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ARTICLE

Obstetric outcome after oocyte vitrification and warming for fertility preservation in women with cancer

Maria Martinez [a], Susana Rabadan [a], Javier Domingo [b], Ana Cobo [c], Antonio Pellicer [c], Juan A Garcia-Velasco [a,*]

[a] *IVI-Madrid, Rey Juan Carlos University, Av. del Talgo 68, 28023 Madrid, Spain*; [b] *IVI-Las Palmas, Av. Juan Carlos I, 17 35019, Las Palmas de Gran Canaria, Spain*; [c] *IVI-Valencia, Plaza de la Policía Local, 3 46025 Valencia, Spain*

* Corresponding author. *E-mail address:* juan.garcia.velasco@ivi.es (JA Garcia-Velasco).

Maria Martinez studied medicine and specialized in obstetrics and gynaecology in Madrid, Spain. She received her initial training at Assisted Reproduction in IVI Madrid and at IVI Valencia, and has been working at IVI Madrid since 2007. She specializes in fertility preservation in oncology patients.

Abstract Obstetric outcome of first pregnancies achieved after vitrification and warming oocytes from women being treated for cancer was evaluated. Of a total of 493 women who consulted for fertility preservation, 357 had their oocytes cryopreserved after being diagnosed with cancer, and 11 returned after being cured for assisted reproduction treatments (eight had breast cancer, one Hodgkin lymphoma, one endometrial adenocarcinoma, and one thyroid cancer). The oocyte survival rate was 92.3%, the fertilization rate was 76.6%, and the mean number of embryos transferred was 1.8 ± 0.7. Beta-human chorionic gonadotropin was detected in seven out of the 11 embryo transfers carried out. Four ongoing pregnancies were achieved and delivered at term with normal fetal weight and no major or minor malformations. Women diagnosed with cancer who have their eggs cryopreserved before anti-cancer treatment have good assisted reproductive technology performance and good perinatal outcomes. Cryopreservation of oocytes seems to be a good alternative for fertility preservation in these women.

KEYWORDS: fertility preservation, oocyte, perinatal outcome, vitrification

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Introduction

Cancer is a disease with a high prevalence and a tremendous affect on our society. Until recently, it was considered a long-term incurable disease. In the past decades, survival rates of many different oncological diseases have drastically improved. Patients and physicians now focus on surviving the disease, and also on quality of life after survival, such as fertility.

The incidence of breast cancer in the USA is increasing in women aged less than 40 years, currently representing 7% of cases; however, survival rates are greater than 70% (Del Mastro et al., 2011; Linet et al., 1999; Rodríguez-Wallberg and Oktay, 2010; Sonmezer and Oktay, 2006; Surveillance, Epidemiology and End Results Program, 2013, 2006. USA: Division of Cancer Control and Population Sciences, National Cancer Institute, 2013). Around 250,000 cancer survivors are women between the ages of 20 and 39 years (Linet et al., 1999; National Cancer Institute, 2006), of which 42% will develop premature ovarian failure (Eskander et al., 2011; Larsen et al., 2003). Therefore, the effect of radiotherapy and chemotherapy on the gonads and the uterus is crucial to understanding the future fertility potential of these patients.

Fertility preservation is a new area in reproductive medicine. Cryopreservation of oocytes or ovarian tissue gives oncological patients at high risk of becoming infertile after their treatment the possibility of becoming pregnant with their own gametes. Different fertility preservation strategies have been described, ranging from surgical ovarian transposition to ovarian quiescence with gonadotrophin-releasing hormone (GnRH) agonists, in-vitro oocyte maturation, freezing of ovarian tissue, or oocyte and embryo vitrification (Donnez and Dolmans, 2013). Among the different alternatives, cryopreservation of eggs has been extremely successful, with excellent survival rates and similar rates of fertilization, implantation and pregnancy as fresh oocytes in many different IVF indications (Cobo et al., 2008, 2010; Garcia-Velasco et al., 2013; Rienzi et al., 2012). Oocyte cryopreservation is significantly simpler and does not require a laparoscopic approach under general anaesthesia. Another advantage is that oocyte cryopreservation can be applied in women without a partner, and allows avoidance of ethical and legal complications, which are often related to embryo cryopreservation. Since the American Society of Clinical Oncology (Loren et al., 2013) and the Practice Committees of the American Society for Reproductive Medicine (2013) decided that this procedure is not experimental – unlike freezing ovarian tissue (Loren et al., 2013) – many different centers throughout the world are offering oocyte vitrification as an option for fertility preservation in women with cancer.

In this study, the first results are presented of patients who had oocytes vitrified for oncological reasons, and who, after being treated for their condition and realizing that their fertility was compromised, returned to have their oocytes warmed to try to achieve a pregnancy.

Materials and methods

Between May 2007 and November 2012, 493 women were selected for inclusion in our fertility preservation programme for women with cancer. The mean age of patients was 31.9 years (range 15–43 years). All had recently been diagnosed with cancer and were about to start oncological treatment with chemotherapy, radiotherapy, or both. In all cases, written informed consent was obtained from the patient as well as authorization from the clinical oncologist to proceed with ovarian stimulation. If there was disagreement with the oncologist, the procedure was not carried out. This study was exempt from Institutional Review Board as existing information had been recorded in such a manner that participants could not be identified directly or through identifiers to investigators. The most frequent indication for fertility preservation in our programme was breast cancer (67%) followed by Hodgkin lymphoma (11%). Most patients opted for oocyte vitrification to preserve their fertility (357/493 [72.4%]). A total of 375 controlled ovarian stimulation cycles were carried out. The remaining either had their ovarian tissue frozen or decided not to have either their oocytes or ovarian tissue cryopreserved.

Ovarian stimulation protocol

In non-hormone-dependent cancers, an ovarian stimulation protocol was started with 150–225 IU/day of recombinant FSH (Gonal F; Merck-Serono) on day 2 or 3 of a spontaneous cycle under GnRH antagonist protocol (Domingo et al., 2012). In 'hormone-dependent' cancer patients (i.e. all breast, ovarian, and endometrial cancers irrespective of the hormone receptor status), aromatase inhibitors were used for ovarian stimulation. Letrozole 5 mg/day (Femara 2.5 mg; Novartis, Spain) was administered orally starting on the second or third day of a spontaneous cycle until the day of triggering and then until the first day of menstruation after oocyte retrieval. After 2 days of letrozole administration, 150–225 IU/day of recombinant FSH (Gonal F; Merck-Serono) was added. A GnRH antagonist 0.25 mg/day (Cetrotide; Merck-Serono) was administered when the leading follicle reached 14 mm, and final oocyte maturation was triggered with 0.2 mg of the GnRH agonist, triptorelin (Decapeptyl 0.1; Ipsen-Pharma, Spain) as soon as two follicles were 20 mm or greater. No complications or moderate or severe side-effects were noted.

Oocyte vitrification and warming

The Cryotop method was used for oocyte vitrification as described by Kuwayama et al. (2005) with minimal modifications. Oocytes were denuded by enzymatic means 2 h after ovum retrieval. They were then equilibrated at room temperature for 15 min in 7.5% (v/v) ethylene glycol plus 7.5% dimethylsulphoxide in tissue culture medium (TCM) 199 plus 20% synthetic serum substitute (SSS) (Kitazato, Tokyo, Japan). After 12 min, the oocytes were checked for rehydration. If complete, the oocytes were subjected to the vitrification step. Oocytes were then placed in vitrification solution containing 15% ethylene glycol plus 15% dimethylsulphoxide plus 0.5 M sucrose. After 1 min in this solution, the oocytes were placed on a Cryotop strip and immediately submerged in liquid nitrogen. No more than four oocytes per Cryotop were loaded. When the patient was ready to attempt to conceive, all