

A Comparison of Success Rates of Embryo Transfer on Weekdays and Weekends

Pinar Solmaz Hasdemir, M.D.^{1*}, Melek Bulut Kamali, R.N.², Esat Calik, M.D.¹,
Hasan Tayfun Ozcakil, M.D.^{1,2}

1. Celal Bayar University Medical School, Department of Obstetrics and Gynecology,
Manisa, Turkey

2. Celal Bayar University Infertility Research and Treatment Center,
Grand Medical Hospital IVF Center, Manisa, Turkey

Abstract

Background: The aim of this study is to examine the effect of the embryo transfer (ET) day on clinical pregnancy success rates in *in vitro* fertilization-ET (IVF-ET) cycles.

Materials and Methods: In this retrospective study, we divided patients with infertility who underwent IVF-ET with fresh embryos into two groups depending on whether the ET was performed on weekdays or weekends. The main outcome measure was to compare the clinical pregnancy rates of patients with similar demographic and clinical characteristics who underwent ET on weekdays or weekends.

Results: A total of 188 patients underwent IVF-ET on weekdays (n=156) or weekends (n=32). Both groups had similar demographic and cycle characteristics. The overall pregnancy rate was 42.8%. Among the study groups, the weekday group had a 40.2% ET success rate and the weekend group had a 54.8% success rate (P=0.517). Although no statistically significant difference existed between the two groups, we observed an absolute 14.6% increase in pregnancy rate for ETs performed during weekends compared to those performed on weekdays, with a 35% statistical power.

Conclusion: ETs performed during weekends were more successful than ETs performed during weekdays with an absolute 14.6% increase in clinical pregnancy rate. This finding should be confirmed by conducting further studies with larger groups of patients.

Keywords: Embryo Transfer, *In Vitro* Fertilization, Pregnancy

Citation: Hasdemir PS, Kamali MB, Calic E, Ozcakil HT. A comparison of success rates of embryo transfer on weekdays and weekends. *Int J Fertil Steril*. 2016; 10(1): 48-52.

Introduction

Infertility is a common health care problem with a prevalence of 4 to 14% worldwide (1). Improvements in the success rates of the *in vitro* fertilization-embryo transfer (IVF-ET) cycles can benefit couples from the physical, psychological and financial points of view. Thus, every possible factor which can potentially improve the success of an ET should be considered.

IVF-ET cycles were started at the beginning of the natural cycle in the first years of assisted reproductive technologies. Conventional ovarian hyperstimulation was later replaced by controlled ovarian stimulation to avoid the need for clinical and laboratory staff to be on duty during weekends (2). Since then, no studies have compared pregnancy success rates between weekdays and weekends. To the best of our knowledge, this is the first study

Received: 21 Feb 2015, Accepted: 4 May 2015

*Corresponding Address: Celal Bayar University Medical School,
Department of Obstetrics and Gynecology, Manisa, 45000 Turkey
Email: solmaziyildiz@yahoo.com



Royan Institute
International Journal of Fertility and Sterility
Vol 10, No 1, Apr-Jun 2016, Pages: 48-52

that compares the effect of the ET day on clinical pregnancy success rates in IVF-ET cycles.

Materials and Methods

This was a retrospective observational study based on a review of medical records from Celal Bayar University Infertility Research and In vitro Fertilization Center. We included patients who referred to our clinic because of primary or secondary infertility and underwent assisted reproduction (IVF-ET) with a gonadotropin-releasing hormone (GnRH) antagonist protocol between August 2013 and January 2015.

A total of 188 patients were divided into two groups, depending on whether the ET performed on weekdays (n=156) or weekends (n=32). Clinical characteristics that included age, duration of infertility, and body-mass index (BMI) were collected for each patient. The results of sperm analysis were collected from each patient. We defined abnormal sperm analysis as any abnormality in one of the following parameters: total count, morphology and/or motility. Serum follicle-stimulating hormone (FSH), estradiol (E₂) and luteinizing hormone (LH) levels were measured at the beginning of the ovulation induction and at the day of human chorionic gonadotropin (hCG) administration (E₂ and LH). Ovulation induction protocol, oocyte retrieval days, ET days, endometrial thickness at the beginning of ovulation induction and day of oocyte retrieval, and clinical pregnancy rates were collected for each patient. Only first ovulation induction cycle of each patient was included in the study.

Exclusion criteria for IVF-ET were high serum FSH (>13 mIU/mL), serum LH (>13 mIU/mL) or serum E₂ (>80 pg/mL) levels, use of long or short ovulation induction protocols, patients with unavailable or arrested embryos, chemical pregnancies and pregnancies with gestational sac without fetal heart beat. Also excluded were patients with IVF-ET cycles with cryopreserved embryos and those with a history of >4 IVF cycle failures.

Ovulation induction protocol

We used the antagonist protocol in each patient with the same ovulation induction agents. Ovulation induction was started with recombinant FSH (r-FSH, Puregon®, Australia) or human menopausal gonadotropin (HMG, Menogon®, Switzer-

land). GnRH antagonist (Orgalutran®, Australia, 0.25 mg/day) was added to the cycle on 5th to 7th day depending on the clinical characteristics of the patient. Ovulation was triggered by intramuscular hCG (Pregnyl®, Germany, 10000 IU) when at least two follicles larger than 17 mm in diameter were detected on ultrasound. Oocyte retrieval was performed 36 hours after the injection by the same operator. ETs were performed between the 2nd and 5th days after oocyte retrieval depending on the embryo characteristics; all transfers were performed with the same technique, equipment, and by the same operator. One embryo was transferred in one cycle in patients younger than 35 years of age and two embryos (in case of available two good quality embryos) in patients equal or older than 35 years of age based on legal arrangements in Turkey. Patients received luteal phase support by micronized vaginal progesterone (Progestan, 800 mg/day) from the day of oocyte retrieval which continued until a pregnancy test was performed.

Main outcome measure

This study compared the pregnancy rates of patients with similar clinical and cycle characteristics who underwent ET on weekdays versus weekends. We considered the primary outcome measure to be the clinical pregnancy rate. A blood pregnancy test was performed 9 to 12 days after ET and ultrasound was performed 2 weeks later if the pregnancy test was positive. Clinical pregnancy was defined as presence of a gestational sac with a fetal heart beat.

Ethical consent

The research protocol was approved by the Institutional Review Board of Celal Bayar University Medical School (no. 20478486-302) on August 27, 2014.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics 15.0 (SPSS Inc., USA). The Shapiro-Wilk test was used to calculate whether the numeric variables had normal distribution. For normally distributed variables, we used the student's t test to analyze any differences in the distributions of the patients' characteristics. The Mann-Whitney U test assessed abnormally dis-

tributed variables. Cross-tables and chi square analysis were employed in the evaluation of the categorical data. P value<0.05 was considered statistically significant. A power analysis was made and the effect size measured to determine the timing (weekdays versus weekends) of ET on the pregnancy success rate.

Results

Overall, there was a 42.8% pregnancy rate. The rate of clinical pregnancy was 40.2% in the weekdays group and 54.8% in the weekend group (P=0.517) with a power of 35% and an effect size of 15%. Although there was no statistically significant difference between the two groups, an absolute 14.6% increase in success rate existed for ETs performed during weekends compared to those performed on weekdays.

Table 1 summarizes the baseline and cycle characteristics of the study population. Abnormal

sperm analysis results existed in 69.5% of those in the ET weekdays group versus 72.4% of those in the ET weekend group (P=0.755). Both groups had a history of 0-5 intra-uterine insemination (IUI) treatments and/or 0-3 IVF programs. The percentage of IUI treatments and/or IVF programs were similar in both groups, with 54.4% of patients who underwent IUI in the weekdays group compared to 43.8% in the weekend group (P=0.442) and 29.9% who underwent IVF in the weekdays group compared to 31.2% who underwent IVF in the weekend group (P=0.885). The type of transferred embryos were cleaved-staged embryos in 83.9% and blastocysts in 16.1% in the weekdays group and cleaved-staged embryos in 87.5% and blastocysts in 12.5% in the weekend group. A single embryo was transferred in 78.2% of weekday patients and in 93.7% of the weekends group. Two embryos were transferred in 21.8% of weekday patients and in 6.3% of patients in the weekends group.

Table 1: Baseline and cycle characteristics of the patients that underwent embryo transfer on weekdays and weekends

	ET weekdays n=156	ET weekends n=32	P value
Age of women (Y)	31.17 ± 4.34*	29.87 ± 3.91*	0.119
Age of man (Y)	33.90 ± 4.39*	32.48 ± 4.19*	0.125
Duration of infertility (Y)	5.50 (1-20)**	6 (1-22)**	0.963
BMI	25.72 ± 4.41*	24.31 ± 3.79*	0.095
Baseline FSH level (mIU/mL)	7.36 ± 3.19*	7.79 ± 2.19*	0.565
Baseline E ₂ level (pg/mL)	51.57 ± 33.61*	46.89 ± 22.06*	0.555
Baseline LH level (mIU/mL)	5.15 ± 2.83*	4.99 ± 1.92*	0.805
Baseline endometrial thickness (mm)	5.38 ± 2.51*	5.58 ± 2.06*	0.737
Dosage of induction agent (IU/day)	187.50 (100-300)**	175 (100-300)**	0.150
Retrieved follicle (n)	7.40 ± 4.75*	7 ± 3.38*	0.723
M2 oocytes (n)	6.05 ± 3.68*	5.26 ± 2.66*	0.376
Grade 1 embryos (n)	2.9 ± 3.38*	3 ± 2.69*	0.909
Fertilization rate	4.18 ± 2.61*	3.84 ± 1.77*	0.590
E ₂ level at hCG day (pg/mL)	1335.75 ± 910.33*	1321.22 ± 884.97*	0.935
LH level at hCG day (mIU/mL)	3.22 ± 3.11*	6.64 ± 9.44*	0.146
Endometrial thickness (mm)	9.87 ± 2.56*	9.44 ± 2.61*	0.388
Mean transferred embryo (n)	1.29 ± 0.45*	1.15 ± 0.37*	0.174
ET day after OPU	3 (2-6)**	3 (2-5)**	0.344

*; Mean ± SD, **; Median (minimum-maximum), BMI; Body-mass index, M2; Metaphase II, ET; Embryo transfer, OPU; Ovum pick-up, P<0.05 was considered to be statistically significant, FSH; Follicle-stimulating hormone, LH; Luteinizing hormone, E₂; Estradiol and hCG; Human chorionic gonadotropin.

Discussion

IVF involves a complex series of steps, including controlled ovarian hyperstimulation, oocyte retrieval, fertilization, embryo culture, and uterine transfer. Many studies have described factors that influence the success rate of implantation and clinical pregnancy rates in IVF-ET cycles (3-16), including endometrial receptivity (4-6), treatments targeted to improve implantation (5, 7, 8), the ET technique (9, 10), transfer day of the conception material (11, 12), serum E₂ level during the IVF cycle (4th day) (13), decrease in serum E₂ level after hCG administration (14), the relationship between E₂ and LH levels (15), and type of the agent used in ovulation induction (16).

Craig et al. (17) recently showed that acupuncture on the day of ET had a detrimental effect on clinical pregnancy rates, although a Cochrane analysis did not confirm this finding (18). Manheimer et al. (19) have reported a small positive effect of acupuncture on ET rates. Acupuncture is known to increase nitric oxide (NO) production and vasodilator effect via relaxation of the smooth muscles of the vessels (20). It is clear from the current literature that many factors which affect the success of IVF-ET procedures remain to be clarified.

Uterine receptivity and implantation is one of the most enigmatic parts of the fertilization process. The junctional zone (JZ), or subendometrial layer of the myometrium, is the most popular part of the uterus related to this subject. The degree of JZ contractility has been shown to change through the ovarian cycle. Increased contractility just before ET significantly reduces the success rate of ET (12, 21). It is known that uterine manipulation during ET has a negative effect on pregnancy rates and is possibly related to increased uterine JZ contractility with mechanical effect (10, 22). JZ contractility may be regulated by local synthesis of NO within the uterus and high progesterone levels. It is believed to be related to uterine receptivity although the mechanism is unclear (23). A higher implantation success rate with frozen-thawed ETs has been shown in recent studies. This is thought to be related to the potential detrimental effect of endometrial receptivity induced by the high hormonal environment in fresh ET cycles (5, 24).

We believe that every possible factor which can potentially improve the success of ET should be

considered. To the best of our knowledge, there is no data that compares the success rate of ET performed on weekdays versus weekends. We have found an absolute 14.6% increase in success rate for ETs performed during weekends compared to those performed on weekdays. There is no known possible factor for increasing the implantation rate during weekends. The factors that underline the difference in the current study should be investigated. This difference may be due to patient and/or IVF team related factors. Saturdays are more relaxing days in terms of crowdedness and work load. This may help to perform easier ETs with less JZ contractions. A relaxing clinic environment as well as patient mood during the weekends may decrease patient anxiety and positively effect hormonal status related to the implantation process.

There are several limitations in this study. Miscarriage after fetal heart beats and live birth rates were not determined. The number of patients in the study population was relatively low. According to the statistical power analysis, a 35% power was reached in this study. In order to reach a statistical significance with a 14.6% difference between the two groups, 485 patients in the weekdays group and 97 patients in weekend group were required. A nearly three-fold higher patient number would be needed to reach statistical significance. In order to reach this number of patients, approximately a 5-year study would be needed at our center. Therefore, the current study findings should be confirmed with studies powered with larger numbers of patients.

Conclusion

ETs performed during the weekends compared to weekdays can be more successful. We strongly believe that large prospective studies are required to demonstrate whether ETs performed during the weekends are more successful in terms of clinical pregnancy rates compared to those performed on weekdays and, if so, to identify the potential reasons that improve the success rate of IVF-ET cycles.

Acknowledgements

The authors would like to thank to Mehmet N. Orman for professional statistical analysis. There was no financial support and conflict of interest in this study.

References

1. Bahamondes L, Makuch MY. Infertility care and the introduction of new reproductive technologies in poor resource settings. *Reprod Biol Endocrinol*. 2014; 12: 87.
2. Zorn JR, Boyer P, Guichard A. Never on a Sunday: programming for IVF-ET and GIFT. *Lancet*. 1987; 1(8529): 385-386.
3. Tobler KJ, Zhao Y, Weissman A, Majumdar A, Leong M, Shoham Z. Worldwide survey of IVF practices: trigger, retrieval and embryo transfer techniques. *Arch Gynecol Obstet*. 2014; 290(3): 561-568.
4. Kim A, Jung H, Choi WJ, Hong SN, Kim HY. Detection of endometrial and subendometrial vasculature on the day of embryo transfer and prediction of pregnancy during fresh in vitro fertilization cycles. *Taiwan J Obstet Gynecol*. 2014; 53(3): 360-365.
5. Roque M, Valle M, Guimarães F, Sampaio M, Geber S. Freeze-all policy: fresh vs. frozen-thawed embryo transfer. *Fertil Steril*. 2015; 103(5): 1190-1193.
6. Miller PB, Parnell BA, Bushnell G, Tallman N, Forstein DA, Higdon HL, et al. Endometrial receptivity defects during IVF cycles with and without letrozole. *Hum Reprod*. 2012; 27(3): 881-888.
7. Mansour R, Tawab N, Kamal O, El-Faissal Y, Serour A, Aboulghar M, et al. Intrauterine injection of human chorionic gonadotropin before embryo transfer significantly improves the implantation and pregnancy rates in in vitro fertilization/intracytoplasmic sperm injection: a prospective randomized study. *Fertil Steril*. 2011; 96(6): 1370-1374.
8. Vuong TN, Phung HT, Ho MT. Recombinant follicle-stimulating hormone and recombinant luteinizing hormone versus recombinant follicle-stimulating hormone alone during GnRH antagonist ovarian stimulation in patients aged ≥ 35 years: a randomized controlled trial. *Hum Reprod*. 2015; 30(5): 1188-1195.
9. Kang SM, Lee SW, Jeong HJ, Yoon SH, Koh MW, Lim JH, et al. Clinical outcomes of elective single morula embryo transfer versus elective single blastocyst embryo transfer in IVF-ET. *J Assist Reprod Genet*. 2012; 29(5): 423-428.
10. Ghaffari F, Kiani K, Bahmanabadi A, Akhoond M. Comparison of easy and difficult embryo transfer outcomes in in vitro fertilization cycles. *Int J Fertil Steril*. 2013; 6(4): 232-237.
11. Halvaei I, Khalili MA, Razi MH, Agha-Rahimi A, Nottola SA. Impact of different embryo loading techniques on pregnancy rates in in vitro fertilization/embryo transfer cycles. *J Hum Reprod Sci*. 2013; 6(1): 65-69.
12. Lesny P, Killick SR. The junctional zone of the uterus and its contractions. *BJOG*. 2004; 111(11): 1182-1189.
13. Phelps JY, Levine AS, Hickman TN, Zacur HA, Wallach EE, Hinton EL. Day 4 estradiol levels predict pregnancy success in women undergoing controlled ovarian hyperstimulation for IVF. *Fertil Steril*. 1998; 69(6): 1015-1019.
14. Kondapalli LA, Molinaro TA, Sammel MD, Dokras A. A decrease in serum estradiol levels after human chorionic gonadotrophin administration predicts significantly lower clinical pregnancy and live birth rates in in vitro fertilization cycles. *Hum Reprod*. 2012; 27(9): 2690-2697.
15. Ye H, Huang GN, Zeng PH, Pei L. IVF/ICSI outcomes between cycles with luteal estradiol (E2) pre-treatment before GnRH antagonist protocol and standard long GnRH agonist protocol: a prospective and randomized study. *J Assist Reprod Genet*. 2009; 26(2-3): 105-111.
16. Daya S. Updated meta-analysis of recombinant follicle-stimulating hormone (FSH) versus urinary FSH for ovarian stimulation in assisted reproduction. *Fertil Steril*. 2002; 77(4): 711-714.
17. Craig LB, Rubin LE, Peck JD, Anderson M, Marshall LA, Soules MR. Acupuncture performed before and after embryo transfer: a randomized controlled trial. *J Reprod Med*. 2014; 59(5-6): 313-320.
18. Cheong YC, Dix S, Hung Yu Ng E, Ledger WL, Farquhar C. Acupuncture and assisted reproductive technology. *Cochrane Database Syst Rev*. 2013; 26; 7: CD006920.
19. Manheimer E, van der Windt D, Cheng K, Stafford K, Liu J, Tierney J, et al. The effects of acupuncture on rates of clinical pregnancy among women undergoing in vitro fertilization: a systematic review and meta-analysis. *Hum Reprod Update*. 2013; 19(6): 696-713.
20. Lundeberg T. Acupuncture mechanisms in tissue healing: contribution of NO and CGRP. *Acupunct Med*. 2013; 31(1): 7-8.
21. Fanchin R, Righini C, Olivennes F, Taylor S, de Ziegler D, Frydman R. Uterine contractions at the time of embryo transfer alter pregnancy rates after in-vitro fertilization. *Hum Reprod*. 1998; 13(7): 1968-1974.
22. Lesny P, Killick SR, Tetlow RL, Robinson J, Maguiness SD. Embryo transfer and uterine junctional zone contractions. *Hum Reprod Update*. 1999; 5(1): 87-88.
23. Lesny P, Killick SR, Tetlow RL, Manton DJ, Robinson J, Maguiness SD. Ultrasound evaluation of the uterine zonal anatomy during in-vitro fertilization and embryo transfer. *Hum Reprod*. 1999; 14(6): 1593-1598.
24. Shapiro BS, Daneshmand ST, Garner FC, Aguirre M, Hudson C. Clinical rationale for cryopreservation of entire embryo cohorts in lieu of fresh transfer. *Fertil Steril*. 2014; 102(1): 3-9.