OPEN ACCESS Freely available online

Clinics in Mother and Child Health

Commentary Article

Male Fertility Preservation: How far are we from the Clinics?

Stefan Schlatt* , **Swati Sharma**

Centre of Reproductive Medicine and Andrology, Institute of Reproductive and Regenerative Biology, Münster Germany

DESCRIPTION

Male factor infertility contributes to nearly half of the failed conception and pregnancy attempts. The primary reason attributed in adult males is constant decline in semen quality and sperm count during the past 50 years due to various known and unknown causes [1]. Adult patients producing mature gametes (fertilization competent spermatozoa) have the option to cryopreserve semen for future ART treatments.

In contrast, there is a big cohort of adult infertile men like azoospermic patients and prepubertal boys undergoing cytotoxic treatment or genetic abnormalities like Klinefelter's syndrome, who do not produce mature gametes and do not have any option to father their biological children in the future. However, due to availability of advanced cancer therapies and treatment options, the survival rate of such prepubertal cancer patients is over 85 %, but infertility leads to a decline in their overall quality of life [2].

Since cryo-banking of human pre-pubertal testicular tissue was initiated prior to administering cancer therapies, researchers are contemplating on identifying and establishing effective strategies which can be employed for clinical fertility preservation [3].

There are several cell-based and tissue-based experimental ex vivo approaches (iPS-cell based, spermatogonial stem cell-based, 2D- or 3D-organoid and tissue-based strategies) currently being developed to achieve complete spermatogenesis in primates [4-6]. Most of these *in vitro* approaches like spermatogonial stem cell culture or tissue culture are neither well-established nor can they yet be considered safe and efficient to initiate clinical applications. Currently, testicular grafting and germ cell transplantation are the only two strategies which can be applied for fertility preservation in primate models and have been validated in monkeys [7-9].

The risk of reintroducing or auto-transplanting back malignant cells in patients makes it challenging to implement these strategies in high-risk infertile patient groups, like cancer survivors who undergo chemotherapy or radiation treatment. The best way forward for clinical translation will be to initiate testicular and germ cell auto-transplantation in infertile patients suffering from low-risk or non-malignant diseases (like sickle-cell disease patients).

This is specifically relevant for those patients undergoing bone-marrow transplantation as they are regularly facing permanent infertility. In parallel, more efficient strategies (employing genome and transcriptome analysis tools like in situ spatial transcriptomics) need to be developed and applied to reliably detect remnants of malignant cells in cell-fractions or gonadal tissues envisaged to be transferred back into high-risk patient groups to restore fertility after cure and recovery from the disease.

Moreover, attempts to establish high throughput culture strategies in combination with miniaturized bioengineered microchip systems or using biomaterials need to be intensified, to investigate and understand biological mechanisms involved in spermatogenesis. As availability of human testicular tissue is limited for male fertility preservation research, various strategies can be adapted to overcome this technical barrier. Animal and tissue sparing multiplex systems can be developed to efficiently use limited tissue material available for various research applications [10].

Wherever normal human tissue material is not accessible, testicular tissue from well-established nonhuman primate models like macaque and marmoset monkeys can be extensively used for preclinical and translational research applications to explore testicular function [11]. Further, more advanced technological tools like artificial intelligence (AI) and big data can be efficiently implemented in reproductive biology research. Such advanced predictive modeling tools can be employed to answer various research questions, including to predict the scale or damaging impact of various degrees of gonadotoxic therapies on testicular function and fertility potential in young prepubertal cancer patients.

Thus, ex vivo models (using limited experimental samples) in combination with high-throughput advanced predictive tools can be efficiently exploited to develop clinically competent, effective, and robust strategies to investigate germ cell dynamics and to develop functional spermatozoa for infertile patients.

Correspondence to: Prof. Dr. rer. nat. Stefan Schlatt, Center for Reproductive Medicine and Andrology, Institute of Reproductive and Regenerative Biology, Albert-Schweitzer-Campus 1, Building D11, 48149 **Münster** , Germany, Tel: +49 251 8356099, Fax: +49 251 8354800; E-mail: stefan.schlatt@ukmuenster.de

Received: January 04, 2020; **Accepted:** January 18, 2020; **Published:** January 25, 2020

Citation: Schlatt S, Sharma S (2021) Male Fertility Preservation: How far are we from the Clinics? Clinics Mother Child Health. 17:372

REFERENCES

1. Levine H, Jørgensen, Andrade AM, Mendiola J, Derri DM, Mindlis I, et al. Temporal trends in sperm count: a systematic review and meta-regression analysis. Human Reproduction Update. 2017;23(6): 646-659.
2. Goossens E, Jahnukainen K, Mitchell RT, Van Pelt AMM, Pennings G, Rives N, et al. Fertility Preservation in boys: recent developments and new insights. Hum Reprod Open. 2020;2020(3): hoaa016.
3. Picton HM, Wyns C, Anderson RA, Goossens E, Jahnukainen K, Kliesch S, et al. A European perspective on testicular tissue cryopreservation for fertility preservation in prepubertal and adolescent boys. Hum Reprod. 2015;30(11):2463-2475.
4. Sharma S, Wistuba J, Pock T, Schlatt S, Neuhaus N. Spermatogonial stem cells: updates from specification to clinical relevance. Hum Reprod Update. 2019;25(3):275-297.
5. Mincheva M, Klaverkamp SR, Wistuba J, Redmann K, Stukenborg JB, Kliesch S, et al. Reassembly of adult human testicular cells: can testis cord-like structures be created in vitro? Mol Hum Reprod. 2018;24(2): 55-63.
6. Mall EM, Rotte N, Yoon J, Klaverkamp SR, Rőpke A, Wistuba J, et al. A novel xeno-organoid approach: exploring the crosstalk between human iPSC-derived PGC-like and rat testicular cells. Mol Hum Reprod. 2020;26(12):879-893.
7. Hermann BP, Sukhwani M, Winkler F, Pascarella JN, Peters KA, Sheng Y, et al. Spermatogonial stem cell transplantation into rhesus testes regenerates spermatogenesis producing functional sperm. Cell Stem Cell, 2012;11(5):715-726
8. Fayomi AP, Peters K, Sukhwani M, Pulaski VH, Shetty G, Meistrich ML. Autologous grafting of cryopreserved prepubertal rhesus testis produces sperm and offspring. Science. 2019;363(6433):1314-1319.
9. Neuhaus N, Schlatt S. Stem cell-based options to preserve male fertility. Science, 2019;363(6433):1283-1284.
10. Sharma S, Venzac B, Burgers T, Le Gac S, Schlatt S. Microfluidics in male reproduction: is ex vivo culture of primate testis tissue a future strategy for ART or toxicology research? Mol Hum Reprod. 2020;26(3):179-192.
11. Mincheva M, Wistuba J, Brenker C, Schlatt S. Challenging human somatic testicular cell reassembly by protein kinase inhibition-setting up a functional in vitro test system. Scientific Reports. 2020;10(1): 8935.