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Use of testosterone therapy in transgender men undergoing fertility preservation and assisted reproductive technology

Transgender (TG) people are individuals whose gender identity does not align with the sex to which they were assigned at birth. In the United States, there are about 1.6 million adults and youth that identify as TG and approximately 480,000 that identify as TG men (1). These individuals may feel the desire to undergo changes with their genitalia and secondary sexual characteristics to conform with their gender identity. As part of this transition, they may choose gender-affirming hormone therapy (GAHT) and/or gender-affirming surgery (GAS) at an appropriate time. In TG men, GAHT involves the use of masculinizing hormone therapy provided by exogenous testosterone (T). Moreover, GAS entails 3 components, 1. chest surgery to create a male chest, 2. genital surgery typically involving hysterectomy with possible oophorectomy and genital reconstruction, and 3. non-genital, non-breast surgical interventions.

TG persons may desire to have children and access fertility services for fertility preservation (FP) and reproduction. The World Professional Association for Transgender Health (WPATH) and the Endocrine Society recommend counseling TG persons regarding effect of GAS and GAHT on future fertility and discussing FP options prior to undergoing transition. The available options for TG men include oocyte, embryo, and ovarian tissue cryopreservation.

In individuals who have begun transition, discontinuation of GAHT may be necessary prior to undergoing FP or assisted reproduction, however there is no firm guidance providing recommendation as to the need of discontinuing testosterone and for how long. Limited data is available in attempts to address this gap in knowledge. Leung et al. demonstrated comparable cycle outcomes in TG patients with prior GAHT compared to matched cis-gender patients undergoing assisted reproductive technology. On average, TG men stopped GAHT 4 months prior to treatment but the minimum time without T was 1 month; nonetheless, patients were still required to discontinue exogenous T therapy prior to treatment (2). Approximately 37% of TG patients with ovaries would undergo oocyte cryopreservation if offered, but many patients forego this procedure due to the fear of reversal of androgen-induced changes by discontinuation of T and gender dysphoria (3).Therefore, there is a need to answer the following questions: is there a need to discontinue GAHT and if so, for how long should therapy be discontinued in TG men seeking FP or assisted reproduction?

The first paper reviewed, “Timing of testosterone discontinuation and assisted reproductive technology outcomes in transgender patients: a cohort study” by Albar et al., presents a retrospective cohort study of 18 TG men undergoing FP after discontinuation of T therapy for at least one month. The average time on T supplementation was 44 months, while the mean time off T prior to starting treatment was 7.7 weeks. A median total number of oocytes obtained was 11, and the median number of mature oocytes was 7.5. Using a linear regression model, no significant association was noted with the outcome of mature oocytes and time being off T (4).

The second paper reviewed, “Fertility treatment outcomes in transgender men with a history of testosterone therapy” by Ghofranian et al., is a descriptive, retrospective cohort study of TG men undergoing fertility treatment with IVF, embryo cryopreservation, co-IVF, oocyte cryopreservation, and intrauterine insemination (IUI). Of 77 patients that were initially screened, 11 patients were included in the analysis due to history of GAHT. The total time on exogenous T ranged from 3 weeks to 120 months, whereas the time off T ranged from 2 weeks to 24 months. The authors found no

correlation between the time on or off GAHT with exogenous T, total gonadotropin used, and number of retrieved oocytes. Furthermore, high-quality blastocysts were produced from patients undergoing IVF or embryo cryopreservation and live births were reported from patients undergoing IUI (5).

There is still limited data assessing FP and assisted reproduction in TG men with a history of GAHT. The studies presented here seek to address the gap in knowledge regarding prior use of exogenous testosterone therapy and fertility treatment outcomes. While they both found no significant association with prior use of exogenous T and cycle outcome parameters, such as retrieved and mature oocytes, they are limited by the small size of the sample participants. Many previous studies on fertility care in TG men are constrained by the small number of patients presenting for evaluation and a further attrition in the patients that then undergo any treatment, which raises concern for the statistical power of these studies.

Furthermore, case reports have described TG men undergoing FP and assisted reproduction with discontinuation of testosterone just immediately before planning FP treatment and also with concomitant use of T throughout the ovarian stimulation. Given the concern of stopping testosterone expressed by these patients, further research is definitively needed to determine if T can be continued throughout FP treatments without impairing cycle outcomes.

Conclusion

These studies demonstrate that prior use of and time of discontinuation of GAHT via exogenous testosterone in TG undergoing FP and assisted reproduction were not associated with negative impact on cycle outcomes, including mature and retrieved oocytes. Additionally, live births were reported in patients undergoing assisted reproduction with prior use of testosterone therapy. In summary, although there is limited evidence, GAHT can be discontinued as little as 2 weeks prior to starting treatment without impacting cycle outcomes. With only case reports providing evidence of successful FP cycles in TG male patients who chose to continue GAHT during stimulation, additional research is needed to determine whether T can be continued during stimulation without impacting cycle outcomes. Overall, TG patients and providers can be reassured that prior use of GAHT before undergoing FP or assisted reproduction does not impair the outcome of their cycles with brief discontinuation of treatment.

References

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*Please note: The newsletter reflects the opinion of the author and not of the ISFP.