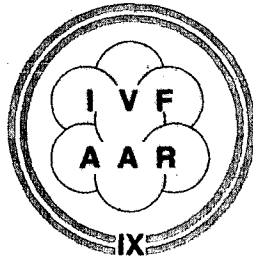


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IXth

Deep-fundal rather than mid-fundal placement of embryos increases ectopic but not intrauterine pregnancy rate (1)

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SUMMARY

A randomized prospective study was performed to compare the effects of a mid-fundal versus a deep-fundal transfer technique on subsequent intrauterine and ectopic pregnancy rates (PRs) following in vitro fertilization (IVF). The clinical intrauterine PR following the deep-fundal transfer was 12.4%/cycle with a 1.5% ectopic PR (which represented 12.2% of the pregnancies) versus 14.2% intrauterine pregnancies/cycle with a 0.4% ectopic rate (representing 3% of pregnancies) following mid-fundal transfers. The mid-fundal technique appears superior to deep-fundal procedures because of a lower percentage of ectopic pregnancies without any sacrifice of the intrauterine PR following mid-fundal transfers.

INTRODUCTION

Part of the quality control for the Cooper Center for In Vitro Fertilization is to evaluate separately the pregnancy rates (PRs) per retrieval and per transfer according to physicians. One physician appeared to have the highest PR/transfer and after evaluating the techniques it was

determined that this particular physician, in contrast to the others, did not use a mid-fundal transfer technique, but instead delivered the embryos <5mm from the fundus.

Based on this retrospective analysis, a prospective study was designed to compare intrauterine pregnancy (IUP) rates and ectopic pregnancy (EP) rates following mid-fundal vs deep-fundal embryo transfers following IVF.

MATERIALS AND METHODS

Five physicians participated in this study. Two were designated to use a deep-fundal transfer and the other three physicians the mid-fundal technique (>15mm from fundus). Three controlled ovarian hyperstimulation (COH) regimens were used for fresh ETs; luteal phase leuprolide acetate (LA) - gonadotropin regimen (90% of cycles), short flare technique, hMG only, and clomiphene citrate (CC)-gonadotropins. The patients were assigned to the two groups randomly, regardless of their COH regimens. Therefore, both groups contained similar proportions of patients on different COH regimens.

Embryo Transfer Procedure

The short Frydman Embryo Transfer Set (CCD International, Natick, MA) was used for embryo replacement into the uterus. The set consists of a cannula with a removable metal stylet and an ET catheter with an inner steel tube in the upper part of the catheter. The cannula is inserted into the cervix and the stylet is removed.

In the IVF laboratory the catheter is attached to a 1 mL syringe and rinsed up to the metal rod with ET media. Embryo transfer media consists of Hepes buffered human tubal fluid medium (Irvine Scientific #1092, Irvine, California). Air is introduced into the syringe up to the 0.05 mL mark. A 5 uL column of transfer media is aspirated into the catheter followed by the same volume of air. The embryos are placed in an organ culture dish in 1 mL of transfer media and then loaded into the catheter in 5 uL of transfer media. This column with embryos is followed by 5 uL of air and a final column of 5 uL of transfer media.

The embryologist hands the transfer catheter through a window in the IVF laboratory into the transfer room. The physician places the catheter into the uterus and expels the embryos and the extra 0.05 mL of air. The uterine depth from the external os had been previously determined during a mock transfer procedure. The distance from the fundus during the actual transfers was based on the external os-fundus depth measured in the prior mock transfer. The catheter is held in this position for one minute after the transfer to allow the embryos to fall away from the catheter. The catheter and cannula are removed from the uterus and handed back to the embryologist. The embryologist rinses the catheter and cannula with embryo transfer media to ensure that no embryos remained inside.

RESULTS AND CONCLUSIONS

There were 1590 transfers evaluated (including fresh and frozen

ETs). There were 200 (12.5%) clinical pregnancies (gestational sac seen intrauterine) and 14 EPs (7.0% of all pregnancies were EPs). The deep-fundal technique was used in 660 ETs and mid-fundal in 930 ETs. There were 82 pregnancies using deep-fundal technique (12.4%) and 132 pregnancies (14.2%) for the mid-fundal transfer group. Ten EPs occurred in 660 (1.5%) deep-fundal transfers and 4 in 930 (0.4%) mid-fundal transfers. Thus, 10 of 82 (12.2%) pregnancies following deep-fundal transfer resulted in EPs compared to only 4 of 132 (3%) with the mid-fundal technique. The difference in the rate of EPs with the two techniques of transfer was significant (Fisher's Exact Test, $P = 0.029$).

Tubal disease was noted in 49% vs 46.5% of those receiving deep vs mid-cavity transfer, respectively. All EPs occurred in women with tubal pathology.

The number and percentage of ectopics according to COH regimen used (irrespective of mid-fundal or deep-fundal transfer technique) were as follows: luteal phase LA - 11 EPs (7%), hMG - 2 (3%), and flare technique - 1 (3.2%). Considering the very low number of the ectopics with hMG and flare techniques, and low proportion of transfers performed with these techniques, the difference probably could not be considered significant.

The relationship of the transfer techniques in ET to the success and complications of IVF has been a subject of interest and discussion since the introduction of this technology.

Yovich et al. (2) evaluated the same two transfer techniques we evaluated in this study and found 4 of 24 pregnancies were ectopic (25%) with deep-fundal transfers versus only one ectopic in 56 (1.7%) using mid-fundal transfer (2). Interestingly, 2 of the 14 pregnancies in the study presented herein were heterotopic pregnancies. Dimitry et al. (3) reported heterotopic pregnancies in 9 of 312 IVF (2.9%) pregnancies despite the fact that heterotopic pregnancy has been estimated to be as infrequent as 1/30,000 (4). The 4.2% rate of EPs in mid-fundal transfer in this study is consistent with the 4.0% risk of EPs reported by Cohen et al. in 1163 IVF pregnancies (5).

We had five physicians participating in this study. Ideally the study would have been less biased if only a single physician would have done both types of transfers during the whole study. This would have precluded an adequate sample size in a reasonable length of time. However, to overcome this possible difficulty we evaluated the results of the transfers by the two physicians who were performing the deep transfers, since they changed to the mid-cavity technique at the termination of the reported study. Out of 285 ETs performed by the mid-cavity method they had 70 pregnancies (PR = 24.5%/ET) and two cases of ectopics (2.8%). This confirms the increased risk of the deep-fundal transfer in leading to EPs. Since no higher intrauterine PR was found with the deep method, the mid-cavity approach is the preferred technique.

The explanation behind the higher ectopic rate in deep-fundal method might be the closer proximity of the embryos to the tubes and that the fundal contact might exacerbate the uterine activity which could force the embryos in a retrograde direction.

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