 2014. © 2014 Elsevier Inc.

Use of testosterone supplementation therapy (TST) has become increasingly common among younger men.[1] Idiopathic biochemical hypogonadism, defined by a total testosterone level <300 ng/dL, is observed in just over a third of all men aged 45-54 years.[2] The diagnosis of hypogonadism and its treatment with TST has grown remarkably in recent years, as testosterone prescriptions have increased over 500% since 1993.[3] The age group with the most rapid rate of increased utilization is men aged 40-49 years, with testosterone prescriptions increasing more than 4.2-fold between 2001 and 2011. In 2011, this equated to a total prevalence of 2.3% in this age group alone.[1]

Men undergo vasectomy at an average age of 31 years,[4] whereas the average age for vasectomy reversal (VR) is 41 years.[5,6] Some men within this window will be diagnosed with hypogonadism and treated with TST. Nearly all men will have some degree of suppression of spermatogenesis during treatment with TST. Exogenous testosterone typically results in atrophy of the germinal epithelium in normal men with varying degrees of suppression of spermatogenesis, including azoospermia, within several months.[7,8] The level of suppression is partly dependent on the type of testosterone preparation, with topical preparations typically displaying a smaller degree of suppression of gonadotropins and thus spermatogenesis than injectable or implantable testosterone preparations.[9] Sperm concentrations usually recover to pretreatment levels after the cessation of TST; however, recovery could take up to 2 years,[10] and permanent detrimental effects to spermatogenesis are possible.[11,12] The use of TST before VR may impact vasal fluid findings by suppressing spermatogenesis, which could complicate intraoperative decision making on the method of

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reconstruction, and, therefore, may impair postoperative patency and pregnancy rates.

There is currently no available data for the management of exogenous testosterone-suppressed spermatogenesis in vasectomized men seeking VR. The vasectomized patient represents a particularly difficult patient in whom to assess spermatogenesis, and therefore the serum testosterone and gonadotropins, represents the most accurate initial assessment. Medical testicular salvage therapy to recover spermatogenesis in hypogonadotropic hypogonadal men may be accomplished with clomiphene citrate (CC)[13] and/or human chorionic gonadotropin (hCG).[14] If doubt persists whether spermatogenesis has recovered after treatment with testicular salvage therapy, a testicular sperm aspiration (TESA) in the office may be performed. Although TESA is more invasive, it can provide a definitive demonstration of spermatogenesis and represents a particularly helpful diagnostic test for the dilemma of uncertainty of active spermatogenesis in patients with obstructive azoospermia secondary to vasectomy.[15]

VR outcomes after TST and considerations for preoperative management have not been previously reported. Because of the increased diagnosis and treatment of androgen deficiency, we hypothesize that a growing proportion of men desiring VR will have been treated with TST. Because the effects of exogenous androgens adversely impact spermatogenesis,[12] we postulated that the use of TST may play a factor in VR outcomes. We also sought to retrospectively describe a method of testicular salvage therapy to potentially reinitiate spermatogenesis as well as a method to assess for the presence of spermatogenesis before VR.

In this study, we describe the results of a retrospective case series of the VR outcomes in men previously on TST with a goal to demonstrate a proof of concept of a preoperative evaluation and treatment strategy using medical management with testicular salvage therapy, and TESA in select cases, to increase the success rate of VR after TST.

METHODS

After obtaining institutional review board approval, a retrospective chart review was conducted of consecutive VR cases performed in a large academic urology practice. All surgeries were performed by a single fellowship-trained microsurgeon between December 2009 and May 2013. Patients were included in the study if a history of prior TST was identified during the obstructive interval between vasectomy and VR. All patients must have had 2 separate hormone profiles along with postoperative semen analysis data available. Patients were excluded if any of these criteria were not met.

Preoperative data collected included demographics, length of obstructive interval, and the formulation and length of time of TST. Because TST for all patients was prescribed by an outside facility before the patients presenting for evaluation for VR, specific prescription details including dose, usage and compliance, and improvements in symptoms and testosterone levels while on TST were not available for all patients and was therefore not included for analysis. Baseline laboratory values assessed included total testosterone level, calculated free testosterone level, luteinizing hormone (LH) level, follicle stimulating hormone (FSH) level, estradiol level, and sex hormone binding globulin level. After TST was discontinued, patients underwent medical testicular salvage therapy with CC 25 mg daily, with or without hCG 3000 units subcutaneously every other day. Both CC and hCG were recommended to all patients, with some patients taking both as recommended and others taking only CC because of patient factors such as cost considerations. It should be noted that this particular combination regimen of off-label medications has not been previously reported in the literature and only represents the authors' practice. The regimen and the length of time on medical testicular salvage therapy were recorded. Patients returned for a secondary physical examination and laboratory assessment before VR.

After approximately 3 months of testicular salvage therapy, if the recovery of spermatogenesis was clinically uncertain based on the subjective changes in testicular volume or in the hormonal profile, patients underwent TESA before VR. TESA was performed as an office-based procedure with local anesthesia on a single testicle with a single entry passage of the needle. After administration of a spermatic cord block and subcutaneous skin block with 1% lidocaine, an 18-ga 1.5-inch needle primed with sperm wash media and fixed to a fine needle aspirate piston syringe was passed into the testicular parenchyma and moved in and out with a sawing motion approximately 5 times while holding the vacuum suction on the piston syringe. The aspirate was then examined on a slide by a certified andrologist with a phase microscope at 40 times magnification for the determination of active spermatogenesis.

After the secondary preoperative assessment confirmed an improvement in the physical examination and the hormonal profile or a positive TESA was performed, all patients underwent microsurgical VR by a single fellowship-trained microsurgeon with either a 2-layered vasovasostomy (VV) or intussuscepted end-to-side epididymovasostomy (EV), techniques of which were previously described in detail.[16] Intraoperative data abstracted included the methods of reconstruction and the characteristics of the intravasal fluid (including its consistency and the presence or absence of sperm or sperm parts). Results of postoperative semen analyses and the achievement of pregnancy were similarly recorded.

Data were analyzed by computation of appropriate descriptive summary statistics with measures of dispersion reported as interquartile range (IQR) owing to the small sample size. Comparisons between groups were performed using the Student *t* test. The threshold for statistical significance was defined as a 1-tailed P value $<.05$.

RESULTS

Retrospective chart review identified a total of 265 patients who underwent VR between December 2009 and May 2013. Of those, 10 patients (2.7%) had a documented history of TST. After 4 patients were excluded for incomplete data, a total of 6 patients were included for analysis (Table 1). Median age at VR was 38.5 years (IQR, 36.8-40.5 years), with a median obstructive interval of 7.5 years (IQR, 5.5-8.8 years). All 6 men had previously fathered children before their vasectomy.