IS THE OUTCOME OF ICSI CYCLES AFFECTED BY EMBRYO TRANSFER TECHNIQUE?

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ABSTRACT

Objective: To evaluate the effect of tenaculum usage during embryo transfer, on pregnancy rates of intracytoplasmic sperm injection (ICSI) cycles.

Methods: Thirty-eight ICSI cases in which cervix uteri were held with tenaculum during embryo transfer were compared to 76 cases in which embryo transfer was performed easily by a transfer catheter.

Results: Both groups were comparable for female age, etiology of infertility, and number of embryos transferred. Sixteen of the thirty-eight women (42.1%) in the former group became β-hCG test positive; however, only 14 cases (36.8%) progressed to clinical pregnancy. In the latter group, 30 of the 76 cases (39.5%) were β-hCG test positive, and 25 cases (32.9%) turned into clinical pregnancy. There was no significant difference among the biochemical or clinical pregnancy rates of the two groups ($p>0.05$).

Conclusion: In comparison of the two groups with similar characteristics, holding the cervix uteri with tenaculum during embryo transfer, a procedure that might induce prostaglandin secretion and cause minimal bleeding, did not create a significant difference between the pregnancy rates of the two groups. Therefore, correcting the position of the cervix and the uterus during embryo transfer, by holding with an instrument may be advisable instead of a hard and long transfer by only using the transfer catheter.

Key Words: ICSI, Embryo transfer, Pregnancy rate, Tenaculum, Catheter

INTRODUCTION

Embryo transfer is one of the most critical stages of an intracytoplasmic sperm injection (ICSI) cycle, thus it has been thoroughly analyzed by many authors. The most common parameters investigated and found to be influencing the pregnancy rates are the number of embryos to be transferred, the route of transfer, location of transfer, and multiple transfers (1-5). Difficult embryo transfer is a leading cause of multiple transfers for retained embryos in the transfer catheter (4).

This study has been designed to investigate the effect of tenaculum application for traction of the cervix, on the pregnancy rate of ICSI cycles. We have found that straightening the uterocervical angle by traction of the cervix permits easier transfer in some cases and has no deleterious effect on the pregnancy rate.

MATERIALS AND METHODS

One hundred and fourteen consecutive ICSI cases below the age of 40 years who have undergone embryo transfer between July 1997 and September 1997 in the International Hospital IVF unit were included in the study. Four cases where cervical dilatation had to be performed were excluded from the study.

All patients received a gonadotropin releasing hormone agonist (GnRHa) either as a long or as a flare-up protocol. Follicle development was stimulated using LH + FSH, pure FSH or a combination of both. Ten thousand IU of hCG (Pregnyl, Organon) was administered when the leading follicle reached at least 18 mm in mean diameter and serum E2 levels exceeded 1000 pg/ml.

Oocyte aspirations were performed transvaginally 35-36 hours after hCG injection. Retrieved oocytes were microinjected 4 hours after the collection time.

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All embryos were observed daily and scored according to the following system: Embryo score consists of two components; number of blastomers multiplied by grade of blastomeres. Grading is done in four groups. Grade 1 embryos are without fragments and with even blastomeres: they receive a score of 4 for grading. Grade 2 embryos have a fragmentation or uneven blastomare rate of up to 10%, score 3. Grade 3 and 4 embryos carry 10-50% and >50% fragmentation with scores of 2 and 1, respectively. Day 2 embryos contain 4 and day 3 embryos contain 8 blastomeres, optimally. To make the day 2 and day 3 transfers comparable, the embryo score of an individual embryo is given as the percentage of that day's optimum embryo score. For example a grade 2 embryo with 8 blastomeres on day 3 receives a score of (3x8) 24 which when divided by the optimum score (32) gives 75%. Mean embryo score is calculated as the mean of all embryos transferred.

Up to four embryos were replaced after 48 to 72 hours of oocyte collection. The outer sheath of a soft embryo transfer catheter was placed into the cervical canal, the tip being flush with the internal cervical os. In case of difficulty, the cervix was held with a tenaculum very gently and the uterus was pulled forward to straighten the uterocervical angle. When this procedure also failed a harder transfer catheter was used. As soon as the outher sheath was in place, the inner piece with the embryos was brought by the embryologist, and the transfer was performed to a location of 1 cm. before the uterine fundus, a distance measured previously.

The luteal phase was supported with injections of progesterone in oil (50 mg IM daily). Pregnancy test was performed on the 13th day after embryo transfer by measuring the blood β-hCG level. A clinical pregnancy was defined by observation of a gestational sac and a fetal heart beat.

Statistical analysis was performed by two-tailed independent Student's t-test for numerical values, and Chi-square test with Pearson coefficient was used for non-parametric values.

RESULTS

In seventy-six of the 114 cases, embryo transfer was performed easily by a soft catheter (Group A). Among the remaining 38 cases (Group B) where the soft catheter did not pass through the internal cervical os, traction of the cervix by a tenaculum provided a smooth transfer in 22 cases; however, in 16 cases a harder catheter along with tenaculum usage was necessary to perform the transfer.

Groups A and B were comparable for mean age, 31.7 years and 32.5 years, respectively (Table I). Mean number of embryos transferred in both groups were 3.1 per transfer (Table I). Mean embryo scores were also comparable 81.3 ± 15.7% and 78.4±13.8% for groups A and B, respectively.

Etiology of infertility was dominated by male factor 85.5% in group A and 76.3% in group B. Other factors were also distributed similarly in both groups (Table II).

Comparison of either biochemical (only β-hCG positive, no gestational sac) or clinical (fetal cardiac activity present) pregnancy rates were statistically not significant (p>0.05) (Table III).

Within group B, although statistically not significant because of small number of cases, a marked difference was observed between the pregnancy rates of cases where a soft catheter or a hard catheter was used (p>0.05) (Table IV).

Table I. Comparison of mean age, mean number and grade of embryos transferred between group A (embryo transfer **without** tenaculum usage) and group B (embryo transfer **with** tenaculum usage). SD: standard deviation. N.S.: not significant (p>=0.05).

Variable	Group	Mean	±SD	Min.	Max.	p value
Age	A	31.7	4.6	21	39	N.S.
	B	32.5	4.9	22	39	
ET	A	3.1	1.1	1	4	N.S.
	B	3.1	1.0	1	4	
Embryo	A	81.3%	15.7%	40.6%	100.0%	N.S.
Score	B	78.4%	13.8%	43.8%	100.0%	

Table II. Distribution of etiology in group A (embryo transfer **without** tenaculum usage) and group B (embryo transfer **with** tenaculum usage) patients.

Etiology	Group A (%)	Group B (%)
Male	65 (85.5)	29 (76.3)
Tubal	6 (7.9)	5 (13.2)
Anovulation	3 (3.9)	1 (2.6)
Other	2 (2.7)	3 (7.9)

Table III. Comparison of biochemical (only β-hCG positive, no gestational sac) and clinical (fetal cardiac activity present) pregnancy rates between group A (embryo transfer **without** tenaculum usage) and group B (embryo transfer **with** tenaculum usage) (p>=0.05).

Pregnancy	Group A (%)	Group B (%)
Not pregnant	46 (60.5)	22 (57.9)
Biochemical pregnancy	5 (6.6)	2 (5.3)
Clinical pregnancy	25 (32.9)	14 (36.8)

Table IV. Biochemical (only β-hCG positive, no gestational sac) and clinical (fetal cardiac activity present) pregnancy rates within group B (embryo transfer **with** tenaculum usage) comparing soft and hard catheter usage (p>=0.05).

Pregnancy	Soft catheter (%)	Hard catheter (%)
Not pregnant	10 (45.5)	12 (75.0)
Biochemical pregnancy	1 (4.5)	1 (6.3)
Clinical pregnancy	11 (50.0)	3 (18.8)

DISCUSSION

Since fertilization and cleavage rates have improved by recent developments in the embryology laboratory, implantation has become the limiting factor for pregnancy rates remaining still around 30-40%. Although our knowledge is very restricted about implantation, embryo transfer is a procedure shown to be effective in implantation rate (5). Therefore, we may improve our pregnancy rates by performing adequate embryo transfer techniques.

Difficult embryo transfers have been shown to decrease pregnancy rates and also cause retention of embryos within the catheter leading to multiple transfers (4,5). Nabi et al., have stated presence of mucus or blood on the transfer catheter after the procedure and difficulty in passing the internal cervical os, as the main factors for retained embryos. They have found no significant difference between the pregnancy rates of single transfer cases and multiple transfer cases, 24.7% and 23.2% respectively (4). In contrast, Viscer et al., have found the pregnancy rate of immediate retransfer cases as low as 3.0% compared to the 20.3% of single transfer cases and 10.5% of retransfer cases after 24 hours (5).

We have applied traction on the cervix by gently holding with a tenaculum after failure of passage through the internal cervical os by a soft catheter and manipulation of speculum. As shown by Johnson et al., a limited traction force on the cervix decreases the uterocervical angle from 75° to 10°, which in turn provides a straight route for the catheter (6). Although other methods such as dilatation beforehand by laminaria or filling the bladder to straighten the anteverted uteri have been tried, these resulted either in reduced pregnancy rates or further difficult transfers (7-9).

In our cases, the overall pregnancy rate of the tenaculum group (42.1%) was slightly higher than the control roup (39.5%) without a statistically significant difference. These comparable results show that neither the chemical stimuli nor the minimal bleeding that might be created by holding of the cervix impairs the implantation procedure.

However, a marked difference was observed between the overall pregnancy rates of the soft (54.5%) and hard catheter (25.1%) cases among the tenaculum group. Since the number of cases was limited in this group, a further study is necessary to investigate the real effects of different catheters.

Applying traction on the cervix by a tenaculum during embryo transfer, in cases where passage through the internal cervical os has failed by a soft catheter, aids in performing the transfer without deteriorating pregnancy rates. In addition, by decreasing the frequency of multiple transfers for retained embryos, patient frustration and reduced pregnancy rates are also prevented.

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