Elective Fertility Preservation for Non-medical Reasons

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The reproductive behaviour is changing worldwide. Parenthood has increasingly become an issue of personal preference. The main contributing factor is the introduction of effective oral contraceptives, which has allowed women to remain longer in education and participate in the labour force market. On top of professional matters, social and financial issues are also related to motherhood delay.

It is well known that female fertility declines with increasing age, particularly after 35 years of age, due to a decrease of the follicle pool and to the inability to maintain the chromosomal integrity (1). Therefore, childbearing postponement has led to an increase in the number of IVF cycles performed in women of advanced age. However, IVF cannot fully compensate for the age-related fertility decline, with cumulative live birth rates after an IVF cycle of 16% at 40 years, 7% at 42 years and below 2% over 43 years (2). Thus, motherhood postponement has an impact both on the family size and on the risk of involuntary childlessness, with an estimated incidence of 7% in some European countries (3).

Elective oocyte cryopreservation emerges as a back-up strategy for women desiring to delay motherhood and not willing to proceed to oocyte donation in a future time. It provides in these women the opportunity to have a biological child avoiding multiple unsuccessful infertility treatments. It enhances women's reproductive autonomy and contributes to diminish gender inequality associated to the differences in age-related fertility decline observed in men and women (4). Most women seeking for non-medical oocyte cryopreservation are university educated, in professional employment and without a stable relationship (1).

Patients willing to undergo this procedure should be informed about the age-related success rates, the medical risks due to controlled ovarian hyperstimulation and oocyte retrieval and its cost-effectiveness.

Success rates are strongly related to age at vitrification and the number of vitrified oocytes. According to a live birth rate model built with more than 500 women, in order to have a 75%

chance of at least one child, the number of vitrified oocytes should be 10 at age 34, 20 at age 37 and 61 at age 42 (5). Unfortunately, according to the vast majority of studies, most women undergoing elective oocyte cryopreservation do so from 35 years onwards and the mean number of vitrified oocytes per patient is around 10 (6,7). According to one of the largest studies analysing outcomes after thawing, cumulative live birth rates (CLBR) per patient for women <36 years is 68.8%, decreasing to 25.5% at 36 and over. If we take 10 oocytes as an example, CLBR would be 42.8% for women <36 years and 25.2% for those aged 36 and over (6).

As far as the risks are concerned, the odds of developing ovarian hyperstimulation syndrome is extremely low due to the use of GnRH antagonist for ovulation triggering and to the fact that no pregnancy will follow ovarian stimulation. On the other hand, oocyte retrieval has a complication rate <1% (infection, damage to organs, ovarian torsion, bleeding) (8). Treatment burden for patients can be diminished by a random start of stimulation, the use of long-term acting gonadotrophins for ovarian stimulation and progestins for LH peak prevention (9). To date, no increased risk in congenital abnormalities in the offspring has been reported with the use of vitrified oocytes. Data on long-term oocyte storage and on long-term offspring health can emerge only with time and use of the treatment (4, 10).

Cost-effectiveness will depend on utilization rate and the initial cost of the procedure. From a biological point of view, the ideal age to cryopreserve is below 35 years, obtaining the maximal benefit if oocytes are used after the age of 40 (11, 12). Nevertheless, from a cost-effectiveness point of view, it has been reported that the ideal age is 37 (12). Another study concluded that this action is cost-effective if performed at age 35, when compared to IVF over 39 years, if at least 61% of women return (13).

There are several ethical concerns surrounding non-medical fertility preservation, such as the accumulation of unused cryopreserved oocytes due to the low utilization rate, which has been reported to be of 12% (6). Additionally, there are obstetric risks related to pregnancy at advanced maternal age, particularly above age 45 (14). There are concerns too regarding the children born to advance-aged parents. Nonetheless, all those fears are not unique to non-medical oocyte cryopreservation but are common to those for patients of advanced age undergoing an IVF with own or donated oocytes. Another important issue refers to the fact that this strategy might lead to a false perception of an insurance policy against age-related infertility (7). Lastly, there is an unavoidable dilemma about the funding of these procedures as it unlikely that public health systems, with limited resources, can provide full or partial coverage, although in some countries IVF at advanced age with fresh oocytes is fully covered. Accurate information

regarding all the above-mentioned topics is warranted when assessing patients seeking for this procedure. Whether oocyte cryopreservation is justified or not should be based on its efficiency and safety rather than on the underlying cause (15), even if some authors wonder if, far from being the proper solution to the problem, it will create further challenges (16).

Patients should be informed that their best chances of having a child are through natural conception at young ages. However, for those wishing to delay motherhood, education about age-related fertility decline is needed and doctors should explain oocyte cryopreservation as a preventive measure with its risks, costs and age-specific success rates. Patients have to be aware that success is not guaranteed but compared to IVF at advanced ages, elective non-medical oocyte cryopreservation yields higher success rates, above all if carried out at a young age, and compared to oocyte reception, it allows maintaining a genetic link.

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