SHORT COMMUNICATION

GREENVILLE, SOUTH CAROLINA

Cook Versus Edwards–Wallace: Are There Differences in Flexible Catheters?

INTRODUCTION

The most important 10 min in an assisted reproductive technology (ART) procedure may be the last 10 min—the embryo transfer. Bongso suggests that pregnancy rates for in vitro production (IVP) clinics are determined by proper stimulation, culturing techniques, and atraumatic embryo transfers (1). Focusing on the latter, (a) we compare our clinical pregnancy rates after embryo transfer with the Cook soft-pass catheter and the Edwards–Wallace catheter, and (b) because two other independent studies with the same research question report similar findings (2,3), we combine our data with theirs to compare these two popular embryo transfer catheters.

MATERIALS AND METHODS

Patient Population

This prospective, randomized study included gametes from 105 couples undergoing 117 IVP procedures. Patients were distributed evenly between the two catheter groups, according to age, proportion undergoing intracytoplasmic sperm injection (ICSI), and risk factors (Table I). Our institutional review committee approved the study, and patients signed consent forms.

In Vitro Production Conditions at REI

We described our IVP techniques earlier (4). Briefly, patients received gonadotropin to initiate

ovulation after midluteal, leuprolide acetate suppression. Data from the transvaginal ultrasound of the ovaries and serum estradiol levels provided insight into the gonadotropin response. Once two or more follicles reached ≥ 16 mm, the patients received 10,000 IU of hCG intramuscularly. Follicle aspiration occurred 34 to 35 hr later, with the recovered oocytes being evaluated for maturity.

For those patients who underwent in vitro fertilization (IVF), we added 20,000 motile spermatozoa to each 50- μ l drop of Human Tubal Fluid (HTF; Irvine Scientific, Santa Ana, CA) containing a mature oocyte. After 16 to 18 hr, we stripped the cumulus cells from and observed each oocyte for two or more pronuclei, the indicator of fertilization. We placed each two-pronuclei zygote into a single 50- μ l drop of HTF and cultured it for an additional 2 or 5 days.

For those patients who underwent intracytoplasmic sperm injection (ICSI), we placed each denuded oocyte into a 50- μ l drop of Sperm Washing Medium (Irvine Scientific, Santa Ana, CA). We then added motile spermatozoa to a 50- μ l drop of 7.5% polyvinylpyrrolidone (PVP; Irvine Scientific, Santa Ana, CA). A spermatozoon was immobilized in the PVP, aspirated, and then injected into the oocyte. Following ICSI, each oocyte was handled in the same manner as those undergoing IVF, with the exception that stripping of the oocytes was not required.

Following culture, we evaluated the embryos for cell stage and grade. For day 3 embryos, the total number of blastomeres determined the cell stage; the size, shape, granularity, and fragmentation of the blastomeres determined the cell quality (1 = best, 5 = poorest). For day 6 embryos, similar criteria delineated cell stage and grade. Normally, cell stage ranged from early blastocysts to hatching blastocysts. Cell grade included thickness of the zona pellucida, percentage fragmentation, number of cells touching the perivitelline space, “quilting pattern” among the blastomeres, and an embryonic disc.

Prior to the start of the study, we randomized patients in blocks of eight using a computer program. We transferred embryos with the most advanced cell

Table I. Patient Characteristics of Women by Assigned Catheter Group

Patient characteristic	Cook catheter group	Wallace catheter group	<i>P</i> value
Number in group	52	53	—
Age (years ± SD)	32.4 ± 5.0	32.7 ± 4.3	0.76
% intracytoplasmic sperm injection	51.9 (27/52)	58.5 (31/53)	0.56
Risk factors			0.96
% with tubal factor	28.8 (15/52)	28.3 (15/53)	0.99
% with ovulatory dysfunction	21.2 (11/52)	17.0 (9/53)	0.63
% with endometriosis	21.2 (11/52)	22.6 (12/53)	0.99
% with male factor	17.3 (9/52)	17.0 (9/53)	0.99
% with uterine factor	1.9 (1/52)	0.0 (0/53)	0.50
% with unexplained infertility	1.9 (1/52)	1.9 (1/53)	0.99
Other	7.7 (4/52)	13.2 (7/53)	0.53

stages and best grade with the Cook Soft-pass catheter (Catalog No. J-SPPE-681710; Cook OB/GYN, Spencer, IN) or the Edwards–Wallace catheter (Catalog No. ME 1816; Cooper Surgical, Shelton, CT). A fetal sac 4 weeks post-embryo transfer indicated a clinical pregnancy.

Statistical Analysis

We evaluated the data initially by an intention-to-treat analysis that retained the original group assignment, regardless of the actual catheter used. Six patients randomized to the Edwards–Wallace catheter group received a Cook catheter for embryo transfer, while one patient randomized to the Cook catheter group received a catheter other than an Edwards–Wallace or a Cook. We assessed statistical significance by Fisher’s exact test for categorical variables and Student’s *t* test for continuous variables, and we assumed independence for these tests.

RESULTS

Greenville Hospital System Data

Physicians recovered a mean of 16.8 oocytes from 55 couples who would eventually use the Cook catheter. These oocytes yielded an average of 9.3 zygotes from 49% IVF and 51% ICSI. We transferred 201 embryos (3.2 embryos/transfer) averaging 6.9 cells and a grade of 2.1 into these individuals. Similarly,

the physicians recovered a mean of 16.3 oocytes from 49 couples that would eventually use the Edwards–Wallace catheter. These oocytes yielded an average of 8.5 zygotes from 36% IVF and 64% ICSI. We transferred 170 embryos (3.2 embryos/transfer) averaging 7.2 cells and a grade of 2.0 into these patients. Neither the number of oocytes retrieved, the number of zygotes produced, the percentage ICSI, the number of embryos transferred, the cell stage, nor the grade differed (*P* = 0.76, *P* = 0.40, *P* = 0.56, *P* = 0.85, *P* = 0.34, and *P* = 0.16, respectively) for the two groups of patients. The clinical pregnancy rate for the Cook catheter group was 48% (30/63), while the clinical pregnancy rate for the Wallace catheter group was 53% (28/53). These clinical pregnancy rates did not differ significantly (*P* = 0.71).

Employing the intention-to-treat approach, we discovered a 6% increase in pregnancy rate with the Edwards–Wallace catheter compared to the Cook catheter, but the increase was not statistically significant (*P* = 0.58; Table II). When analyzing the actual catheters used, again we discovered a similar positive increase (5%) in favor of the Wallace catheter group, but again, the groups did not differ significantly (*P* = 0.71; Table II). Although a higher proportion of Edwards–Wallace catheter patients underwent ICSI, the higher (although not statistically significant) pregnancy rate for the Edwards–Wallace patients was sustained with (50% versus 44%) or without (58% versus 53%), ICSI (Mantel–Haenszel *P* = 0.68).

Grouped Data

Although the previous studies (2,3) were published only in abstract form, the prospective, randomized clinical trials appear similar to ours. Therefore, we added our data to these previous reports and determined that the Cook catheter group had a combined 39% (85/220) pregnancy rate, while the Edwards–Wallace catheter group had a combined pregnancy rate of 43% (89/209; Table II). However, these groups did not differ (*P* = 0.43).

DISCUSSION

We compared two flexible embryo transfer catheters in a prospective, randomized trial and determined that the pregnancy rates did not differ. Two other independent groups reported similar results. None of these three studies had the statistical power to detect other than a very large difference in clinical

Table II. Pregnancy Rates in Three In Vitro Production Programs by Type of Embryo Transfer Catheter

Investigator	Proportion with a clinical pregnancy (number pregnant/number of procedures)			
	Cook catheter	Wallace catheter	Difference	P value
Greenville Hospital System	47%	53%	6%	0.58
Intended catheters	(27/58)	(31/59)		
Actual catheters used ^a	48%	53%	5%	0.71
	(30/63)	(28/53)		
Grunert <i>et al.</i> (1998), actual catheter used	32%	39%	7%	0.53
	(16/50)	(19/49)		
Mayer <i>et al.</i> (1999), actual catheters used	36%	39%	3%	0.78
	(39/107)	(42/107)		
Total of actual catheters used	39%	43%	4%	0.43
	(85/220)	(89/209)		

^a One patient used a catheter other than a Cook or Wallace and was excluded from these data.

pregnancy rate between the two catheter groups. Because these two independent groups conducted prospective, randomized clinical trials similar to ours, we combined the data.

The combined difference in pregnancy rates between the two catheter groups is 4 to 5%. To demonstrate a significant difference of 5% between the two catheters, 1616 patients per group would be required. The current combined data (215 patients per group) have the statistical power to detect a difference $\geq 14\%$ (assuming a background pregnancy rate of 35%, a Type I error of 5%, and a Type II error of 20%).

Although not statistically significant, the Edwards–Wallace catheter group has a slightly higher pregnancy rate than the Cook catheter group in all three of the investigating ART centers. Whether the difference is sufficient to recommend the Wallace catheter over the Cook catheter depends on additional factors such as ease of use, patient comfort, and catheter cost. Perhaps clinics should adopt the policy that we have chosen, using the less expensive Cook catheter for the mock transfer and the Wallace catheter for the actual embryo transfer. This practice reduces the cost while giving any potential benefit in pregnancy rate to the patient. A multicenter trial would be required to evaluate pregnancy differences between catheters of the order of 3 to 7% (Table II), a difference that, while not statistically significant, is clinically important.

In conclusion, in three separate trials, pregnancy rates do not differ for patients undergoing embryo transfer with the Cook Soft-pass catheter or the Edwards–Wallace catheter.

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