

Monday, October 17, 2005
4:00 p.m.

O-122

Ongoing Pregnancy Rate is Significantly Higher With Day 5 Embryo Transfer Than After Day 3 Embryo Transfer, When More Than Three Embryos are Available on the Third Day of Embryo Culture. E. G. Papanikolaou Sr., G. Verheyen, M. Camus, A. Van Steirteghem, P. Devroey, H. Tournaye. Dutch speaking, Free University of Brussels, Brussels, Belgium.

OBJECTIVE: To study whether patients with at least four good quality embryos on day 3 would benefit in terms of ongoing pregnancy rate, from an extension of culture to day 5, and eventually from undergoing a blastocyst stage transfer.

DESIGN: Prospective randomized controlled trial.

MATERIALS AND METHODS: Between January 2001 and November 2003, 301 patients seeking infertility treatment were assessed eligible (female age ≤ 37 years; rank trial ≤ 3 ; FSH on day 3 of the cycle ≤ 12 ; ejaculated sperm origin; equal number ($n=2$) embryos transferred in each group) for participating in the study. Overall, 164 patients fulfilled the criteria on the third day of embryo-culture and were randomized to have either a cleavage stage embryo transfer (D3 group, $n=84$) or a blastocyst stage embryo transfer (D5 group, $n=80$). Good quality embryos were defined as having minimum 6 cells in the morning of day 3 with maximum 20% of anucleate fragments. Multifollicular ovarian stimulation (multi-FOS) was performed with a GnRH-agonist protocol in 44% of the patients, whereas in the remaining 56% of the patients a GnRH-antagonist protocol was used. An ongoing pregnancy was defined as each pregnancy showing a positive heart beat at ultrasound after 12 weeks of gestation. Fisher's exact test was used to analyse nominal variables while continuous variables were compared using independent Student's t-test or Mann Whitney test. Analysis was by intention to treat.

RESULTS: The two groups were comparable with regard to the age, the infertility aetiology, the stimulation protocol used, the duration of stimulation, and the total dose of gonadotrophins administered. All patients in both groups had embryo transfer. Both clinical pregnancy rate (52.5% vs. 32.1%; OR: 2.33, 95%CI: 1.23-4.40) and ongoing pregnancy rate (51.3% vs. 27.4%; OR: 2.78, 95%CI: 1.45-5.34) were significantly higher in the D5 group compared to the D3 group, respectively. Similarly, implantation rate was higher after D5 transfer compared to D3 embryo transfer (37.3% vs. 20.6%, $p<0.001$). A high (42.9%) initial multiple pregnancy rate in blastocyst group (compared with 29.6% in D3 group) resulted in more than one third of the ongoing pregnancies after Day 5 transfer being twins (36.8%).

CONCLUSION: The threshold of four good embryos on the third day of embryo culture appears to be reassuring criterion that the patient will undergo an embryo transfer at day 5 and moreover will have a higher chance of achieving an ongoing pregnancy compared to day 3 transfer. The reason for the higher success rate with blastocysts might mainly be due to a selection process (a high proportion of morphologically top quality embryos on day 3 of culture will be chromosomically abnormal). However, as a result of the high implantation potential, blastocyst transfer in selected patients may lead to an unacceptable high rate of multiple pregnancies. Therefore, it appears that reducing high order pregnancies without compromising pregnancy outcome, by implementing single blastocyst transfer in a population similar to the one involved in the present study, is a realistic goal.

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Monday, October 17, 2005
4:15 p.m.

O-123

Impact of Prophylactic Antibiotics on the Incidence of Bacterial Contamination of Embryo Transfer Catheters and Subsequent Pregnancy Outcome Rates After ART. N. Brook, J. Edgeworth, Y. Khalaf, E. Wharf, P. Braude. Guys and St Thomas's Hospital, London, United Kingdom.

OBJECTIVE: To determine the impact of prophylactic antibiotics (co-amoxiclav) given prior to embryo transfer on bacterial contamination rates of the embryo transfer catheter, and on pregnancy rates.

DESIGN: 342 patients were randomised on the day of egg collection using opaque sealed envelopes randomisation to receive either 750mg of co-amoxiclav the night before embryo transfer and 750mg 2 hours prior to embryo transfer, or no antibiotics. Exclusion criteria were allergy to penicillin, antibiotics being indicated during transvaginal oocyte retrieval, or declined to take part. Patients were included for one cycle only. Patients underwent standard ultrasound guided trans-cervical embryo transfer on either day 2 or 3 following oocyte retrieval. The Guy's and St Thomas' Hospital Ethics Committee and Research and Development Department (EC04/033) approved the trial.

MATERIALS AND METHODS: Routine preparation and cleaning of the vagina and endocervix was undertaken in the same way for all patients. The physician was blinded to which arm of the study the patient was allocated. Embryos were transferred to the mid-cavity of the uterus under ultrasound guidance. Following withdrawal of the catheter and confirmation that the embryos had been transferred, the distal 2cm of the catheter tip was cut using sterile scissors and rolled using sterile forceps on to an agar plate and then placed in broth solution for bacterial incubation for 48 hours. Microbiological assessment of the plates was performed by a single observer blinded to the randomisation, who identified the organism(s) isolated, and quantified the severity of the contamination. Results were recorded as no growth, gram-negative growth or gram-positive growth, the latter subdivided in three categories - light, moderate and heavy growth. Statistical analysis was performed on completion of recruitment using the two-sample Wilcoxon rank-sum test.

RESULTS: The two patient groups had similar demographics of age, number of previous cycles and type of treatment. Of the 342 patients recruited to the trial, catheter analysis was performed on 277 (81%). The remainder were excluded due to failed fertilisation (22), inadvertent discarding or loss of catheter tips (39), protocol violations (4) or candidal growth on catheter tip (1). 147 patients had co-amoxiclav (group 1) and 130 did not (group 2). There was no statistical difference in contamination rates of the catheter tip (52.3% group 1 vs 61.5% group 2), or pregnancy rates in the two groups (46.3% group 1 vs 43.8% group 2). The presence of gram-negative bacteria did not have a statistical impact on the likelihood of achieving a pregnancy (45.4% group 1 vs 51.7% group 2), but the presence of a severe gram-positive infection was associated with a significant reduction in the likelihood of achieving a pregnancy (Light growth OR 0.69, moderate growth OR 0.63, heavy growth OR 0.33 ($P<0.047$)).

CONCLUSION: This study does not support the hypothesis that routine antibiotic prophylactics at the time of embryo transfer increases the likelihood of a successful pregnancy outcome. Even the presence of gram-negative bacterial contamination did not reduce the pregnancy rate significantly but a heavy bacterial contamination with gram-positive organisms did. However identification of these women at the time of embryo transfer is difficult.

Supported by: None

Monday, October 17, 2005
4:30 p.m.

O-124

Ultrasound-guided Versus Clinical Touch Embryo Transfer: A Systematic Review & Meta-analysis. A. M. Abou-Setta, H. G. Al-Inany, R. T. Mansour, M. M. Aboulghar, G. I. Serour, M. A. Aboulghar. The Egyptian IVF-ET Center, Cairo, Egypt.

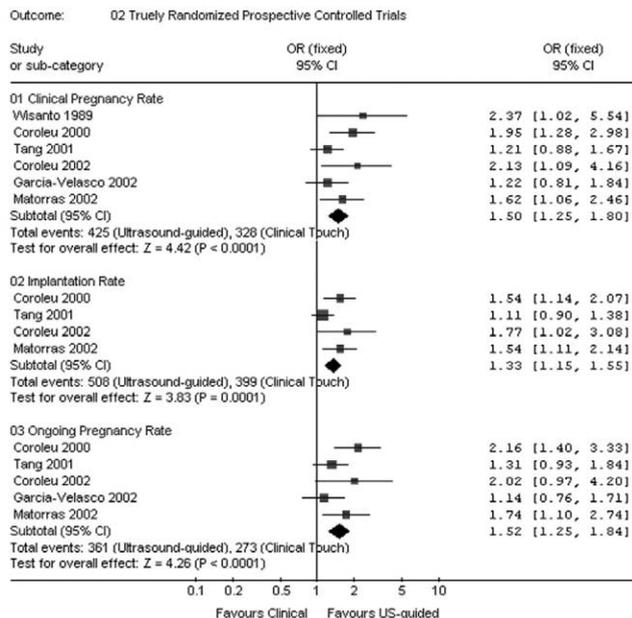
OBJECTIVE: Embryo transfer is considered as the most crucial step in IVF/ICSI cycles. The amount of high quality literature concerning ultrasound guidance during embryo transfer is both limited and conflicting.

DESIGN: Systematic review and meta-analysis of randomized, controlled trials comparing US-guided ET with clinical touch ET.

MATERIALS AND METHODS: A computerized search was conducted using MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL) on the Cochrane Library Issue 2, 2005, the National Research Register (NRR) and the Medical Research Council's Clinical

Trials Register. Furthermore, the reference lists of all known primary studies and review articles were also examined to identify additional relevant citations. In addition, a hand search of the citation lists of relevant publications, review articles; abstracts of scientific meetings and included studies were searched for trials.

RESULTS: A total of 15 randomized controlled trials (RCTs) evaluating the use of abdominal US-guided vs. clinical touch embryo transfer were located (12 full-text papers and 3 conference abstracts) including 8,381 embryo transfers. Since the quality of randomization was determined to be improper in five studies, or not clear from the manuscript in four studies, only six studies were determined to have described a proper method of randomization. As for the primary outcome measures (clinical pregnancy rate, implantation rate and ongoing pregnancy rate), using the fixed, or random effect model (where appropriate), pooling of the results demonstrated a statistically significant increased chance of clinical pregnancy [(P < 0.00001; O.R = 1.54, 95% CI = 1.37 - 1.74)], implantation [(P = 0.007; O.R = 1.28, 95% CI = 1.07 - 1.54)], and ongoing pregnancy [(P < 0.0001; O.R = 1.50, 95% CI = 1.25 - 1.79)] following embryo transfer using the US-guidance vs. clinical touch: Furthermore, when only the truly randomized controlled trials were analyzed, the results were still in favor of using ultrasound guidance: clinical pregnancy rate [(P < 0.0001; O.R = 1.50, 95% CI = 1.25 - 1.80)], implantation rate [(P = 0.0001; O.R = 1.33, 95% CI = 1.15 - 1.55)], and ongoing pregnancy rate [(P < 0.0001; O.R = 1.52, 95% CI = 1.25 - 1.84)] following embryo transfer using the US-guidance vs. clinical touch. As for the secondary outcome measures (multiple pregnancy rate, ectopic pregnancy rate and rate of difficult transfer), there was no statistical significant difference between the two groups. Lastly, a series of subgroup analyses have been performed to determine the difference between fresh, frozen-thawed and donor oocyte trials. In addition, each study was critically appraised and given a validation score.



CONCLUSION: Using ultrasound guidance during ET results in a significantly higher PR, IR and OPR as compared to clinical touch.
Supported by: None

Monday, October 17, 2005
 4:45 p.m.

O-125

The Success in IVF When Utilizing Autologous Endometrial Coculture (AECC) is not Secondary to a Local Endometrial Injury. S. D. Spandorfer, Y. Delgado, J. Park, R. Clark, Z. Rosenwaks. Cornell University Medical Center, New York, NY; Flushing Hospital, Flushing, NY.

OBJECTIVE: The success after IVF depends on many factors. We have developed a unique coculture system utilizing the patient's own endometrial cells and successfully applied this to our clinical IVF-ET program (J Rep Med, 2004). Previous work has suggested that an endometrial biopsy in the cycle prior to IVF is associated with a doubling of IVF success rate (Fertil Steril 79: 1317). This has prompted us to speculate that our success with AECC may be secondary to a local endometrial injury effect specifically limited to those patients undergoing a biopsy in the cycle prior to their IVF cycle.

DESIGN: Retrospective analysis of 665 consecutive IVF cycles utilizing AECC comparing outcome and effectiveness of AECC based on performing the endometrial biopsy in the immediate menstrual cycle preceding the IVF cycle or at a time before this (at least 2 cycles before the IVF cycle).

MATERIALS AND METHODS: Embryos from each of 665 patients allocated to growth on AECC were analyzed for outcome. All patients had previously undergone failed IVF cycles. During a luteal phase biopsy (5-12 days after LH surge) made prior to the treatment cycle, glandular (G) and stromal (S) endometrial cells were isolated by enzymatic digestion and separated based on differential sedimentation rates. These cells were cryopreserved, then plated as a 50%/50% combination of G and S cells prior to embryo exposure. Three hundred patients underwent a biopsy in the cycle before IVF, while the remaining 365 patients underwent their biopsy at least more than 2 cycles prior to their IVF cycle.

RESULTS: The mean age of the patients was 37.02 (± 3.8) years with an average number of 3.1 (± 1.8) failed IVF cycles. Embryos grown on AECC demonstrated a significant improvement in number of blastomeres and fragmentation when compared to embryos grown in conventional media without AECC (5.9 ± 1.0 vs. 4.7 ± 1.1 blastomeres and 11.6% ± 5.3 vs. 21.6% ± 7.2 frag; P < 0.001). Nineteen of the patients (19/665; 2.86%) did not have a transfer. An overall pregnancy rate of 51.9% and an overall clinical pregnancy (positive fetal heart) of 42.1% were found per patient

