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Article

Does oocyte donation compared with autologous oocyte IVF pregnancies have a higher risk of preeclampsia?

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KEY MESSAGE

Singleton pregnancies after oocyte donation are associated with a significantly higher risk of preeclampsia, pregnancy-induced hypertension and caesarean section compared with pregnancies using autologous oocytes. Fertility practitioners and obstetricians should take this information into consideration when counselling patients interested in receiving donated oocytes and during the follow-up of their pregnancies.

A B S T R A C T

The aim of this study was to evaluate whether pregnancies resulting from oocyte donation have a higher risk of preeclampsia compared with pregnancies after IVF using autologous oocytes. Propensity score matching on maternal age and parity was carried out on a one to one basis, and a total of 144 singleton pregnancies resulting in delivery beyond 22 gestational weeks, achieved by oocyte donation, were compared with 144 pregnancies achieved through IVF and intracytoplasmic sperm injection with the use of autologous oocytes. All pregnancies were achieved after fresh embryo transfer. Obstetric and neonatal outcomes were compared for each pregnancy. Singleton pregnancies after oocyte donation were associated with a significantly higher risk for preeclampsia (OR 2.4, CI 1.02 to 5.8; $P = 0.046$), as well as for pregnancy-induced hypertension (OR 5.3, CI 1.1 to 25.2; $P = 0.036$), and caesarean delivery (OR 2.3, CI 1.4 to 3.7; $P = 0.001$) compared with pregnancies using autologous oocytes.

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Introduction

Oocyte donation constitutes an integral part of modern assisted reproductive care. The first human pregnancy after the transfer of a donated oocyte fertilized *in vitro* to a cyclic recipient was reported by an Australian group in 1983 (Trounson et al., 1983). Although oocyte donation was initially carried out in patients with premature ovarian failure, indications have more recently expanded to older patients with ovarian insufficiency or patients with recurrent failures in IVF (Antinori et al., 1993; Barri et al., 1992; Borini et al., 1995; Pados et al., 1994; Sauer, 1995).

Since the first clinical application of oocyte donation, several studies have evaluated the obstetric and neonatal outcomes of this procedure. One of the first studies that assessed the evolution and outcome of pregnancies from oocyte donation reported a high incidence of obstetric and neonatal complications, such as first-trimester bleeding (34.6%), preeclampsia (32.7%), intrauterine growth restriction (IUGR) (11.5%) and caesarean section (63.5%) (Pados et al., 1994).

Results of subsequent studies, however, have varied between investigators. In studies focusing on the outcome of singleton pregnancies after oocyte donation, the incidence of preeclampsia ranges from 9.8 to 12% (Le Ray et al., 2012; Malchau et al., 2013; Stoop et al., 2012). In studies focusing on pregnancy-induced hypertension (PIH), the incidence of preeclampsia ranges from 13 to 30% (Keegan et al., 2007; Söderström-Anttila et al., 1998; Stoop et al., 2012; Wiggins and Main, 2005; Wolff et al., 1997). It should be emphasized that certain maternal conditions such as Turner syndrome are characterised by a higher incidence of some obstetrical complications such as PIH, preeclampsia and caesarean section (Alvaro Mercadal et al., 2011; Chevalier et al., 2011).

Comparison of complication rates between oocyte donation, and IVF and intracytoplasmic sperm injection (ICSI) pregnancies using autologous oocytes, have produced discrepant results. Studies focusing on differences in preeclampsia rates between oocyte donation pregnancies and IVF–ICSI pregnancies with autologous oocytes have found them to be significantly higher after donated ovum compared with pregnancies after IVF using autologous oocytes (Klatsky et al., 2010; Malchau et al., 2013) whereas others have not (Krieg et al., 2008; Stoop et al., 2012; Wiggins and Main, 2005). Most studies support that singleton pregnancies from oocyte donation present a significantly higher risk of PIH (Keegan et al., 2007; Levron et al., 2014; Söderström-Anttila et al., 1998; Wiggins and Main, 2005), whereas Stoop et al. (2012) found no significant difference. These discrepancies are probably a result of the differences in methodology used, i.e. use of different analysis strategies, small number of participants or problematic matching of participants with the controls. To properly estimate the risk of these complications with oocyte donation, important confounders, such as age, parity and multiplicity (singleton versus multiple pregnancies) must be controlled for when comparing oocyte recipients (who are usually older and nulliparus) with patients undergoing IVF using their own gametes. To date, however, only a small fraction of studies have done this (Klatsky et al., 2010; Stoop et al., 2012). Therefore, it is evident that additional well-matched studies with clear comparisons between case and control groups are needed to provide a conclusive answer to this important clinical question.

The aim of the present study was to assess the occurrence of preeclampsia and other obstetric and neonatal outcomes after oocyte donation and after IVF with autologous oocytes.

Materials and methods

Study design

This retrospective study was conducted at the Fertility Clinic of the Erasme Hospital of the French-speaking Free University of Brussels. The study group consisted of all women with singleton pregnancies achieved after oocyte donation who gave birth to a baby of more than 22 weeks of gestation, between 1991 and 2013. The control group was extracted from women with singleton pregnancies achieved after IVF–ICSI who gave birth to babies of more than 22 weeks' gestation with a delivery at the Erasme Hospital during the same period.

Selection methods and inclusion criteria

During this period, data for 239 singleton pregnancies achieved after oocyte donation and 799 singleton pregnancies achieved after IVF–ICSI with autologous oocytes were available and were included for analysis in this study.

Patients who underwent IVF and ICSI techniques were included in the same group, as no significant differences in the incidence of obstetric or neonatal complications in singleton pregnancies resulting from these techniques have been reported (Bonduelle et al., 2002; Nouri et al., 2013).

All patients in the control group delivered at the maternity ward of the Erasme Hospital, and data about their assisted reproduction technique cycles, pregnancies and deliveries were extracted from the electronic database *Gyneco2000*. Some patients in the study group were followed and delivered in the same unit or elsewhere. When patients delivered in other units, a questionnaire was sent to their gynaecologist and their responses were scanned into the Medical Viewer programme of the Erasme Hospital. In some cases, the files were incomplete, so patients, their physicians, or both, were contacted to retrieve the missing information; however, the dataset remained incomplete.

Exclusion criteria

Exclusion criteria were multiple pregnancies, the application of testicular sperm extraction (TESE) and cycles with preimplantation genetic diagnosis. Patients undergoing cycles of preimplantation genetic diagnosis were heterogeneous, and included mothers with genetic diseases that could interfere with obstetric outcomes. They also included patients with normal fertility and therefore comparison with infertile IVF couples could not be made. Similarly, pregnancies achieved with the use of TESE may not have similar obstetric outcomes compared with pregnancies in which no TESE was needed. Therefore, the rate of caesarean section has been previously shown to be lower in pregnancies with TESE compared with pregnancies from ejaculated sperm (Fedder et al., 2013). As differences in obstetric and neonatal outcomes between pregnancies after fresh and frozen embryo transfer have been reported (Maheshwari et al., 2012; Wennerholm et al., 2013), pregnancies achieved after the use of cryopreserved embryos were excluded. As the incidence of PIH and preeclampsia seems to be higher in patients with Turner's syndrome compared with pregnant women who have undergone oocyte donation who do not have Turner syndrome, patients with this syndrome were excluded (Alvaro Mercadal et al., 2011; Chevalier *et al*, 2011).