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ARTICLE

Fertility preservation in patients with haematological disorders: a retrospective cohort study☆

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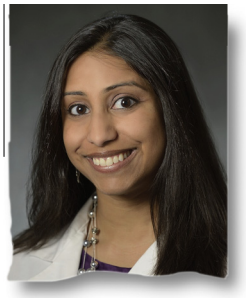

Dr Senapati completed her medical school training at the Ohio State University and residency training at the University of Pennsylvania. She is currently a fellow in the reproductive endocrinology and infertility at the University of Pennsylvania.

Abstract This study investigated the factors associated with utilization of fertility preservation and the differences in treatments and outcomes by prior chemotherapy exposure in patients with haematological diseases. This study included all 67 women with haematological diseases seen for fertility preservation consultation at two university hospitals between 2006 and 2011. Of the total, 49% had lymphoma, 33% had leukaemia, 7% had myelodysplastic syndrome and 4% had aplastic anaemia; 46% had prior chemotherapy; and 33% were planning for bone marrow transplantation, 33% pursued ovarian stimulation and 7% used ovarian tissue banking; and 48% of patients did not pursue fertility preservation treatment. All five cycle cancellations were in the post-chemotherapy group: three patients with leukaemia and two with lymphoma. Patients with prior chemotherapy had lower baseline antral follicle count (10 versus 22) and received more gonadotrophins to achieve similar peak oestradiol concentrations, with no difference in oocyte yield (10.5 versus 10) after adjustment for age. Embryo yield was similar between those who had prior chemotherapy and those who had not. Half of the patients with haematological diseases who present for fertility preservation have been exposed to chemotherapy. While ovarian reserve is likely impaired in this group, oocyte yield may be acceptable.

KEYWORDS: cancer, fertility preservation, haematological disease, IVF, ovarian reserve

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Introduction

Over 130,000 reproductive-age women are diagnosed with cancer in the USA annually (Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) Research Data (1973–2008), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2011, based on the November 2010 submission), with haematological cancers accounting for 18% of new diagnoses in women under the age of 45 (Kohler et al., 2011). In the paediatric and adolescent populations, US cancer statistics suggest that incidence of leukaemia is increasing 0.5% per year (American Cancer Society, 2011). While various therapeutic protocols for haematological malignancies are available, many include alkylating agents which have been associated with gonadotoxicity and infertility (Meirow and Nugent, 2001). In addition, various non-malignant haematological disorders such as sickle cell disease require gonadotoxic treatment strategies similar to those used for haematological malignancies (Bhatia and Walters, 2008; Walters and Sullivan, 2010). Improvements in treatment regimens have resulted in greater survival in patients with these disorders, thereby increasing the importance of long-term quality of life and future fertility to survivors (Letourneau et al., 2011; Loren et al., 2013). Indeed, studies suggest that the majority of cancer patients are concerned about the risk of infertility associated with treatment, and a third report that concerns about the risk of infertility have an impact on their treatment decisions (Partridge et al., 2004).

Over the past decade, there has been increasing interest in methods to expand the reproductive options of patients facing gonadotoxic therapies. While embryo cryopreservation is the standard option for adult females with a committed partner, oocyte cryopreservation is now widely accepted as well; additionally, ovarian tissue cryopreservation is another experimental option for patients without a committed partner (Lee et al., 2006). However, patients with haematological disorders present unique challenges to fertility preservation counselling and management. These individuals are often too ill at diagnosis to be eligible for fertility preservation treatment, which typically require a delay in therapy for days to weeks and involve minor surgical procedures, which pose increased risks in patients with abnormal haematological parameters. Moreover, even if leukaemia patients are eligible for ovarian tissue cryopreservation, there is concern about reseeding malignant cells with future autologous transplantation of tissue (Dolmans et al., 2010; Greve et al., 2012; Mueller et al., 2005; Salle et al., 2003; Schmidt et al., 2011; Shaw et al., 1996). Leuprolide acetate down-regulation administered prior to chemotherapy is another option, but the long-term benefits with respect to fertility preservation remain unclear (Beck-Fruchter et al., 2008; Chen et al., 2011). While patients with lymphoma are better candidates for fertility preservation treatment, often initial therapies like ABVD (adriamycin, bleomycin, vincristine and doxorubicin) do not have a substantial risk of infertility and, therefore, there is less motivation to pursue fertility preservation (Hodgson et al., 2007). For these reasons, often patients present for fertility preservation consultation only after a relapse in disease has been diagnosed after initial therapy, and sterilizing stem cell transplantation has been recommended. Hence, individuals with haematological malignancies often are seen after having already been exposed to gonadotoxic therapies (Maltaris et al., 2007).

The American Society of Clinical Oncology has recommended that providers discuss the fertility risks and fertility preservation options with patients facing gonadotoxic therapies; however, there are little data on clinical outcomes to guide recommendations for specific populations (Lee et al., 2006). There is a growing body of evidence regarding fertility preservation outcomes in breast cancer patients (Azim et al., 2008; Hill et al., 2012; Letourneau et al., 2011; Oktay et al., 2005, 2006; von Wolff et al., 2011; Westphal and Wapnir, 2012); however, the natural course of the disease and treatment are very different from haematological conditions, making it difficult to extrapolate data to patients with these disorders. Specifically, there are limited data about the fertility preservation choices and response to ovarian stimulation for women with haematological malignancies, particularly for those who have previously been exposed to chemotherapy (Dolmans et al., 2005; Ginsburg et al., 2001; Klock et al., 2010; Rossi et al., 2011).

The objective of this study was to identify factors that influence the utilization of fertility preservation treatment in patients with haematological disorders who present for fertility preservation consultation and to compare fertility preservation treatment choices and ovarian stimulation parameters between patients who present before or after exposure to chemotherapy.

Materials and methods

This retrospective cohort study identified all female patients with haematological disorders who were referred for fertility preservation consultation at two university centres from 2006 to 2011. Institutional Review Board approval was obtained at both study sites before the start of this study (IRB no. 809406, first approved 16 February 2009, University of Pennsylvania; 4 August 2009, University of North Carolina Chapel Hill). Patients were included if they were post-menarchal, had been recently diagnosed with a haematological disease and had impending chemotherapy treatment.

Medical records were abstracted to obtain detailed demographic and treatment specific data. Recorded data included: patient age at first fertility preservation consultation, race, gravidity, parity, body mass index (BMI) and partner status (by patient self-report). Disease specific information recorded included: haematological diagnosis, treatments prior to presentation for fertility preservation consultation, the time from last treatment, impending treatment plans and fertility preservation strategy pursued. For patients who elected to undergo ovarian stimulation for oocyte or embryo cryopreservation, stimulation parameters including baseline antral follicle count, cycle day 3–5 FSH, total gonadotrophins used during stimulation, duration of stimulation, peak serum oestradiol (pg/ml), oocyte yield (MII), embryo yield and cycle cancellation rates were collected.