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Research Article

Comparing Two Soft Embryo Transfer Catheters: Results of Patients that Received Oocytes from the Same Donor

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Abstract

We compared the efficacy of two different soft catheters on pregnancy rates and designed this study to remove factors that could interfere in the results, i.e., oocyte/embryo quality, endometrial preparation and operator interference. A total of 68 patients undergoing fresh embryo transfer, in oocyte donation cycles were prospectively studied. Every two patients received oocytes from the same donor and were sequentially allocated to either the Frydman or Sidney IVF catheter. Duration of endometrial preparation, number of oocytes, fertilization rate and transferred embryos were similar in both groups. The overall pregnancy rate was 45.5% (31/68), 10 in the Frydman catheter group (29.4%) and 21 in the Sidney IVF catheter group (61.7%). Clinical pregnancy rate was significantly higher in patients who used Sidney IVF catheter compared to those who used Frydman catheter. Out of the 34 pairs of patients, there were 19 discordant pairs. In four cases pregnancy occurred only in the Frydman catheter group and in 15 cases only in the Sidney catheter group. The other 6 pregnancies occurred in patients of both groups ($p = 0.02$). The choice of embryo transfer catheter may affect the outcome of ART cycles as our study suggests that some soft catheters have better results than others.

Keywords: Embryo transfer; Soft catheter; Oocyte donation; Pregnancy rates

Introduction

Embryo Transfer (ET) is the final step and probably one of the most important procedures in assisted reproduction. Many factors have been shown to influence the success of ET, such as embryo quality, the technique used, the experience of the operator, and the difficulty of the procedure [1-6]. The choice of the catheter is also very important for a good prognosis after embryo transfer; therefore, the ideal catheter must not cause trauma to the endocervix or endometrium after its passage through the cervix [7]. Moreover, the type of catheter was rated the third and the fourth most important variable in embryo transfer, in two surveys performed in two different countries [8,9].

Several ET catheters are available and they differ in length, caliber, location of distal port, malleability and degree of stiffness, and all are composed of nontoxic plastic. Many studies have compared the use of different ET catheters and a higher chance of clinical pregnancy was observed when soft ET catheters were used [10,11]. Recent prospective randomized trials compared two types of soft catheters and did not find difference in pregnancy rates between them [12-16]. Although these studies were prospective and randomized the most important factors could not be removed, i.e, the oocyte/embryo quality, endometrial preparation and operator interference.

Therefore, we designed this study aiming to detect whether embryos derived from oocytes retrieved from the same donor would yield different outcome when transferred into different recipients, using two different types of soft catheter, thus detecting a considerable effect of the type of soft tissue catheter used in achieving successful embryo transfer results.

Material and Methods

Patients

A total of 68 infertile and nulligravid patients who were undergoing first attempt of Oocyte Donation (OD) cycles for infertility treatment were included in this prospective study, performed at ORIGEN, Centre of Reproductive Medicine, Belo Horizonte, Brazil. The study was approved by the local ethics committee, according to Brazilian ethics and legal regulation, and each patient signed an informed consent form. All patients underwent complete infertility evaluation and only women with FSH >15 IU/l were included in the study. ICSI was performed for all couples.

The inclusion criterion for the study was that two patients received oocytes from the same donor within the same cycle, and the embryo transfer was performed with different soft catheters. Couples with male factor infertility, uterine fibroids, tubal infertility, were not included. At the day of embryo transfer, the two patients were sequentially allocated to use either Frydman or Sidney IVF catheter for embryo transfer. For the first patient we used Frydman and for the second we used Sidney IVF.

Ovulation induction

All donors had the same long protocol for ovulation induction using the same hormones and the same criteria for dose tailoring. Treatment started with subcutaneous administration of 3.75 mg of GnRHa (Triptorelin, Gonapeptyl, Ferring, Brazil) for suppression of pituitary function on day 2 of the menstrual cycle. To confirm down-regulation, serum estradiol (E_2) levels and vaginal ultrasound were performed 10 days later. If the E_2 concentration was < 30 pg/ml and the ultrasound showed an endometrial thickness of < 3 mm, pituitary suppression was confirmed. If patients were not down regulated, serum E_2 and vaginal ultrasound were repeated every other day until suppression was achieved [17].

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After confirmation of suppression, patients were superovulated with daily recombinant FSH (rFSH – GonalF – Serono - Brazil) subcutaneous injections. The starting dose was 225 IU and the dose was tailored according to the ovarian response measured by E_2 levels and follicular growth monitored by vaginal ultrasound (Tosbee- Toshiba-Japan). Recombinant hCG (rhCG- 250 mcg - Ovidrel – Serono - Brazil) was given when at least 12 follicles reached a mean size of 17 mm with concordant E_2 levels (~ 200 pg/mL per follicle) [18]. Oocyte retrieval was performed approximately 34 hours after rhCG injection.

ICSI and embryo culture

Oocyte retrieval was performed ~34 h after rhCG injection by vaginal ultrasound guided aspiration. Oocytes were inseminated by ICSI as reported previously [19]. Briefly, after complete removal of the corona cells oocytes were placed in a fresh droplet of culture medium. Micromanipulation procedure was carried out on the heated stage of an inverted microscope at x400 magnification (Nikon Diaphot, Japan) adapted with a pair of hydraulic micromanipulators and a motor-driven course control (Narishige, Japan). A single sperm was aspirated into the injection micropipette from a drop of HEPES buffered media *(Hepes-buffered Earle's balanced salt solution* - Sigma, USA) containing 10% polyvinylpyrrolidone (PVP - Irvine, USA). Once in the droplet containing the oocyte, the holding micropipette was lowered and the oocyte was held in place. The injection pipette was then pushed through the zona pellucida into the cytoplasm and a single spermatozoon was injected. Inseminated oocytes are moved to droplets of culture media under mineral oil in Petri dishes, at 37°C, under a gas phase of 6% CO_2.

On the following day, i.e. 17-19 h later (day 1), the oocytes were inspected for normal fertilization by the presence of two pronuclei. The embryos were cultured in Earle's Balanced Salt Solution (EBSS, Sigma) with 10% synthetic serum substitutive at 37°C in a Petri dish (Falcon–BD, USA) under mineral oil (Sigma), under a gas phase of 6% CO_2, and were checked daily for classification based on standard morphological parameters until transfer [20]. On day 2 after oocyte retrieval, the embryos were examined and three of them were selected for embryo transfer.

Endometrial preparation

All patients included in the study had normal hysteroscopy before starting the treatment, and had the same endometrial preparation. All had normal tubes. Patients were submitted to vaginal ultrasound and measurement of E_2 levels. If the E_2 concentration was < 30 pg/ml and the ultrasound showed an endometrial thickness of < 3 mm, treatment started with estradiol valerate (E_2V - Primogyna – Schering – Brazil). Patients started with 2 mg per day from day 1-5, then the dose was increased to 4 mg per day form day 6 - 10, and increased to 6 mg per day from day 11 until 12 weeks of pregnancy [21]. After 15 days endometrial preparation was confirmed if E_2 levels were > 250 pg/ml and vaginal ultrasound showed an endometrial thickness > 8mm.

Embryo transfer

All embryo transfers were performed on day 2 after ICSI under abdominal ultrasound guidance. The cervical mucus was carefully removed away before transfer using saline solution (0.9%). All transfers were performed by the same physician, in order to avoid any possible inter operator variations [5]. The Frydman embryo transfer catheter (1306045 - CCD – France) used was a soft 18 cm long catheter with an external diameter of 1.53 mm with an open end. The Sydney IVF catheter system set (G18740 K-JETS 7019-SIVF – Cook – USA) consisted of a double lumen catheter set. The external guiding is 17 cm long and the internal catheter is 23 cm long with an external diameter of 0.92 mm.

Luteal Phase Support

Luteal phase support started on the day of oocyte retrieval. All patientes received vaginal micronized progesterone in gel (Crinone 8%, Serono, Brazil) for a single daily administration. Progesterone was used for at least 13 days, when a pregnancy test was performed, and until 12 weeks if pregnancy was confirmed [22].

Pregnancy

Serum β-HCG concentrations were measured 14 days after ICSI. Confirmation of pregnancy was made by vaginal ultrasonography at 2 and 4 weeks, when a fetal heart beat was observed. All pregnancies were followed at least for 20 weeks. The primary outcome measurement considered for analysis was the pregnancy rate, defined as the percentage of pregnancies with a fetal heart beat per embryo transfer.

Statistical analysis

For statistical analysis, Wilcoxon test was used to compare the clinical and laboratorial parameters between the two groups. To compare the effect of the catheters on the pregnancy rates the McNemar test was used. The results are presented as mean ± SD. Difference was considered significant when $p<0.05$.

Results

The mean age of the patients in the Frydman catheter group was 42.06 ± 6.6 (range – 24-52) and in the Sidney catheter group was 42.5 ± 5.5 (range – 30-56). The difference was not significant. The BMI was similar in all groups. Duration of endometrial preparation in the patients of the Frydman Catheter group was 35.6 ± 8.5 days (range – 16-51) and in the patients of the Sidney catheter group was 34.1 ± 9.3 days (range – 16-47). The difference was not significant. The mean endometrial thickness observed in the patients of the Frydman Catheter group was 9.88 ± 1.2mm (range – 8-12) and in the patients of the Sidney catheter group was 9.94 ± 1.2 days (range – 8-12). The difference was not significant. All recipients received 6 MII oocytes and the mean number of fertilized oocytes was similar in both groups. All patients had 3 good quality embryos transferred. All transfers were easy, none had blood at the tip of the catheter, retained embryos that needed to be replaced and none had insertion failure. The overall pregnancy rate was 45.5% (31/68), 10 in the Frydman catheter group (29.4%) and 21 in the Sidney catheter group (61.7%) (Table 1). In this study there were 19 discordant pairs. In four cases pregnancy occurred only in the Frydman catheter group and in 15 cases only in the Sidney catheter group. The other 6 pregnancies occurred in patients of both groups (p = 0.02).

Parameter	Frydman catheter group	Sidney catheter group	p
No. of patients	34	34	
Age	42.06 ± 6.6 (24-52)	42.5 ± 5.5 (30-56)	0.52[a]
Body mass index	29.44 ± 3.9 (23.4–41.2)	29.13 ± 3.7 (24.2–42.2)	0.67[a]
Duration of endometrial preparation (days)	35.6 ± 8.5 (16-51)	34.1 ± 9.3 (16-47)	0.49[a]
Fertilized oocytes	4.6 ± 1.3	4.5 ± 1.4	0.61[a]
Pregnancy rate	29.4%	61.7%	0.02[b]

Results are mean ± SD (range)
[a]Wilcoxon test
[b]McNemar test

Table 1: Patient characteristics and assisted reproduction treatment outcomes according to type of soft catheter used for embryo transfer.

Discussion

Many factors are involved in the implantation process and the most important are probably oocyte and embryo quality. Other factors might also influence implantation capacity, such as endometrial preparation, sperm quality, the technique used for ET and the experience of the operator. These factors inevitably play a role when a comparison between different catheters is performed. For this reason we designed this study to try to remove these factors when comparing two different soft ET catheters. As a result, we observed a higher pregnancy rate when used the Sidney IVF soft catheter.

Several studies and two large meta-analysis were performed to compare the use of soft and hard catheters and concluded that soft catheter leads to a higher chance of pregnancy. The first one [10] evaluated 10 randomized controlled trials that compared soft and hard ET catheters in 4141 embryo transfers. The authors demonstrated an increased chance of clinical pregnancy when ET was performed with soft catheter. The other study [11] evaluated seven trials that compared soft and hard ET catheters and also demonstrated an increased chance of clinical pregnancy when soft ET catheters were used. For this reason, we decided to use only soft catheters.

More recently, some prospective randomized trials compared two types of soft catheters. McIlveen et al. [12] evaluated 150 women undergoing ET with the Edwards-Wallace or Sidney IVF catheters and found no significant difference in pregnancy rates. Rhodes et al. [13] randomized 100 women to use both Edwards-Wallace or Sidney IVF catheters and the outcome of pregnancy were not significantly different. However the study did not have the power to detect a difference in clinical PR between the two catheter groups. Ata et al. [14] compared 260 women undergoing embryo transfer with Edwards-Wallace and Labotect catheters. Although they observed a difference in the pregnancy rate (44.6 versus 34.6%) no statistical significance was observed. Saldeen et al. [16] evaluated 400 ET randomized to use Edwards-Wallace or Sidney IVF catheters. No significant differences in the clinical pregnancy rates and live-birth rates were found. El-Shawarby et al. [15] evaluated 308 patients undergoing ET with the Edwards-Wallace or Rocket Embryon catheter and observed that pregnancy rate was similar in both groups. Therefore, our study is probably the first to observe a significant difference between two soft ET catheters.

This fact can be explained by the methodological difference between the studies, as our study was designed to compare pairs of patients that received oocytes from the same donor, each one with a different catheter for ET. Moreover the group of patients included in our study was very homogeneous. As each pair of patients received oocytes from the same donor, all had normal sperm, normal uterus and all had the same number of good quality embryos transferred, and these factors did not interfere or at most had a small impact on the results. Also, as all patients had the same endometrial preparation and the same operator performed all embryo transfers using the same technique, we avoided these interferences [1-6]. Therefore, the only interference was the type of catheter used for ET. Although the proposed design for the study was too restrictive, the number of patients included was enough to reach statistical significance.

In summary, our study suggests that some soft catheters have better results than others. However, more studies with larger number of patients are necessary to confirm our findings. Also, the forthcoming studies should use the same methodology, in order to remove the factors that potentially interfere with the results.

References

1. Schoolcraft WB, Surrey ES, Gardner DK (2001) Embryo transfer: techniques and variables affecting success. Fertil Steril 76: 863-870.
2. Wood EG, Batzer FR, Go KJ, Gutmann JN, Corson SL (2000) Ultrasound-guided soft catheter embryo transfers will improve pregnancy rates in in-vitro fertilization. Hum Reprod 15: 107-112.
3. Mansour RT, Aboulghar MA (2002) Optimizing the embryo transfer technique. Hum Reprod 17: 1149-1153.
4. Buckett WM (2003) A meta-analysis of ultrasound-guided versus clinical touch embryo transfer. Fertil Steril 80: 1037-1041.
5. Yao Z, Vansteelandt S, Van der Elst J, Coetsier T, Dhont M, et al. (2009) The efficacy of the embryo transfer catheter in IVF and ICSI is operator-dependent: a randomized clinical trial. Hum Reprod 24: 880-887.
6. Glujovsky D, Pesce R, Fiszbajn G, Sueldo C, Hart RJ, et al. (2010) Endometrial preparation for women undergoing embryo transfer with frozen embryos or embryos derived from donor oocytes. Cochrane Database Syst Rev : CD006359.
7. Lemgruber M, Sampaio M, Valle M (2002) Hysteroscopic evaluation of the effect of three different embryo transfer catheters on the endometrium. Fertil Steril 78: S233.
8. Kovacs GT (1999) What factors are important for successful embryo transfer after in-vitro fertilization? Hum Reprod 14: 590-592.
9. Salha OH, Lamb VK, Balen AH (2001) A postal survey of embryo transfer practice in the UK. Hum Reprod 16: 686-690.
10. Abou-Setta AM, Al-Inany HG, Mansour RT, Serour GI, Aboulghar MA (2005) Soft versus firm embryo transfer catheters for assisted reproduction: a systematic review and meta-analysis. Hum Reprod 20: 3114-3121.
11. Buckett WM (2006) A review and meta-analysis of prospective trials comparing different catheters used for embryo transfer. Fertil Steril 85: 728-734.
12. McIlveen M, Lok FD, Pritchard J, Lashen H (2005) Modern embryo transfer catheters and pregnancy outcome: a prospective randomized trial. Fertil Steril 84: 996-1000.
13. Rhodes TL, Higdon HL 3rd, Boone WR (2007) Comparison of pregnancy rates for two embryo-transfer catheters. Fertil Steril 87: 411-416.
14. Ata B, Isiklar A, Balaban B, Urman B (2007) Prospective randomized comparison of Wallace and Labotect embryo transfer catheters. Reprod Biomed Online 14: 471-476.
15. El-Shawarby SA, Ravhon A, Skull J, Ellenbogen A, Trew G, et al. (2008) A prospective randomized controlled trial of Wallace and Rocket embryo transfer catheters. Reprod Biomed Online 17: 549-552.
16. Saldeen P, Abou-Setta AM, Bergh T, Sundström P, Holte J (2008) A prospective randomized controlled trial comparing two embryo transfer catheters in an ART program. Fertil Steril 90: 599-603.
17. Geber S, Sales L, Sampaio M (2002a) Comparison between a single dose of goserelin (depot) and multiple daily doses of leuprolide acetate for pituitary suppression in IVF treatment: a clinical endocrinological study of the ovarian response. J Assist Reprod Genet 19: 313-318.
18. Geber S, Ferreira DP, Spyer Prates LF, Sales L, Sampaio M (2002) Effects of previous ovarian surgery for endometriosis on the outcome of assisted reproduction treatment. Reprod Biomed Online 5: 162-166.
19. Geber S, Sales L, Sampaio MA (2002) Laboratory techniques for human embryos. Reprod Biomed Online 5: 211-218.
20. Veeck L (1999) The morphological assesment of human oocytes and early concepti. In: Keel BA, Webster RW, editors. Handbook of laboratory diagnosis and treatment infertility. Boca Raton, FL: CR Press 353-369.
21. Sampaío MA, Geber S (2001) Births after transfer of zona-free blastocysts in oocyte donation cycles. J Assist Reprod Genet 18: 156-159.
22. Geber S, Moreira AC, de Paula SO, Sampaio M (2007) Comparison between two forms of vaginally administered progesterone for luteal phase support in assisted reproduction cycles. Reprod Biomed Online 14: 155-158.