Testosterone therapy at the time of vasectomy reversal

Impact on intraoperative decision-making and interpretation of postoperative outcomes

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ABSTRACT

INTRODUCTION: During vasectomy reversal (VR), accurate intraoperative microscopic assessment of the vasal fluid for sperm presence and quality is essential in determining the indication for a vasovasostomy (VV) or vasoepididymostomy (VE). The use of testosterone therapy (TT), known to supress spermatogenesis, can potentially interfere with this determination. This initiative evaluated the impact of TT on vasal and epididymal fluid sperm characteristics and intraoperative decision-making among men on TT at the time of VR.

METHODS: Of 2622 consecutive VRs performed from 2007–2023, patients actively using TT at the time of VR were identified. Details as to the type, dose, and duration of TT were documented. All patients were counselled regarding the impact of TT on spermatogenesis and encouraged to discontinue TT if possible. During VR, vasal and epididymal fluid (as indicated) was sampled and each aspirate underwent microscopic evaluation for sperm presence and quality, and categorized as: motile sperm/intact-non-motile sperm/sperm parts/no sperm. Rates of sperm presence/absence in the vasal/epididymal fluid, frequency of VV/VE, postoperative patency (presence of motile sperm), and semen parameters were compared among patients on TT vs. clinically matched patients not using TT at the time of VR.

RESULTS: Among the 2622 VRs reviewed, 54 men (2%) reported using TT at the time of their VR. Despite its impact on spermatogenesis, intraoperative microscopic analysis of the reproductive fluid (vasal or epididymal) identified the presence of sperm in 95% (51/54) of patients. Testis biopsy confirmed sperm production among three patients with absence of sperm within the vasal or epididymal fluid. Rates of VV or VE did not significantly differ among men using TT at the time of VR compared to non-users. Postoperative patency rates (TT: 78 % vs. no TT: 93%) and mean total motile sperm counts (TMC) were lower among patients using TT at the time of VR (7.9 vs. 28.3, p=0.02).

CONCLUSIONS: Use of TT at the time of VR does not appear to impact rates of intraoperative microscopic identification of sperm within the reproductive fluid or the indication for VV/VE. Postoperative patency rates and TMC may be lowered by use of TT. Moreover, the determination to the etiology azoospermia postoperatively (production vs. obstruction) may be clouded by the use of TT during VR.

INTRODUCTION

Testosterone therapy (TT) is known to have a contraceptive effect on sperm production.[1-3]

Exogenous testosterone administration initiates negative feedback on the pituitary gland, dampening both follicle stimulation hormone (FSH) and luteinizing hormone (LH) release from the anterior pituitary. Consequently, signaling of endogenous testosterone production and testicular spermatogenesis is diminished, often resulting in severe oligospermia or azoospermia within the ejaculate.[1,2] Among men who have undergone vasectomy, using the ejaculate as an indicator as to the specific impact of TT on spermatogenesis is challenging, as the occlusive nature of the vasectomy in and of itself is expected to result in azoospermia.[4]

During vasectomy reversal (VR), accurate intraoperative microscopic assessment of the vasal fluid for sperm presence and quality is essential in determining the indication for a vasovasostomy (VV) or vasoepididymostomy (VE).[5,6] Contemporary guidelines (American Society for Reproductive Medicine [ASRM])[7] generally recommend that a VV be performed if the presence of sperm or sperm parts are identified within the aspirate of fluid expressed from the testicular end vas, whereas a VE is indicated if no sperm are identified within the vasal fluid.[7] A noted exception, favoring VV, is the absence of sperm within clear and copious vasal fluid. The suppressive

KEY MESSAGES

- Use of TT at the time of VR does not appear to impact microscopic identification of sperm within the reproductive fluid or the indication for VV/VE.
- Postoperative patency rates and total motile sperm counts may be lowered by use of TT, and TT discontinuation, if possible, is generally advised for optimal reproductive outcomes following VR.
- The determination of the azoospermia etiology postoperatively (production vs. obstruction) may be clouded using TT during VR. In such circumstances, cessation of TT may be informative.

impact of TT on testicular sperm production can potentially interfere with this determination and theoretically lead to erroneous intraoperative decision-making.[1] For example, in a patient on TT at the time of VR, the absence of sperm within an intraoperative fluid aspirate from the testicular end vas could be indicative of either epididymal obstruction or diminished spermatogenesis consequent to TT in the absence of epididymal obstruction. Consequently, a clear indication for VV or VE would be uncertain.

The current initiative evaluated the impact TT on vasal and epididymal fluid sperm characteristics and intraoperative decision-making among men on TT at the time of VR.

METHODS

This study received research ethics board approval for infertility research at the Sinai Health System at the University of Toronto. A retrospective evaluation of a prospectively maintained patient data series of VR surgeries performed by a single surgeon (EG) from 2007–2023 was analyzed.

Patients

Of 2622 consecutive VRs, patients actively using TT at the time of VR were identified. Details as to the type, dose, and duration of TT were documented. Prior to reversal surgery, all patients were counselled by an experienced testosterone specialist regarding the potential suppressive impact of TT on spermatogenesis and encouraged to discontinue TT if possible, with alternative treatments discussed. Patients using human chorionic gonadotrophin (HCG) or a selective estrogen receptor modulator (SERM) concurrent with or as a transition from TT were excluded from this analysis. Testosterone levels were not specifically measured by the VR surgeon as part of the study protocol prior to surgery.

During VR, vasal fluid was manually expressed and sampled from the freshly transected testicular-end vas and the vasal fluid quality was characterized (thick-paste/opaque/translucent/clear).[5] The vasal fluid volume was documented as copious/minimal.[5] Immediately following vasal fluid aspiration, each sample underwent intraoperative bench microscopic evaluation at 200 power to determine sperm presence (yes/no) and vasal sperm quality — categorized as motile sperm/intact non-motile sperm/sperm parts (sperm heads or tails)/no sperm (ASRM guidelines).[7] As indicated, fluid from the epididymal tubules was similarly analyzed and categorized. Testis tissue biopsy was performed only among patients demonstrating an absence of sperm within both the vasal and epididymal fluid samples.

Rates of sperm presence/absence in the vasal/epididymal fluid, frequency of VV/VE, postoperative patency (presence of motile sperm in the ejaculate), and semen parameters were compared among patients on TT vs. clinically matched (age and vasal occlusion interval) patients not using TT at the time of VR. Postoperative semen analyses were performed starting at three months following surgery. All patients using TT at the time of their VR remained on TT for postoperative semen testing. SPSS software was used to support the statistical analysis as part of this study.

RESULTS

Among the 2622 VRs performed during the study time frame, 54 men (2%) reported using TT at the time of their VR. The mean patient age was 43 years and the mean vasal occlusion interval (time form vasectomy to VR) was 6.7 years. Prior to VR, the average time on TT was 39 months, with topical gels used by 62% of patients (25–100 mg/day), injectables by 26% (cypionate or enanthate 100–200 mg biweekly), intra-nasal administration by 6% (11–33 mg/day), axillary by 4% (60 mg/day), and oral agents by 2% (120 mg/day). Dosing was within manufacturers' guidelines for all testosterone products used. All patients reported biological fatherhood prior to both their VR and initiation of TT.

Despite the known impact of TT on spermatogenesis, intraoperative microscopic analysis of the reproduc-

tive fluid (vasal or epididymal) identified the presence of sperm in 95% (51/54) of all patient subjects. Among these patients, 86% (44/51) had sperm identified within the vasal fluid and had a VV performed, while the remaining 14% (7/51) of men had evidence of sperm within the epididymal fluid aspirate and underwent VE. Testis biopsy confirmed sperm production among the three (5%) patients with an absence of sperm within both the vasal or epididymal fluid. Among these patients, all had a VV completed. Collectively, 100% of men on TT demonstrated evidence of spermatogenesis at the time of VR.

Compared to clinically matched non-users of TT, rates of VV or VE did not significantly differ among men using TT at the time of VR. Postoperative patency rates (TT: 78 % vs. No TT: 93%) and mean total motile sperm counts (TMC) were lower among patients using TT at the time of VR (TT: 7.9 vs. No TT 28.3, p=0.02). Clinical, operative, and postoperative characteristic of the testosterone and non-testosterone VR cohorts is summarized in Table 1.

DISCUSSION

The current study sought to evaluate the impact TT use at the time of VR on vasal and epididymal fluid sperm characteristics and the potential influence of such use on intraoperative decision-making and surgical outcomes. Despite the known suppressive influence of TT on spermatogenesis, overall, we found that sperm production was preserved (although likely diminished), with sperm identifiable in the reproductive tract in all patients at the time of VR. Consequently, the established evidence-based intraoperative algorithms for determining the indication for VV or VE during VR remain informative.[6,7] As such, rates of VV or VE should be relatively uninfluenced by TT use at the time of VR, as demonstrated in the current study.

With respect to postoperative outcomes, our analysis does highlight the suppressive nature of TT use (vs. non users) on TMC and patency rates.[1] Accordingly, patients should be counselled that optimization of fertilization potential and conception is best achieved through discontinuation of TT. The route of testosterone administration or product type did not impact the primary outcomes of this study.

Appreciating that TT in and of itself can lead to the absence of sperm within the ejaculate, determining the etiology of post-VR azoospermia presents a diagnostic challenge to the clinician tasked with differentiating a deficit in sperm production form persistent reproductive tract obstruction. Under these circumstances, cessation of TT and allowing time for the reproductive hormonal axis to recover may be informative. Recovery of spermatogenesis following TT discontinuation would be consistent with hormonal suppression of sperm production as a consequence of TT, while persistent azoospermia would suggest anastomotic failure.

The current investigation represents the largest analysis of the impact of TT on VR outcomes published to date. Consistent with the findings of the current study, a retrospective case series of 14 men by Bash et al reported high rates of VV (96%) and sustained patency rates among patients using TT prior to VR.[8] Moreover, Coward et al reported an overall patency rate of 83%, with spontaneous pregnancy rates of 50% among six men with prior TT, suggesting that VR after TT can have outcomes comparable to those in the general population.[9]

Limitations

With respect to study limitations, the authors acknowledge that measurement of serum testosterone levels and reproductive gonadotropins (LH, FSH) may have offered a more comprehensive understanding as to the

Table 1. Clinical and operative characteristic of testosterone and no testosterone VR cohorts

	Mean age	Mean vasal occlusion interval	VV/VE	% sperm identified in vasal or epididymal fluid	% patent	Total motile sperm count
Testosterone	43 years	6.7 years	87%/13%	95% *5% had sperm identified in testis tissue	78% overall VV: 81% VE: 57%	7.9
No testosterone	42 years	7 years	85%/15%	100%	93% overall VV: 97% VE: 62%	28.3 (p=0.02)

VE: vasoepididymostomy; VR: vasectomy reversal; VV: vasovasostomy.

nature and degree of testosterone absorption and suppression of hypothermic-pituitary-gonadal hormonal axis in this patient population. Such information may allow for individualized counselling and prognostication with respect to TT use and impact on sperm production.

Moreover, testis biopsy specimens were only evaluated for the presence or absence of sperm in order to guide real-time, intraoperative decision-making related to the indication for VV or VE and not for comprehensive histologic staging of spermatogenesis.

Finally, our methodology may have resulted in unnecessary epididymal violation in a limited number of patients. Learning from the study data, a reasonable forward-thinking approach would be only to sample epididymal fluid among patients demonstrating an absence of sperm within the vasal fluid but sperm presence on testis biopsy. In this case, a VE would be indicated.

CONCLUSIONS

Use of TT at the time of VR does not appear to impact rates of intraoperative microscopic identification of sperm within the reproductive fluid or the indication for VV/VE. Postoperative patency rates and total motile sperm counts may be lowered by use of TT, and TT discontinuation, if possible, is generally advised for optimal reproductive outcomes following VR. Finally, the determination of azoospermia etiology postoperatively (production vs. obstruction) may be clouded by the use of TT during VR. In such circumstances, cessation of TT may be informative.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer reviewed.

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