Letters to the Editor

References


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Reply: Ultrasound guided embryo transfer does not offer any benefit in clinical outcome: a randomized controlled study

Sir

We thank Drs Ata and Urman for their interest in our study (Kosmas et al., 2007). For the study design, trial committee had to consider two major aspects. Embryo transfer performance is linked with the clinician (Hearns-Stokes et al., 2000), and a certain number of embryo transfers is required for achieving competence equal to experienced providers (Papageorgiou et al., 2001). Therefore, we limited our study to one experienced clinician who performed all embryo transfer.

Decreased uterine contractility during embryo transfer (Fanchin et al., 2001), day of embryo transfer and number of embryos transferred are all factors that play an important role for successful embryo transfers.

Pseudo-randomization methods were the randomization choice in those studies that show a significant positive effect (Buckett, 2003). Pseudo-randomization included randomization based on availability of the ultrasound machine (Prapas et al., 2001), the transfer room (Prapas et al., 2001), ultrasonographer availability (Kan et al., 1999) and randomization done by alternative allocation of patients to each group (Sallam et al., 2002). It is important to understand that pseudo-randomization can introduce significant bias into statistical analysis and this bias can be incorporated in the pooled results. A study that used a true randomization (Garcia-Velasco et al., 2002) did not report significant difference in the outcome after embryo transfer with or without ultrasound guidance. Other studies (Prapas et al., 2001) found no significant difference in pregnancy rates for Day 5 embryo transfers with or without ultrasound guidance.

The corresponding author assumes that embryo transfer with full bladder is a different entity than embryo transfer with empty bladder. A recent meta-analysis of three studies (Abou-Setta, 2007) shows significantly higher likelihood of clinical pregnancy [OR 1.55 (95% CI = 1.16–2.08)] and ongoing pregnancy [OR = 1.44 (95% CI = 1.04–2.04)] with a full bladder. From these three, the two randomized studies included, showed no significant difference in clinical pregnancy rates [OR 1.02 (95% CI = 0.59–1.77)] and only adding the third pseudo-randomized study, makes the difference significant in favor a full bladder embryo transfer. Pooled results incorporate the bias of the single study. Under current evidence, full bladder during embryo transfer is not a different entity from empty bladder, regarding pregnancy rates.

All patients in the ultrasound-guided (US) embryo transfer group had embryo transfer under ultrasound guidance. Sixty patients were excluded because of poor or no visibility during embryo transfer (study flowchart).

Anatomical variability was minimal. In 21 patients, the outer cervical os–uterine fundus distance (as measured, in the US embryo transfer group) was <6 cm. Thirteen of them became pregnant. Most of these measurements were between 5 and 6 cm.

A very neat meta-analysis (Abou-Setta et al., 2007) compared US versus clinical touch method. This meta-analysis states that ultrasound guidance improves clinical pregnancy rates [OR 1.50 (95% CI = 1.34–1.67)]. By excluding the trials (n = 12) with unclear method of randomization or pseudo-randomization, the previous significant difference in clinical pregnancy is lower [OR 1.43 (95% CI = 1.21–1.68)] (Random effects model). Also in this meta-analysis, heterogeneity is significant. The number of patients needed to treat to obtain one additional clinical pregnancy with use of ultrasound guidance need to be calculated. On the basis of these facts, results are debatable.

As a conclusion, all randomized controlled trials have to be uniformly designed, performed by a single clinician and transfer an equal amount of embryos the same day (Day 3 or 5).

References


Abou-Setta AM, Mansour RT, Al-Inany HG, Aboulghar MM, Aboulghar MA, Serour GI. Among women undergoing embryo transfer, is the probability of pregnancy and live birth improved with ultrasound guidance over clinical

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On nucleation and implantation: 0% mononucleation or 100% mononucleation in blastomeres is not the whole story

Sir,

We read with great interest the study by Scott et al. (2007) on the importance of evaluating certain morphological parameters in zygotes and early embryos that related to outcome after IVF. One of the major findings of the study was that the nuclear status of an embryo has a strong impact on outcome after embryo transfer and that mononucleation in all blastomeres versus in no blastomere yielded a significant difference in pregnancy rates. This finding is in agreement with our findings on the same issue. However, the pregnancy rate (implantation rate) in our study varied not only with all or none of the blastomeres in a four-cell embryo but also with the percentage of blastomeres being mononucleate. In the study by Scott et al. (2007), pregnancies were achieved only when the embryo showed mononucleation either in all blastomeres or in none of the blastomeres. Thus, their study was only partly in accordance with our study. We find this confusing and wonder whether embryos that showed mononucleation in one, two or three blastomeres in a four-cell embryo were never used for transfer or if such embryos never implanted or if these categories of embryos were not recorded. We believe that these are important questions to clarify since our study, which constituted of single-embryo transfer cycles only, showed a significantly lower pregnancy rate not only in four-cell embryos lacking mononucleation, but also in four-cell embryos displaying mononucleation in one, two or three blastomeres only (20–22% pregnancy/implantation rate), in comparison with four-cell embryos with 100% mononucleation (42% pregnancy/implantation rate).

References


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Reply: On nucleation and implantation: 0% mononucleation or 100% mononucleation in blastomeres is not the whole story

Sir,

We wish to thank Drs Sundström and Saldeen for their comments and concerns regarding the data that we presented. We agree that it is not the entire story and that an embryo that has only one of four blastomeres with multinucleation may, indeed, be able to implant and form a viable fetus. In contrast, an embryo where no nuclei are visible may have multinucleation, and an embryo with only one or two cells where nuclei are visible may again have multinucleation, that is, not seen. However, in our analysis we did not look at the embryo data for outcome but rather looked at outcome and correlated that with embryo data. This was necessary as the initial series was a prospective data collection, in which Day 2 morphology was not used for transfer or if such embryos never implanted or if these categories of embryos were not recorded. We believe that these are important questions to clarify since our study, which constituted of single-embryo transfer cycles only, showed a significantly lower pregnancy rate not only in four-cell embryos lacking mononucleation, but also in four-cell embryos displaying mononucleation in one, two or three blastomeres only (20–22% pregnancy/implantation rate), in comparison with four-cell embryos with 100% mononucleation (42% pregnancy/implantation rate).