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Obstetric and perinatal outcomes of singletons after single blastocyst transfer: is there any difference according to blastocyst morphology?

Céline Bouillon [a,b,c,d,*], ***Noémie Celton*** [a,1], ***Sandra Kassem*** [a], ***Cynthia Frapsauce*** [a], ***Fabrice Guérif*** [a,b,c,d]

[a] *Service de Médecine et Biologie de la Reproduction, CHRU de Tours, F-37044 Tours, France*
[b] *Université François Rabelais de Tours, F-37041 Tours, France*
[c] *INRA, UMR85 PRC, F-37380 Nouzilly, France*
[d] *CNRS, UMR6175 PRC, F 37380 Nouzilly, France*

Dr Bouillon graduated in medicine at Dijon University, France, in 2013. She is currently completing her PhD at Tours University. Since 2013, she has worked as a physician in the Department of Reproductive Medicine and Biology in Tours University Hospital. Her scientific interests include blastocyst development, single-embryo transfer, gonadotropins and cryopreservation.

KEY MESSAGE
It has been shown that blastocyst transfer with poor morphology is associated with reduced implantation. Our results seem to be reassuring, as the transfer of a single morphologically poor blastocyst did not have a deleterious effect on obstetric or perinatal outcome compared with a blastocyst with good or fair morphology.

A B S T R A C T

A strong correlation between blastocyst morphology and implantation has been shown by many studies. The consequences and effects of assisted reproductive techniques on children's short and long-term health have always been a source of discussion. The obstetric and perinatal outcome of singletons according to blastocyst morphology has rarely been evaluated. The aim of this observational study is to determine whether a relationship exists between blastocyst morphology and obstetric and perinatal outcomes. A total of 799 singleton clinical pregnancies were analysed after transfer of a single fresh blastocyst on day 5 between 2006 and 2013. Blastocysts were divided into four groups based on their morphology on day 5: group 1 = good morphology blastocysts; group 2 = fair morphology blastocysts; group 3 = poor morphology blastocysts and group 4 = early (B1/B2) blastocysts. Obstetric and perinatal outcomes were compared between the four groups. After adjustment for some confounding variables, main obstetric and perinatal outcomes after transfer of blastocysts with poor morphological characteristics were not associated with increased adverse obstetric and perinatal events. Sex ratio was significantly higher in group 1 compared with groups 2, 3 and 4, and in Group 2 compared with Group 3 ($P < 0.001$) even after adjustment ($P < 0.05$).

* Corresponding author.
E-mail address: c.bouillon@chu-tours.fr (C Bouillon).
[1] Present address: Service de médecine et biologie de la reproduction, cytogénétique et CECOS de Picardie, CHU Amiens Picardie, site Sud, F 80 054 Amiens Cedex 1, France.

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Introduction

Blastocele expansion, organization of inner cell mass (ICM) and trophectoderm cells are used to evaluate blastocyst quality (Gardner and Schoolcraft, 1999). A strong correlation between blastocyst morphology and implantation has been demonstrated by many studies (Balaban et al., 2000, 2006; Goto et al., 2011; Guerif et al., 2010). Which of the morphological characteristics is the strongest predicting factor for success after blastocyst transfer, however, is still a matter of debate (Ahlström et al., 2011; Hill et al., 2013; Honnma et al., 2012; Richter et al., 2001; Thompson et al., 2013; Van den Abbeel et al., 2013).

The main goal of IVF is the birth of a single healthy child. Indeed, the consequences and the effects of assisted reproductive techniques on children's short- and long-term health have always been a source of discussion. There seems to be an increased risk of prematurity, low birth weight and neonatal mortality among singletons born after assisted reproduction techniques (Ceelen et al., 2008; McDonald et al., 2009; Pinborg et al., 2013; Reddy et al., 2007) compared with the general population. Moreover, some studies have reported an increase in birth defects after IVF (Hansen et al., 2013; Pandey et al., 2012; Wen et al., 2012). It has also been reported that singleton pregnancies resulting from assisted reproduction techniques are at increased frequency of maternal complications (Jackson et al., 2004; Poikkeus et al., 2007; Reddy et al., 2007). It has not been elucidated to date whether such outcomes might be attributable to certain aspects of assisted reproduction techniques itself or to patient infertility (De Geyter et al., 2006; Hayashi et al., 2012; Rimm et al., 2011; Romundstad et al., 2008; Thomson et al., 2005).

Some studies have focused on the stage of the embryo on transfer and compared obstetric and perinatal outcomes between early and late embryo stages (Dar et al, 2013, 2014; Fernando et al., 2012; Källén et al., 2010; Kalra et al., 2012; Oron et al., 2014a, 2015). In some of these studies, preterm singleton birth rates (<37 weeks) (Dar et al, 2013, 2014; Källén et al., 2010; Kalra et al., 2012) and congenital malformation rates (Dar et al., 2014; Källén et al., 2010) were increased after blastocyst transfer compared with cleavage-stage transfer. By contrast, other studies showed no difference between blastocyst transfer and cleavage-stage transfer (Fernando et al., 2012). Detailed embryo morphology, however, was not investigated in any of these studies.

To the best of our knowledge, only a Canadian group has analysed the perinatal outcome of singletons according to blastocyst morphology (Oron et al., 2014a, 2014b, 2015). The number of live births after the transfer of a single poor-quality blastocyst, however, was low (n = 23), and little information was available about obstetric outcome when blastocyst morphology was considered separately. The aim of our study was to evaluate obstetric and perinatal outcomes in four groups defined according to more detailed morphological characteristics (good, fair, poor and early stage) of the single blastocyst transferred. We did not find increased rates of adverse obstetric and perinatal outcomes after transfer of blastocysts with morphologically poor characteristics.

Materials and methods

Study design

This observational study was undertaken at the IVF Unit, Bretonneau University Hospital, Tours, France, between January 2006 and December 2013. The inclusion criteria comprised the following: couples attempting first or second IVF; couples with a single fresh blastocyst transferred on day 5; attempts using non-donor oocytes; and couples achieving a singleton clinical pregnancy.

All couples were given clear information by a physician on the theoretical disadvantages (uncertainty of reaching the blastocyst stage) and advantages (embryo selection after genome activation, more accurate synchrony between blastocyst and endometrium, and lower uterine contraction at the time of blastocyst transfer) of extended culture. Couples were included in the study only once.

After each birth, a questionnaire was sent to the doctor who delivered the patient with questions on pregnancy and perinatal outcomes. It was not possible to obtain pregnancy outcome for 17 patients (2%). Reports of all patients were then regularly updated in our database in accordance with our usual practice. For the patients with a known live birth (n = 651), the questionnaire was completed for 557 patients (85.6%). Trained members of our staff telephoned the obstetrician to obtain missing data for the remaining 94 patients (14.4%) for whom information was lacking.

Ethics statement

It is current practice in our IVF centre to transfer one blastocyst on day 5 for couples attempting first or second IVF, independently of embryo quality on day 2. All participating couples had provided written informed consent to have the study results reported and published. The protocol for this observational study was approved by the Ethics Committee on Research involving Human Subjects of our hospital on 13 October 2016 (Research Project No 2016 065).

IVF procedure

The ovarian stimulation protocol and the main IVF and intracytoplasmic sperm injection procedures used have already been described elsewhere (Guerif et al., 2004). Briefly, embryo culture with sequential media and assessment were carried out as follows: fertilization (day 0) was performed in Sydney IVF Fertilization medium™ (Cook, Brisbane, Australia). The following morning (day 1), the oocytes were individually placed in microdrops (25 µl) in Sydney IVF Cleavage medium™ (Cook, Brisbane, Australia) under Sydney IVF culture oil™ (Cook, Brisbane, Australia). From day 3 to day 5/6, single embryo culture was carried out in microdrops in Sydney IVF Blastocyst medium™ (Cook, Brisbane, Australia) under Sydney IVF culture oil™ (Cook, Brisbane, Australia). All cultures took place in K-Minc incubators™ (Cook, Brisbane, Australia) at 37°C with 6% CO_2, 5% O_2 and 89% N_2.

Assessment of blastocyst morphology

All the subsequent optical assessments were carried out using an inverted microscope with Hoffman modulation contrast (×200 and ×400 magnification). For all couples included in the study, the whole cohort was placed in extended embryo culture with the intention to transfer a single blastocyst. The outcome of extended embryo culture was recorded for each individually cultured embryo. The morphological assessment was based on the expansion of the blastocoele cavity (B1–B6) and the number and cohesiveness of the inner cell mass (ICM) and trophectodermal cells (Gardner and Schoolcraft, 1999). When an embryo had started to expand, i.e. for blastocysts graded as 3–6 (full blastocysts onwards), it was then possible to assign independent scores

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