Ovarian tissue cryopreservation using vitrification and/or in vitro activated technology

Nao Suzuki*
Department of Obstetrics and Gynecology, School of Medicine St. Marianna University, Kanagawa, Japan

*Correspondence address. E-mail: nao@marianna-u.ac.jp

Submitted on July 29, 2015; resubmitted on July 29, 2015; accepted on July 30, 2015

Slow freezing has been a standard method for ovarian tissue cryopreservation and transplantation (OTCP), while vitrification is commonly used for cryopreservation of embryos, oocytes and sperm. We have conducted preclinical studies using cynomolgus monkeys since 2006 (Hashimoto et al., 2010; Suzuki et al., 2012) and clinical studies since 2010, reporting a live birth after OTCP with vitrification (Kawamura et al., 2013; Suzuki et al., 2015). As discussed in their opinion article in this issue of Human Reproduction (Meirow et al., 2015), it seems to be difficult to compare slow freezing with vitrification and determine which is better. The live birth rate might be thought of as a useful parameter for comparing the two procedures, but it is not actually very useful because the number of primordial follicles in ovarian tissues cannot be counted before transplantation. Vitrification can be performed quickly and easily using a commercially available kit without the need for expensive equipment. Such convenience is a great advantage. However, it is important to determine the optimal conditions for vitrification by taking into consideration the safety and efficacy of cryoprotectants.

It may be considered preferable to avoid OTCP in patients with premature ovarian insufficiency (POI) because they only have a small number of primordial follicles. However, we have performed ‘in vitro activated’ (IVA) OTCP (Kawamura et al., 2013; Suzuki et al., 2015) in patients with POI for two reasons. First, POI is a progressive condition and the number of primordial follicles continues to decline. If an ovary is cryopreserved, hormone therapy can be given to induce follicular development and preparations can be made for IVA. Second, ovarian tissues need to be cultured for 48 h for IVA. Because all of the ovarian tissues harvested cannot be activated at the same time, some tissue must be cryopreserved without culture. It is preferable to perform IVA OTCP after harvesting, but residual ovarian tissue needs to be cryopreserved even in such a case. Meirow et al. are concerned about the safety of performing IVA OTCP after one to two cycles of chemotherapy. We do not think that IVA OTCP should be performed near the start of chemotherapy and have never performed it after one or two cycles of treatment. It is recommended that IVA OTCP should be performed when the patient is not undergoing chemotherapy because of the risk of birth abnormalities as Meirow et al. stated. We think that IVA OTCP should be performed in patients with progressive POI, including those with mosaic Turner syndrome, and in cancer patients aged 35 years or older. The International Society for Fertility Preservation (ISFP) and other reports recommend that OTCP should be performed at up to the age of 35–37 years because the number of primordial follicles is reduced by nearly 90% around that age (von Wolff et al., 2011; ISFP Practice Committee, 2012; Wallace et al., 2014). The number of primordial follicles is the key determinant of whether live birth can be achieved after OTCP and the possibility of successful live birth after OTCP increases if patients are younger. When patients are in their late 30s the live birth rate is low after freezing unfertilized eggs, while if fertilized eggs are frozen a considerable number of eggs have to be frozen. Thus we consider that cancer patients aged 35 years or older should try to give birth using IVA OTCP as soon as possible after achieving remission with cancer treatment, and thereafter should undergo conventional OTCP to extend graft survival and obtain normal endocrine function for a long time regardless of their age or the type of cancer. However, there is concern that PI3K/PTEN signaling may induce tumor cell growth in ovarian tissue during IVA. If OTCP can be done in cancer patients without minimal residual disease, then IVA OTCP can be performed under treatment with a PI3K stimulator and PTEN inhibitor. It may be possible to only perform ovarian fragmentation to disrupt Hippo signaling in patients who should have children and raise them as quickly as possible. We are currently investigating the usefulness of transplanting cryopreserved ovarian tissue in cancer patients by using two OTCP methods. Donnez et al. have brought a splendid breakthrough in this field, which is beneficial for young cancer patients around the world (Donnez et al., 2004). We hope that the addition of vitrification and/or IVA for OTCP will enable more cancer patients to have children in the future.

Author’s role
The author contributed to the conception and writing of this comments.
Funding
No external funding was either sought or obtained for this study.

Conflict of interest
None declared.

References


