Original Article

The Effect of Intercourse around Embryo Transfer on Pregnancy Rate in Assisted Reproductive Technology Cycles

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Abstract

Background: Implantation failure is the most important cause of recurrent *in vitro* fertilization/intra cytoplasmic sperm injection (IVF/ICSI) failure. Several reports suggest that intercourse during the peritransfer period might improve pregnancy rates. This study is designed to determine whether intercourse during the peritransfer period will improve pregnancy and implantation rates in patients undergoing IVF or ICSI.

Materials and Methods: In a randomized control trial study, 390 women with at least five years infertility were evaluated. In the study group, 195 patients had intercourse at least once 12 hours after embryo transfer. Implantation and clinical pregnancy rates were compared with 195 patients in the control group who had no intercourse for the entire assisted reproductive technology (ART) cycle.

Results: Implantation rate in the study group was 6.5% in comparison with 5.5% for the control group. Clinical pregnancy rates were not significantly higher in study patients when compared to the control group (14.2% and 11.7% respectively).

Conclusion: The results showed that intercourse during the peritransfer period can not increase pregnancy outcome.

Keywords: Pregnancy Rate, IVF, ICSI, Coitus

Introduction

Embryo implantation is critically dependent on a supportive uterine environment. Uterine receptivity is the culmination of a cellular and molecular transformation mediated locally by paracrine signals under the governance of ovarian steroid hormones, with cells and cytokines of the immune system playing integral roles in this process (1, 2). The implantation rates and subsequent pregnancy rates in *in vitro* fertilization (IVF) programs are lower than those currently seen in the normal fertile population. During IVF treatment regimens, intercourse is not allowed and artificial insemination is normally excluded (3). Semen is now recognized as contributing to endometrial preparation for embryo implantation, through the agency of specific factors in the seminal plasma fraction of the ejaculate. Conventional belief holds that an immune response to ejaculate antigens should interfere with fertilization and establishment of pregnancy. However, evidence now supports the opposing view that insemination acts to activate maternal immune mechanisms exerting a positive effect on reproductive events (4).

More recently, immunologists have wondered whether exposure to proteins in semen helps to prepare a woman's reproductive system for conception and pregnancy. Tremellen and his colleagues have studied one such protein, transforming growth factor - beta (TGF-β) (5). He proposed that immunization with TGF-β through sexual intercourse helps the maternal immune system learn to tolerate molecular signatures, or antigens, in semen by altering the production of inflammatory molecules (cytokines). The cytokines elicited by seminal activation also exert embryotrophic effects and contribute to optimal preimplantation embryo development.

Previous studies have investigated the role of semen exposure in assisted human reproduction. For example, in a study by Bellinge, patient insemination increased pregnancy rates in an IVF program (3). Tucker concluded that post operative artificial insemination improved gamete intra fallopian transfer (GIFT) outcome (6). In a study by Tremellen, intercourse during assisted human reproduction improved pregnancy outcomes. (embryos that were viable at 6 - 8 weeks) (7). On the other hand, Suna reported that the presence of seminal fluid in patients undergoing intra uterine insemination

(IUI)did not improve pregnancy rates (8).

The purpose of our study is to investigate whether exposure to semen through vaginal intercourse around the time of embryo transfer influences pregnancy rates in ART cycles.

Materials and Methods

The study was approved by the Ethical Committee of Research & Clinical Center for Infertility, Yazd University of Medical Science. A written informed consent was taken from the patients. Amongst couples who underwent IVF or ICSI cycles because of tubal, male, ovarian, endometriosis, unexplained and combined factors, ; 390 patients with a history of at least 5 years infertility were recruited. All patients were down regulated according to the long protocol with gonadotropin-releasing hormone analogue (GnRH–a) subcutaneously (Buserelin, Hoechst, Germany). Subsequently, daily administration of human menopausal gonadotropin (HMG, Menogon, Ferring, Germany) was added. Once an adequate ovarian response had been confirmed (presence of at least 2 - 3 follicles $\geq$ 18 mm in diameter), buserelin and HMG were discontinued and 10,000 IU human chorionic gonadotropin (HCG, Daroupakhsh, Iran) was administered. Transvaginal oocyte retrieval was scheduled 36 - 38 hours after HCG administration, followed by IVF or ICSI procedures to achieve oocyte fertilization. All embryos were cultured under standard condition for 48 hours until they had reached the 2 - 4 cell stage. Patients were randomly divided in two groups on the day of embryo transfer. Random selection to either group was performed by drawing numbered slips of paper from a bag which contained equal numbers for each method. The study group patients had intercourse at least once during the 12 hours after embryo transfer, whereas the control group patients abstained from intercourse for the entire ART cycle. Embryo transfer procedures were similar in both groups. All embryos were fresh. Luteal phase was supported by administration of progesterone (Aburaihan, Iran) in oil, 100 mg per day for 14 days. Clinical pregnancy was defined as the presence of a gestational sac or cardiac activity 3 weeks after embryo transfer. For data analysis t test, X^2 and Mann-Whitney tests were used. A value of p<0.05 was considered statistically significant.

Results

Patients were randomly divided in two groups: 195 patients in the study group and 195 in the control group. The mean age was 29.40 ± 4.4 years for the study group and 29.58 ± 4.9 years in the control group (p>0.05). The mean duration of infertility was 8.69 ± 3.8 years (study group) and 8.97 ± 3.9 years (control group; p>0.05). There was no significant differences in etiology of infertility between both groups (p>0.05). The mean number of retrieved oocytes (p>0.05) and transferred embryos (p>0.05) were similar in both groups. The score of transferred embryos and the endometrial thickness on the day of HCG were similar in both groups (p>0.05). Pregnancy results in five study group patients were unknown.

Table 1: Baseline characteristics of the study and control groups

Variables	Groups		
	Study group n = 195	Control group n= 195	p-value
Age (years)	29.40 ± 4.43	29.58 ± 4.91	0.705
Duration of infertility (years)	8.69 ± 3.8	8.97 ± 3.90	NS
Oocyte number	5.47 ± 2.46	6.01 ± 3.29	0.184
Number of transferred embryos	2.497 ± 0.769	2.49 ± 0.741	0.942
Score embryo	17.3 ± 1.66	17.39 ± 1.75	0.632
Endometrial thickness on the day of HCG administration	9.22 ± 0.83	9.39 ± 1.03	0.131

Parameters are presented in Mean ± SD

Table 2: The pregnancy outcome of 385 fresh embryo transfer cycles

Variables	Groups		
	Study group n = 190	Control group n = 195	p-value
Chemical pregnancy (%)	(28/190) 14.7%	(24/195) 12.3%	0.486
Clinical pregnancy (%)	(27/190) 14.2%	(23/195) 11.7%	0.476
Implantation rate (%)	(32/487) 6.5%	(27/487) 5.5%	0.500

Chemical pregnancy was 14.7% in the study and 12.3% in the control group (p>0.05). Clinical pregnancy was 14.2% (study group) and 11.7% (control group; p>0.05). The implantation rate was 6.5% in the study group and 5.5% in the control group (p=0.5). .Five pregnancies in the study and four pregnancies in the control group were twins.

Discussion

Hypothetically, intercourse can impair implantation by two mechanisms: the introduction of infection and initiation of uterine contractions. Intercourse has been linked with ascending uterine infection during late pregnancy (9) and subclinical infection of the upper reproductive tract is associated with poor IVF – embryo transfer outcome (10). During an IVF cycle the uterine cavity is vulnerable to intercourse related infection since the cervical mucous barrier that prevents ascending infection is disrupted by passage of the embryo transfer catheter. On the other hand, uterine myometrial activity is increased during intercourse, especially in the event of female orgasm (11). These contractions may interfere with implantation of the early embryo since high levels of spontaneous uterine activity are associated with poor IVF outcome (12). However, our study showed that intercourse during the peritransfer period of an ART cycle is not harmful to early pregnancy outcome.

On the positive side, intercourse may act to assist implantation. In mammals, insemination results in the transmission of seminal factors that act (in the female reproductive tract,) to promote sperm survival, to˝ condition˝ the female immune response to tolerate the conceptus and to organize molecular and cellular changes in the endometrium for facilitating embryo development and implantation. These events are initiated when signaling agents, which include TGF-B, other cytokines and prostaglandins secreted by seminal vesicles and prostate glands, interact with epithelial cells in the cervix and uterus to activate cytokine synthesis and induce cellular and molecular changes resembling a classic inflammatory cascade. The consequences are the recruitment and activation of macrophages granulocytes and dendritic cells, which have immune regulatory and tissue remodeling roles that culminate in improved endometrial receptivity to the implanting embryo. Cytokines elicited by seminal activity have embryotrophic properties and contribute directly to the optimal development of the early embryo (13, 14). In rodents, a lack of exposure to seminal plasma results in a decrease in the rate of preimplantation embryo cleavage (15) and a reduction in the proportion of transferred em-

bryos that successfully implant (16). In humans, seminal plasma pessaries have been successfully used to enhance implantation rates in women experiencing recurrent miscarriage of unknown origin (17).

Bellinge, in a prospective trial, found that deposition of semen in the high vaginal area results in higher implantation rates in IVF cycles (3). In another prospective trial, Fishel et al found no significant effect of the use of high vaginal insemination at the time of oocyte recovery in patients undergoing IVF (18). However, our study demonstrates no significant difference in the pregnancy rates with or without intercourse. While seminal fluid serves as a medium for assisting sperm transport during intercourse, and may enhance sperm function and survival, our data does not demonstrate that its presence at the time of embryo transfer enhances fertility potential. Our study suggests that the presence of seminal fluid is not essential for the establishment of pregnancy when fertilization occurred outside the body.

In a randomized study by Suna, there is no significant difference in the pregnancy rates with or without the presence of intravaginal seminal fluid in patients undergoing IUI (8). This study shows that the presence of intravaginal seminal fluid at the time of ovulation does not enhance pregnancy establishment when IUI is utilized and extends this observation to natural fertilization. Further investigations are needed to examine the hypothesis that seminal fluid affects successful pregnancy maintenance.

Conclusion

In conclusion, implantation is a complex process involving ovarian steroids, a multitude of paracrine and autocrine factors, and interaction between multiple cell types. The mechanisms of implantation are not precisely known. Problems with implantation and the development of uterine receptivity are common. Implantation failure is multifactorial in its origin and is a problem that is often unrecognized. Any future progress will require extensive clinical investigation regarding the definition of true defects in uterine receptivity. New studies are needed to understand such defects better and to advise better methods to treat infertility.

Acknowledgements

sistance in statistical analysis of the data. This study was supported by a grant from the Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Sciences. The article has not any conflict of interest.

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