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Review

The impact of donor insemination on the risk of preeclampsia: a systematic review and meta-analysis

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ABSTRACT

A systematic review and meta-analysis were performed to evaluate whether women who conceive with donor sperm have an increased risk of preeclampsia compared with those who use their partner's sperm. Studies that compared women who were impregnated by donor and partner sperm were included. The main outcomes assessed were preeclampsia and gestational hypertension rates. Altogether, 10,898 women (2342 pregnancies by donor sperm versus 8556 by the partner's sperm) were included from seven observational studies. Conception using donor sperm was associated with an increased risk of preeclampsia (odds ratio [OR] 1.63, 95% CI 1.36–1.95) compared with using a partner's sperm. No difference was observed in the risk of gestational hypertension (OR 0.94, 95% CI 0.43–2.03). In conclusion, pregnancies achieved by donor sperm significantly increase the risk of preeclampsia, although the underlying mechanisms remain unclear. Additional studies are required to confirm these findings.

Contents

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Introduction

Hypertensive disease in pregnancy affects approximately 10% of human births (15 million pregnancies per year). The major complication, preeclampsia, occurs in approximately 3–5% of pregnancies, and when it progresses to a severe stage, it can lead to serious consequences for both the mother and the fetus [1]. According to a review by the World Health Organization (WHO) [2], 12% of maternal deaths worldwide result from preeclampsia or eclampsia, as does a considerable proportion of maternal morbidity. In addition, preeclampsia and eclampsia significantly contribute to perinatal morbimortality [2,3].

In 1916, Zweifel first described preeclampsia as "*a disease of theories*" [4]. For decades, this disease has been subject to investigation, although its pathogenesis has been difficult to elucidate because of its potential complexity. A number of theories have been advocated, although impaired placentation appears to play a key role. An imbalance in angiogenic factors and oxidative stress has been reported to lead to arterial vasodilatation and endothelial dysfunction, altering the process of placentation [5,6]. In contrast, the immune theory supports the existence of an immune maladaptation in the maternal–fetal interface [7].

Interestingly, a local inflammatory response induced by sperm exposure has been documented [8,9]. In this regard, multiple studies have noted that the incidence of preeclampsia appears to be reduced with repeat exposure to seminal fluid [10,11], as observed among women with a higher number of sexual cohabitations, women using non-barrier contraceptives and women with a history of healthy pregnancy with the same partner [12,13]. These observations have led to the hypothesis that exposure to a partner's sperm exerts a protective effect. Nonetheless, studies aiming to elucidate this issue have reported conflicting results [14,15].

Donor sperm is commonly used in in vitro fertilisation (IVF) and intrauterine insemination (IUI) when severe male factor infertility is detected, as well as in lesbian couples and single women, and occasionally in cases of known genetic abnormalities in the male [16]. Within the subfertile population, a number of authors have assessed whether the use of donor sperm could increase the risk of hypertensive disorders during pregnancy, although the studies show conflicting results.

The aim of this systematic review and meta-analysis was to determine whether insemination using donor sperm can increase the risk of preeclampsia in comparison with those who achieve pregnancy with a partner's sperm.

Materials and methods

The study was exempt from Institutional Review Board approval because it was a systematic review and meta-analysis. We followed the PRISMA guidelines for systematic reviews [17] and MOOSE for observational studies [18] in order to report the results.

Search strategy

Exhaustive searches were performed in MEDLINE (accessed through PubMed) and EMBASE (accessed through Ovid) from their inception until January 2014. The searches combined terms and descriptors related to preeclampsia, donor insemination and in vitro fertilisation with donor sperm. The search strategy was modified to comply with the requirements of each database. Furthermore, we screened the reference lists of all of the relevant articles and overviews to identify additional relevant citations. The search was restricted to articles published in English or Spanish. The complete search strategy is available upon request from the authors.

Eligibility criteria

The review included studies regardless of their design that analysed pregnant women who had conceived with donor sperm compared with pregnant women who had conceived with their partner's sperm, independent of whether this latter group had conceived spontaneously or through assisted reproductive techniques (ART). We aimed to include studies that compared the rates of developing hypertensive disorders (gestational hypertension, preeclampsia) during pregnancy, as shown in Table 1. Case series and case reports were excluded from our search.

Outcome measures

The main outcome of interest was preeclampsia. Gestational hypertension was a secondary outcome. Outcomes were defined according to the terminology recommended by the SOGC (Society of Obstetricians and Gynaecologists of Canada) [19] and the ISSHP (International Society for the Study of Hypertension in Pregnancy) [20].

Data collection process

The data were collected from the studies using predesigned forms on which the characteristics of the study design, participants, interventions, comparisons and main results were recorded.

Two independent authors (A.S.T. and J.U.A.) assessed all abstracts retrieved from the search and obtained the full manuscripts of citations that fit the inclusion criteria. In a second step,

Table 1
Study eligibility criteria.

Target population	Women of reproductive age
Intervention	Conception using donor sperm versus partner's sperm
Outcome measure	Preeclampsia
	Gestational hypertension
Design	Randomised controlled studies
	Cohort studies
	Case-control studies