IFFS2016 (India)

Fertility Preservation: Ovarian tissue cryopreservation

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More than 60 healthy babies have been born after transplantation of frozen-thawed ovarian tissue (FTOT)(Donnez J and Dolmans MM, J Assist Reprod Genet, 2015). Fifty eight babies were derived from slow freezing and two babies were from the vitrification method. Pregnancy rate per transplantation (PR/T) following slow freezing was around 25% (20/80) in four fertility centers (Donnez J & Dolmans MM, Lancet, 2015). The functional duration of the transplanted tissue is variable; however, the tissue remains active in the majority of women following slow freezing. PR/T and the longevity of the transplanted tissue following the vitrification method are unclear at present. The concentration of cryoprotectants in vitrification is 3-4 times higher than in slow freezing and so we are afraid of toxicity for mothers and babies. We will soon establish an ovarian tissue preservation center in which we will adopt two cryopreservation methods: 1) slow freezing, from the view of safety and actual results, and 2) vitrification, for future prospects. However, we must improve these cryopreservation methods in the near future. We will also adopt a transportation system at 4℃ on ice from a local facility to the center and －196℃ in a dry-shipper from the center to a local facility. We hope to spread fertility preservation using ovarian tissue cryopreservation and this transplantation system to all over Japan.

Minimal Residual Disease (MRD) is a great problem in FTOT in cancer patients. The International Society of Fertility Preservation (ISFP) Practice Committee recommended ovarian tissue cryopreservation for fertility preservation in pre-pubertal females and in emergency cases for post-pubertal females (J Assist Reprod Genet, 2012). Rosendahl et al. (J Assist Reprod Genet, 2013) reported MRD in 7% (31/422) of cases of ovarian tissue cryopreservation: 2/58 in imaging, 1/367 in histology, 1/220 in immunohistochemistry, 21/43 in PCR, and 5/101 in human-animal (human ovarian tissue transplanted into

immuno-deficiency mice). But, up to Jun e 2012, no recurrence had occurred in 33 clinical cases of FTOT. PCR was positive in 20/33 leukemia cases and 1/8 Ewing sarcoma cases, and PCR is very sensitive, especially in leukemia. However, patients shown to be positive by PCR were all negative histologically. Jensen AK et al. (Hum Reprod, 2015) reported three out of 41 women who had received transplantation of FTOT experienced a relapse.. We recommended informed consent for cancer patients, because: 1) the transplanted ovarian tissue is different from the ovarian tissue examined for MRD detection; 2) the amount of resected ovarian tissue analyzed for MRD is very small; 3) MRD detection methods vary (J Mamma Ova Res, in press). In conclusion, freezing and storage of ovarian tissue should be encouraged; transplantation must be performed carefully,; and informed consent is essential.

Key words: Fertility preservation, Slow freezing, Vitrification, Minimal residual disease, Transplantation,