The future of reproductive medicine centers

Observing recent developments and sociological changes in our society, we firmly believe that in the near future reproductive endocrinologists and infertility centers will treat more fertile than infertile couples.

Oocyte vitrification has been successfully introduced in the world of assisted reproduction technology (ART) for many indications. One of them is the so-called "social freezing." Women of different ages have learned that oocyte preservation might be the only way to effectively stop the biological clock that moves against oocyte quality by increasing aneuploidies. We have seen a substantial increase in the number of patients attended for oocyte freezing for social reasons. Although still coming at a later age for fertility preservation (mean ± SD: 36.7±4.2 years), the success rates are good and the age of these patients is decreasing (1). The interest in social freezing has especially increased after some famous companies offered it to their employees as an additional benefit.

We still need more information about the number of eggs that need to be frozen to guarantee a future pregnancy, but today we know that freezing 8 to 10 oocytes provides a reasonable chance of success in women who preserve at a younger age (<36 years) (2). Thus, fertility preservation for non-medical reasons will be performed more and more. This fact, together with societal changes that have delayed the age at childbearing, leads me to predict that women who have frozen oocytes at a younger age will return to make embryos at age 40 to 50 years, a trend we already see in our daily practice.

At the same time, genetic tests introduced in clinical practice will change our reproductive behavior as human beings, both fertile and infertile. We refer to the screening tests for monogenic diseases. Close to 1,150 recessive genes that cause Mendelian diseases have been identified (www.ncbi.nlm.nih.gov/omim). Although they rarely manifest individually, these diseases account for 20% of infant mortality and pediatric hospitalizations.

Initial studies focused on parents from high-risk populations who were offered gene-by-gene carrier screening to search for frequent and specific mutations, resulted in a remarkable decline in the incidence of severe diseases. Today, the advent of high-throughput next-generation sequencing (NGS) makes a comprehensive preconception screening panel more feasible, and allows testing a wide range of conditions that a family history will never reveal. Our group has recently used NGS for targeted DNA sequencing and subsequent analysis of a set of genes causing Mendelian disorders in 2,570 individuals undergoing ART treatment (3). We found an average carrier burden of 2.3 per individual, and more importantly, 5% of the couples using their own gametes were found to have pathogenic variants conferring high risk for six different diseases. These couples mirror what could be expected in the general population.

There is controversy as to whether we should perform these tests in the general ART population, or even in the fertile population. There will be voices claiming that we are starting to intervene in the process of natural reproduction by introducing a selection bias, which will be unacceptable to many. But I'm sure that many more will foresee this technology as a simple and affordable method to avoid diseases and physical, emotional and economical costs to individuals, families and society. Despite many discussions, we are certain that human reproduction, both natural and ART-supported, will be conducted in the future with the aid of previous genetic testing. Needless to say, with appropriate counseling, couples receiving positive tests can avoid having ill children with the use of preimplantation genetic diagnosis (PGD).

Moreover, we know the main cause of implantation failure is embryo aneuploidy. New methods of PGD applied to the chromosomal status, have been shown to be extraordinarily important for successfully replacing a single euploid embryo (4). In addition, we know that endometrial receptivity is important, and we have found that as many as 15% of patients might have a displacement of the window of implantation, a rate which increases to 25% in infertile women (5). With appropriate molecular tools, we can now practice personalized ART with transfer of a single euploid embryo in the right moment for the endometrium.

Therefore, in the near future couples of any fertility status will visit us for genetic counseling before attempting pregnancy. In many cases, the woman will have her oocytes frozen in our center for years because she decided to preserve fertility long ago for social reasons. Once the embryos are created, they will be genetically screened before replacement in the ideal moment. Even for couples attempting natural conception after genetic screening, revolutionary tools are under development to flush the uterus, recover the embryo generated in the reproductive system, screen it genetically, and put back only the normal ones into the uterus.

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