Effect of hyaluronan-enriched transfer medium on take home baby rate after day 3 and day 5 embryo transfers: a prospective randomized study

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Introduction: In 2008 we published a study on the effect of using a hyaluronan-enriched transfer medium (HETM) (Urman et al, 2008) in assisted reproductive technology (ART). The aim of the study was to investigate if there was a significant impact on implantation rate and pregnancy rate after cleavage stage and blastocysts transfers when HETM was used compared to a conventional transfer medium. We found that HETM had a significant positive effect on both pregnancy rate (54.6% vs 48.5%; OR 1.3; 95th CI 1.0-1.6) and implantation rate (32.0% vs 24.7; OR 1.4; 95th CI 1.2-1.7). Recently, the Cochrane Collaboration published a review article on adherence compounds in embryo transfer media for assisted reproductive technologies (Bontekoe, 2010). In this review, 15 randomized controlled studies which investigated the effect of hyaluronan containing transfer media were included. The results showed evidence of improved clinical pregnancy rate with the use of high concentrations of hyaluronan in ART cycles but found no effect on live birth rate. Most studies did not include data on live birth and therefore the conclusion was based on the results from four studies only. In our previous study, delivery rate was not an endpoint. Accordingly, the objective of this study was to follow up the deliveries from the HETM and control group from our previous randomized controlled trial and investigate if there were any differences in take home baby rate between the two groups.

Material and methods: A total of 1,282 fresh cycles were included in the study and the patients were randomized either to the HETM group or to the control group. The clinician and the patient were blinded for the allocation. The study was approved by the Institutional Review Board and informed consent from each patient was obtained. The stimulation protocol, oocyte retrieval and embryo transfer procedures are described in Urman et al, 2008. For hyaluronan-enriched transfer media, EmbryoGlue (Vitrolife, Sweden) was used and for controls G2 version 3 (Vitrolife, Sweden) was used. Data on delivery results were collected from our clinical database and have been analyzed by using Fisher´s exact test to test for differences between groups.

Results: There were no significant differences between the two groups in patient characteristics (Urman et al, 2008). A total of 639 embryo transfers (ET) were included in the HETM group and 643 in the control group. The overall take home baby rate in the HETM group was 48.5% (310/639) compared to 38.4% (247/643) in the control group, $p<0.001$, OR 1.5; 95th CI 1.2-1.9. The take home baby rate for ET day 3 was 40.3% (166/412) in the HETM group and 30.8% (127/413) in the control group, $p<0.01$, OR 1.5; 95th CI 1.1-2.0. The take home baby rate for ET day 5 was 63.4% (144/227) in the HETM group compare to 52.2% (120/230) in the control group, $p<0.05$, OR 1.6; 95th CI 1.1-2.3. In the HETM group, a total of 481 healthy babies were born from 1,718 transferred embryos and 328 healthy babies were born from 1,769 transferred embryos in the control group (28.0% vs 18.5%, $p<0.001$, OR 1.7; 95th CI 1.5-2.0).

Conclusion: From the Cochrane report there is strong evidence that the presence of hyaluronan in the transfer medium has a positive effect on the pregnancy rate. In this study, we conclude that a high concentration of hyaluronan in transfer media also has a positive effect on the take home baby rate. The positive effect was seen for both day 3 transfers and blastocyst transfers.

References: Urman B *et al.* (2008) Fertil Steril, Sep;90(3):604-12

Bontekoe S *et al*. (2010) Cochrane Database Syst Rev, Jul7; (7): CD007421