

Comparative Study between Timed Intercourse and Intrauterine Insemination in Ovulation Stimulated Cycles in Unexplained Infertile Couples

Vadukut Annabelle Sabu¹, Sabrina Mhapankar², Sushil Kumar³

¹Senior Resident, Department of Obstetrics and Gynecology, Mahatma Gandhi Medical College and Hospital, Navi Mumbai, Maharashtra, India, ²Associate Professor, Department of Obstetrics and Gynecology, Mahatma Gandhi Medical College and Hospital, Navi Mumbai, Maharashtra, India, ³Professor and HOD, Department of Obstetrics and Gynecology, Mahatma Gandhi Medical College and Hospital, Navi Mumbai, Maharashtra, India

Abstract

Background and Objectives: It cannot be stressed enough that infertility is a problem of the couple and not an individual alone. IUI as a mode of artificial insemination is widely used in treating couples with unexplained infertility. The present study was done with the objective of comparing the effectiveness of TI and IUI with husband's sperm in couples with unexplained infertility undergoing superovulation with clomiphene.

Methodology: In this cross-over study, a total of 60 couples with unexplained infertility were subjected to controlled ovarian hyperstimulation with clomiphene and prospectively randomized to receive either TI (Group A) or IUI (Group B). The groups were interchanged when pregnancy was not achieved in either group after three cycles of each intervention.

Results: A positive pregnancy test was seen in both IUI and TI after cross-over. There were seven pregnancies (four in IUI and three in TI), out of which 6 (85.71%) were viable pregnancies, while one was non-viable (14.29%). Both IUI and TI had three viable pregnancies each. The one non-viable pregnancy was from the IUI group.

Interpretation and Conclusions: The findings of the present study showed that both TI and IUI are effective treatment modalities for women with unexplained infertility. Although the addition of IUI to ovulation induction does increase the cycle fecundability, it does not improve the fecundity.

Key words: Controlled ovarian hyperstimulation, Intrauterine insemination, Timed intercourse, Unexplained infertility

INTRODUCTION

Infertility is a failure of the woman to conceive within 1 or more years of regular unprotected intercourse. The highest possibility of conception appears to be with timed intercourse (TI) 1–2 days before ovulation.^[1] Considerable controversy surrounds the simple form of infertility treatment called intrauterine insemination (IUI) and the conditions that respond to it.^[2] Some prefer to use the term subfertility to describe women or couples who are not sterile, but exhibit decreased reproductive efficiency.^[3] "Cycle fecundability is the probability that a cycle will

result in pregnancy and fecundity is the probability that a cycle will result in a live birth."^[3] The timing of sexual intercourse in relation to ovulation has a strong influence on the chance of conception.

Intrauterine insemination (IUI) as a mode of artificial insemination is widely used in treating couples with unexplained infertility for over 200 years. The rationale in all insemination techniques is to deposit motile sperm as close to the oocytes as possible. After the use of new sperm preparation methods and controlled ovarian hyperstimulation, IUI replaced other insemination techniques and became the most widely used method for semination.

METHODOLOGY

In this cross-over study, a total of 60 couples from infertility outpatient department were enrolled and

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Corresponding Author: Dr. Vadukut Annabelle Sabu, Department of Obstetrics and Gynecology, Mahatma Gandhi Medical College and Hospital, Navi Mumbai, Maharashtra, India.

randomly categorized into Group A and Group B after being diagnosed as unexplained infertility. Both the groups (female partner) were given tablet clomiphene citrate (CC) 50 mg OD once a day for 5 days from day 2 to day 6 of the menstrual cycle followed by daily follicular monitoring by transvaginal ultrasound scanning (TVS) starting from day 10 till the day of ovulation. The day of ovulation was determined by TVS. The female partner in both groups received inj. human chorionic gonadotropin (HCG) 5000 IU IM when the Graafian follicular size was around 18–20 mm size.

Group A

The couples were advised to have timed intercourse (TI) for 2 days (once in 24 h) 36 h after the trigger with inj. HCG. The couples underwent three cycles of TI in Group A till conception. Couples with a failure of conception after three cycles underwent three cycles of IUI in Group B.

Group B

The couples were subjected to IUI 36 h after stimulating with inj. HCG. IUI was done using husband semen after preparing the semen sample by the swim-up technique. Three cycles were given for each couple until conception. Failure of conception after three cycles had to undergo three cycles of TI in Group A.

Therefore, this was a cross-over study design as both interventions were applied to both the groups.

Subjects in both groups were asked to follow-up on day 2 of menses or day 10 of missed periods.

Urine pregnancy test (UPT) and TVS for the visualization of the gestation sac were done on day 10 of missed period to confirm pregnancy. A positive UPT test was the determining factor for assessing the effectiveness of the two interventions, i.e., IUI and TI. The pregnancy outcome was analyzed as viable or unviable pregnancy or pregnancy wastage (P wastage). P wastage includes abortions and perinatal mortality as well. The quantitative data are represented as their mean ± SD. The Student's unpaired *t*-test was used for analyzing quantitative data. The significance threshold of *P*-value was set at < 0.05.

RESULTS

In the present study, a total of 60 patients were enrolled and categorized into Group A, where patients initially underwent three cycles of TI till conception, followed by three cycles of IUI until conception and Group B, where patients initially underwent three cycles of IUI until conception followed by three cycles of TI until conception.

In Group A, 4 (13.33%) cases reported positive UPT compared to 3 (10%) cases in Group B. Maximum cases, i.e., 27 (90%) reported negative UPT in Group B as compared to 26 (86.67%) cases in Group A. To test, whether this difference is statistically significant or not, Chi-square test was used as a test of significance. *P* = 0.6876 was statistically not significant.

Table 2 shows the outcome of TI and IUI cycles in Group A. In Group A, 30 patients underwent TI first, of which two got pregnant (6.67%). The remaining 28 went for IUI after cross-over, of which two got pregnant (71.4%). Therefore, out of 58 patients after crossing over, there were 4 (6.9%) pregnancies in Group A.

Table 3 shows the outcome of TI and IUI cycles in Group B. In Group B, 30 patients underwent IUI, of which two got pregnant (6.67%). The remaining 28 were subjected to TI, after cross-over, of which one got pregnant (3.57%). Therefore, out of 58 patients after crossing over, there were 3 (5.17%) pregnancies in Group B.

Table 4 gives the pregnancy outcome in both the study groups who underwent TI and IUI. There were seven pregnancies out of which six viable pregnancies (85.71%) which were in TI cycles and IUI cycles equally and one non-viable pregnancy (14.29%) from the IUI cycles.

Table 5 shows the outcome of TI and IUI cycles with respect to infertility. Out of 57 couples with primary

Table 1: Comparison of UPT in the study groups

UPT	Group A		Group B		Total		P-value*
	n	%	n	%	N	%	
Positive	4	13.33	3	10	7	11.67	0.6876
Negative	26	86.67	27	90	53	88.33	
Total	30	100	30	100	60	100	

*Calculated using the Chi-square test. *P* < .05 considered statistically significant. UPT: Urine pregnancy test

Table 2: Outcome of TI and IUI cycles in Group A

Group A	Number of patients	Number of pregnancies	Percentage of pregnancies
TI	30	2	6.67
IUI	28	2	7.14
Total	58	4	6.9

IUI: Intrauterine insemination, TI: Timed intercourse

Table 3: Outcome of TI and IUI cycles in Group B

Group B	Number of patients	Number of pregnancies	Percentage of pregnancies
IUI	30	2	6.67
TI	28	1	3.57
Total	58	3	5.17

IUI: Intrauterine insemination, TI: Timed intercourse

infertility, there were three pregnancies (1.84%) in patients who underwent 163 cycles of TI. These primary infertile couples underwent 160 cycles of IUI and 4 (2.5%) conceived with that. There were no pregnancies in couples with secondary infertility who underwent TI and IUI.

Table 6 shows the effect of the number of cycles of the treatment of TI and IUI on pregnancy in all patient categories.

TI

Of those patients who had three cycles of TI, there was one pregnancy, while those who had two cycles had two pregnancies. There were no pregnancies with just one cycle of TI.

IUI

Of those patients who had one cycle of IUI, there was one pregnancy, while those who underwent two cycles had three pregnancies. There were no pregnancies with three cycles of IUI.

DISCUSSION

Statistics regarding infertility is it primary or secondary; in general, population are not easy to analyze as a lot of

couples do not seek medical help illustrating the potential for error in hospital-based statistics.

Including the cross-over groups, the conception outcome, i.e., positive UPT, was seen in four cases from Group A (13.33%), and three cases got pregnant from Group B (11.67%) [Table 1].

According to the study groups, after and before cross-over, there were in total four pregnancies, two with both IUI and TI, respectively, in Group A [Table 2]. While in Group B, there were three pregnancies, two pregnancies after IUI, and one after TI [Table 3].

Defining the pregnancy outcome, there were three viable pregnancies and one P wastage with IUI while three viable pregnancies with TI [Table 4].

TI: Out of the three, two were term live births, while one was preterm live birth at the 7th month.

IUI: Out of four pregnancies, three were viable with one twin gestation and one singleton live birth and one preterm breech delivery at 7½ months. There was one pregnancy wastage being missed abortion in the first trimester itself.

Table 4: Table of fecundity and fecundability in both study groups

Pregnancy outcome status	TI		IUI		Total	
	Number of pregnancies	Percentage of pregnancies	Number of pregnancies	Percentage of pregnancies	Number of pregnancies	Percentage of pregnancies
Viable pregnancy	3	100	3	75	6	85.71
Pregnancy wastage	0	0	1	25	1	14.29
Total	3	100	4	100	7	100

IUI: Intrauterine insemination, TI: Timed intercourse

Table 5: Outcome of TI and IUI cycles with respect to infertility category

Category	Number of couples	Timed intercourse			IUI			Total number of pregnancies
		Number of cycles	Number of pregnancies	Percentage of pregnancies	Number of cycles	Number of pregnancies	Percentage of pregnancies	
Primary infertility	57	163	3	1.84	160	4	2.5	7
Secondary infertility	3	9	0	0	9	0	0	0
Total	60	172	3	1.74	169	4	2.37	7

IUI: Intrauterine insemination, TI: Timed intercourse

Table 6: Outcome of the number of cycles of treatment in TI and IUI

Cycle number	Timed intercourse			IUI		
	Number of cycles	Number of pregnancies	Percentage of pregnancies	Number of cycles	Number of pregnancies	Percentage of pregnancies
1	0	0	0	1	1	100
2	4	2	50	6	3	50
3	168	1	0.6	162	0	0
Total	172	3	1.74	169	4	2.37

IUI: Intrauterine insemination, TI: Timed intercourse

Maximum patients were that of primary infertility as compared to secondary. All seven pregnancies were from couples who had primary infertility [Table 5]. Our study had a fixed number of cycles for each intervention. Of those patients who had three cycles of TI, there was one pregnancy, while those who had two cycles had two pregnancies. Of those patients who had one cycle of IUI, there was one pregnancy, while those who underwent two cycles had three pregnancies [Table 6].

Martinez *et al.*^[4] reported the first randomized study on comparison of TI and IUI in gonadotropin-stimulated normal ovulatory cycles without any significant differences. Kirby *et al.*^[5] compared IUI with LH-TI during spontaneous cycles and found no significant improvement in pregnancy rates except in couples with severe semen defect. However, based on meta-analyses of 980 cycles in randomized prospective studies, the addition of IUI to superovulation with gonadotropins in couples with unexplained infertility produced better results than superovulation alone.^[6] Although five of the seven studies included in this meta-analysis failed to show significant benefit of IUI, the overall evaluation of all seven studies revealed a significant increase in the pregnancy rate with the addition of IUI. Our cross-over study showed that the addition of IUI over TI in ovulation stimulated cycles with CC in women with unexplained infertility improves the pregnancy rate, i.e., fecundability, but does not improve the chance of live birth, i.e., fecundity. Most studies have indicated that IUI is only useful if the cause is oligospermia and mild asthenozoospermia.^[7,8] There was a cross-over trial conducted in 1990 by Deaton *et al.*^[9] of CC/IUI versus TI, including 67 couples and 298 treatment cycles. The difference in fecundities was statistically significant, while the pregnancy outcome was not significantly different between the two groups. Another randomized prospective trial of IUI versus TI in superovulated cycles with clomiphene conducted by Agarwal and Mittal^[10] showed that in women with unexplained infertility, the addition of IUI to ovulation induction does not improve conception rates.

There is a scope for further studies and large multicentric randomized controlled trials, including normal ovulatory and superovulated cycles in cases of unexplained infertility.

Further, an in-depth study is essential to determine the benefit, cost-effectiveness, and potential side effects of IUI over TI for unexplained infertility. Furthermore, it can help to adjudge the subtle endocrine/ ovulatory defects which may influence favorable outcome. The mechanism by which IUI, either combined or not with ovarian stimulation, may enhance cycle fecundity in couples with unexplained infertility warrants further elucidation.

CONCLUSIONS

Positive pregnancy outcome was seen both with TI and IUI for ovulation stimulated cycles in unexplained infertile couples. Our cross-over study showed that the addition of IUI over TI in ovulation stimulated cycles with CC in women with unexplained infertility improves the pregnancy rate, i.e., but does not improve the chance of live birth.

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