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Should we consider day-2 and day-3 embryo morphology before day-5 transfer when blastocysts reach a similar good quality?

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KEY MESSAGE

Good-quality blastocyst transfer should be carried out irrespective of embryo quality at cleavage stage (day 2 or day 3), as it may not compromise success rates after IVF and intracytoplasmic sperm injection in a good-prognosis population.

A B S T R A C T

Clinical outcomes of 291 day-5 blastocyst transfers carried out between January 2012 and March 2016 were retrospectively compared according to their quality at day 2 and 3. Inclusion criteria were female age younger than 37 years; first or second IVF and intracytoplasmic sperm injection cycle; quality of the transferred blastocyst: blastocoele B3 or higher; inner-cell-mass A/B; trophectoderm A/B; and known implantation outcome for each transferred blastocyst. Blastocysts were classified into good-quality and poor-quality embryo groups at day 2 and 3. Implantation (38.7% versus 41.4), clinical pregnancy (40.3% versus 45.9%), miscarriage (22.2% versus 26.7%;) and live birth rates (37.4% versus 38.8%) were comparable in day 2 good

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and poor-quality embryo groups. No signficiant differences in morphology of transferred blastocysts at day 3 were found. Multivariable analysis highlighted that poor or good embryo quality at day 2 and day 3 were not predictive of the implantation of good-quality blastocysts (at day 2: adjusted odds ratio = 0.82 CI 95% 0.49 to 1.38; at day 3: adjusted odds ratio = 1.39; CI 95% 0.77 to 2.52). Good-quality blastocyst transfer should, therefore, be carried out irrespective of embryo quality at cleavage stage, as it may not compromise success rates in a good-prognosis population.

Introduction

Over the past decade, improvements in culture conditions have allowed the possibility of extended embryo culture until day 5, which has been increasingly preferred to a transfer at day 2 or day 3. In fact, blastocyst transfer is considered more physiological compared with transfers at cleavage stage, as it theoretically enables a better synchronization between the embryonic stage and the endometrial receptivity (Valbuena et al., 2001). Moreover, it is well known that not all embryos obtained at the early cleavage stage develop into blastocysts. Indeed, the morphological criteria commonly used to select embryos at cleavage stage are insufficient to predict their developmental potential, notably because, in many cases, they fail to discard chromosomally abnormal embryos (Fragouli et al., 2014).

Embryo culture generally improves the selection of good-quality embryos available for fresh transfer, cryopreservation, or both, and displaying a good implantation prognosis. Blastocyst morphology is usually evaluated according to three criteria defined in Gardner and Schoolcraft's classification (Gardner and Schoolcraft, 1999): the degree of blastocoele expansion, graded from B1 to B6; the inner cell mass (ICM); and the trophectoderm morphology, both graded from A to C (A corresponding to the best quality score). A high blastocyst quality has undeniably been related to the success rates after IVF or intracytoplasmic sperm injection (ICSI) attempts (Guerif et al., 2010; Rehman et al., 2007; Van den Abbeel et al., 2013). A longer period of culture, however, requires optimal culture conditions and an efficient blastocyst freezing programme to give patients all the benefit of embryo culture strategy. When these conditions are fulfilled, vitrified–warmed blastocyst transfers might provide equivalent live birth rates (LBR) as fresh transfers (Roy et al., 2014).

The efficiency of embryo culture strategy has already been demonstrated, especially in good-prognosis populations, when numerous good-quality embryos are available at cleavage stage (Glujovsky et al., 2012; Guerif et al., 2009). The overall (Guerif et al., 2009) and individual embryo qualities (Rehman et al., 2007) at cleavage stage, however, do not seem to influence the clinical outcomes after the transfer of a good-quality blastocyst, but data on this particular topic are still too scarce.

Therefore, the aim of the present study was to assess, in a good-prognosis population, the value of considering the individual embryo quality at day 2, day 3, or both, when equivalent good-quality blastocysts were available for a transfer at day 5.

Materials and methods

Study design

A retrospective study of prospectively collected data was conducted in the assisted reproduction technique unit of Jean Verdier University Hospital, Bondy, France, after being approved by the Local Ethics Committee on 18 November 2014.

Two hundred and ninety-one blastocyst transfers (125 fresh blastocyst transfers, 166 cryopreserved blastocyst transfers) carried out between January 2012 and March 2016 were retrospectively analysed. All patients met the following inclusion criteria: female age less than 37 years; first or second IVF–ICSI cycle; quality of the transferred blastocyst: blastocoele B3 or higher, inner cell mass A/B, trophectoderm A/B (according to Gardner and Schoolcraft's criteria) (Gardner and Schoolcraft, 1999); known implantation outcome for each transferred blastocyst (including double blastocyst transfers when implantation rate was 0 or 100%). Patients may have been included twice.

Study groups

Two groups were retrospectively created depending on whether the transferred blastocysts originated from a good-quality embryo at day 2 or day 3 (three to five adequately-sized blastomeres at day 2; six to 10 at day 3, <20% fragmentation, no multinucleation) or from a poor-quality embryo (embryos that did not meet the criteria mentioned above).

Sample size

A difference of 30% was previously reported by Silber (2014) between the implantation rate of good-quality blastocysts deriving from day-3 good-quality embryos (implantation rate = 70%) and day-3 poor-quality embryo (implantation rate = 40%). Therefore, considering an alpha risk less than 0.05 and a power greater than 0.95, we assumed that the sample size required to conclude was at least 69 observations in each group.

IVF procedures

Semen preparation

Semen was prepared, using a two-layer density technique (45% and 90%) of PureSperm (Nidacon International, Göteborg, Sweden) diluted in Ferticult HEPES culture media (FertiPro NV, Beernem, Belgium). After a 20-min centrifugation at 300 g, semen pellet was washed using Ferticult HEPES media (FertiPro N.V) and then centrifuged for 5 min at 600 g.

Ovarian stimulation and oocyte retrieval

Ovarian stimulation was conducted as previously described with standard agonist or antagonist protocols (Huirne et al., 2006; Sifer et al., 2006). In brief, within the 3 months preceding ovarian stimulation, antral follicle counting and serum oestradiol, FSH, and anti-Müllerian (AMH) levels were measured on cycle day 3. During a subsequent cycle, recombinant FSH therapy (Gonal-F, Serono Pharmaceuticals, Boulogne, France) was started at a dosage of 150–300 IU/day for at least 5 days, and continued until the day of HCG (Gonadotrophine Chorionique 'Endo', Organon Pharmaceuticals, Saint-Denis, France, 10,000 IU, IM) administration. From the sixth day of exogenous FSH therapy onwards,