Original Articles

Reproductive Biology Section

"Embryo glue" does not seem to improve chances of subsequent pregnancy in refractory in vitro fertilization cases

J.H. Check, D. Summers-Chase, W. Yuan, K. Swenson, D. Horwath, M. Press

The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at Camden
Cooper Hospital/University Medical Center, Department of Obstetrics and Gynecology
Division of Reproductive Endocrinology & Infertility, Camden, NJ (USA)

Summary

Purpose: To determine if the use of Embryo glue improves implantation and pregnancy rates following embryo transfer (ET) in women who failed to conceive in three previous attempts. *Methods:* A matched controlled study was performed in women undergoing IVF-ET, donor oocyte recipients and women using their own oocytes having fresh or frozen ETs. A woman having Embryo glue was matched with the very next woman not using glue within six months of age and having the same number of previous failed ETs. *Results:* Embryo glue did not seem to improve pregnancy or implantation rates. In fact, in evaluating fresh embryo transfers there was a significantly higher live delivered pregnancy rate in the women not using Embryo glue (39.3%) vs those using the glue (14.3%). *Conclusions:* Embryo glue does not improve pregnancy outcome in women failing in previous IVF cycles.

Key words: Embryo glue; Refractory IVF cases.

Introduction

Implantation following in vitro fertilization-embryo transfer (IVF-ET) is a multistage process involving opposition and adhesions of the blastocysts to the uterine endometrium followed by invasion of the trophoblast. One of the reasons for implantation failure in what appears to be normal morphologic embryos could be chromosomal abnormalities. Another theoretical cause may be the failure to develop a sufficient "sticky" matrix for the embryos to attach to the endometrial wall.

Embryo glue (Vitrolife, Denver, CO), which is composed of various substances with the active ingredient hyaluronan, has been developed and there are claims that it can improve pregnancy rates (PRs) following embryo transfer (ET) [1-3]. Other studies have found no benefit to using Embryo glue as a transfer medium as evidenced by comparable pregnancy and implantation rates [4-6].

The objective of the present study was to determine if the use of Embryo glue improves implantation and PRs following ET in women who failed to conceive despite at least three previous ETs.

Materials and Methods

A matched controlled study was performed to evaluate the efficacy of Embryo glue in women undergoing IVF-ET. The study population included donor oocyte recipients and women using their own oocytes having either fresh or frozen ETs. All women in the study had failed to conceive from at least three prior ETs and had a normal uterine cavity as determined by HSG or saline infusion sonography.

A woman who had used Embryo glue was matched with the very next woman not using glue within six months of age and having the same type of ET (fresh or frozen) and same number of previous failed ETs. Oocyte recipients were paired receiving eggs from the same donor.

Embryo transfer was performed using one of two media; Embryo glue or modified human tubal fluid (HTF) supplemented with 20% serum protein substitute (SPS) (both from Sage BioPharma, Pasadena CA). Both types of media were equilibrated overnight at 37°C, 5.5% CO_2 in air. For Embryo glue ETs, embryos were placed in Embryo glue after assisted hatching was performed, between one to three hours prior to ET, and loaded directly into the catheter from the Embryo glue dish. For all other ETs, embryos were moved to the modified HTF solution immediately prior to loading in the catheter. Wallace catheters were used for all ETs.

Comparison of PRs between the two groups (glue or no glue) was made using chi-square analysis with $p < 0.05$ used to determine significance.

Results

Forty-seven women had ETs using Embryo glue, 28 were fresh ETs and 11 were frozen ETs in women up to age 41; 6 were recipient ETs. Overall, there was a non-significant trend for higher clinical and delivered PRs in women where Embryo glue was not used. The clinical pregnancy rate was 29.8% (14/47) for Embryo glue vs 40.4% (19/47) for conventional transfer media, and a delivered pregnancy rate of 23.4% (11/47) vs 38.3% (18/47), respectively.

Evaluation of the implantation rate also demonstrated the same trend; 16.2% (18/111) for Embryo glue vs 22.8% (26/114) for no glue (p = NS). Data were further analyzed by transfer type- fresh, frozen or egg recipient (Table 1).

Revised manuscript accepted for publication January 19, 2011

Table 1. — *Comparison of outcome by type of ET (fresh or frozen or donor egg) and by use or non-use of Embryo glue.*

	Fresh ETs		Recipient ETs		Frozen ETs	
	Embryo glue	No Glue	Embryo glu	No Glue	Embryo glue	No Glue
# Transfers	28	28	6	6	13	13
# ET	2.3 ± .8	2.4 ± .8	3.2 ± .4	2.8 ± .4	2.9 ± .8	3.2 + .7
Clinical PR	25% (7/28)	39.3% (11/28)	50% (3/6)	50% (3/6)	30.7% (4/13)	38.5% (5/13)
Delivered PR	14.3% (4/28)	39.3% (11/28)	50% (3/6)	50% (3/6)	30.7% (4/13)	30.7% (4/13)
Implantation rate	15.3% (10/65)	23.5% (16/68)	16.7% (3/18)	18.8% (3/16)	17.9% (5/28)	23.3% (7/30)

The only significant difference seen was the delivered pregnancy rate in fresh ETs; significantly more women had a successful delivery when conventional ET media was used, 39.3% (11/28) vs 14.3% (4/28) for Embryo glue ($p < .035$).

Conclusions

These data suggest that Embryo glue does not improve implantation in women who have had at least three prior failed ETs. In fact, a trend for a better outcome was observed when Embryo glue was not used as the transfer media.

We purposely chose women who had failed to conceive despite three or more failed ETs since the possibility exists that a defect in adhesion molecules may be present in only a minority of cases and therefore would be more likely to be manifested in a group with several previous failures to establish a live pregnancy.

References

[1] Schoolcraft W., Lane M., Stevens J., Gardner D.K.: "Increased hyaluronan concentration in the embryo transfer medium results in a significant increase in human embryo rate". *Fertil. Steril.,* 2002, *78* (suppl, 1), 55.

[2] Valojerdi M.R., Karimian L., Yazdi P.E., Gilani M.A., Madani T., Baghestani A.R.: "Efficacy of a human embryo transfer medium: a prospective, randomized clinical trial study". *J. Assist. Reprod. Genet.,* 2006, *23*, 207.

[3] Svobodova M., Brezinova J., Oborna I., Dostal J., Krskova M.: "Embryo glue the transfer medium with hyaluronan in the IVF+ET program". *Ceska Gynekol.,* 2007, *72,* 15.

[4] Simon A., Safran A., Revel A., Aizenman E., Reubinoff B., Porat-Katz A. *et al.*: "Hyaluronic acid can successfully replace albumin as the sole macromolecule in a human embryo transfer medium". *Fertil. Steril.,* 2003, *79,* 1434.

[5] Karimian L., Rezazadeh Valojerdi M., Baghestani A.R., Moeini A.: "A prospective randomized comparison of two commercial embryo transfer medium in IVF/ICSI cycles". *Hum. Reprod.,* 2004, *19* (suppl. 1), i52.

[6] Loutradi K.E., Prassas I., Bili E., Sanopoulou T., Bontis I., Tarlatzis B.C.: "Evaluation of a transfer medium containing high concentration of hyaluronan in human in vitro fertilization". *Fertil. Steril.,* 2007, *87,* 48.

Address reprint requests to:
J.H. CHECK, M.D., Ph.D.
7447 Old York Road
Melrose Park, PA 19027 (USA)
e-mail: laurie@ccivf.com