Original Research Article

Role of intrauterine tubo-peritoneal insemination and intrauterine insemination in the treatment of infertility

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ABSTRACT

Background: Infertility management has become more substantial and relevant with an increase in the number of infertile patients as well as advances in the science of reproduction. The objective of our study was to assess the role of intrauterine tuboperitoneal insemination (IUTPI) and intrauterine insemination (IUI) in the treatment of infertile patients.
Methods: 236 infertile patients, 118 in each group attending the infertility clinic, after applying both inclusion and exclusion criteria were enrolled in the present study. Patients in each study group were given clomiphene citrate for ovarian stimulation followed by injection hCG for triggering ovulation. Insemination with washed husband's sperm was performed about 36-40 hours after hCG administration, using 10ml of inseminate in IUTPI and 0.5ml inseminate in IUI. The patient was then called after 2 weeks for urine pregnancy test (UPT) which, if positive was considered as clinical pregnancy.
Results: Out of the total 236 cases, 42 cases had a positive outcome. Out of these 42 positive cases, 27 were from IUTPI group whereas 15 from IUI group. The pregnancy rate was 22.88% in IUTPI and 12.71% in IUI (p=0.039), which was a statistically significant difference. Endometrial thickness, preovulatory follicle number and prewash sperm motility significantly affected positive outcome in IUTPI. Factors like patient's age, BMI<25, bilateral patent tubes and decreased duration of infertility also positively affected the treatment outcome.
Conclusions: Our study found IUTPI to have better pregnancy rate compared to IUI. IUTPI may become a first line option for treatment of infertile patients.

Keywords: Clinical pregnancy rate, Intrauterine tuboperitoneal insemination, Intrauterine insemination, Infertility

INTRODUCTION

Infertility is defined as one year of unprotected intercourse without conception during child bearing age affecting approximately 7.4% of the population. Intrauterine insemination (IUI) with husband's semen has been widely used as a low cost first line assisted reproductive therapeutic option for infertile couples. A newer modified form of IUI called intrauterine tubo - peritoneal insemination (IUTPI) has been developed for infertile patients using 10ml of the inseminate instead of 0.5ml used in IUI. This procedure is made possible by a specially designed instrument, the Double Nut Bivalve speculum (DNB) which clamps the cervix tightly during the procedure preventing back flow of the inseminate. The objective of our study was to compare the clinical pregnancy rate of IUTPI and IUI in the treatment of infertile patients.[1,2]

METHODS

The present study was a prospective study conducted in the Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur. Out of a total of 236 cases, 118 cases in each group were included. Inclusion criteria included patients suffering from unexplained and mild male factor infertility, minimal and mild endometriosis, ovulatory dysfunctions, ejaculatory failures and atleast one patent fallopian tube. Exclusion criteria included patients with severe oligozoospermia, bilateral tubal obstruction and intrauterine abnormality. After taking a written informed consent, history, detailed clinical examination and relevant investigations patients in each study group were given clomiphene citrate 100mg per day from day2 to day5 of menstrual cycle for ovarian stimulation. 5,000 IU of hCG was administered for triggering ovulation when the diameter of the leading follicle reached atleast 18mm. Cycles with development of 4 or more follicles were cancelled due to risk of ovarian hyperstimulation syndrome(OHSS). Insemination with washed husband's sperm was performed about 36-40 hours after hCG administration. The patient was then called after 2 weeks for urine pregnancy test (UPT) which if positive was considered as clinical pregnancy. The clinical pregnancy rate of each group was calculated and compared using Z test. The two groups were compared using two sample proportions test which showed that both the groups were comparable at baseline with respect to variables like demography, age, BMI, duration of infertility, endometrial thickness, preovulatory follicle no., day of menstrual cycle when hCG injection was given and semen parameters. Software used was SPSS 18.0. P value <0.05 was taken as significant.

RESULTS

236 infertile patients, 118 in each group attending the infertility clinic, after applying both inclusion and exclusion criteria were enrolled in the present study. Out of the total 236 cases, 42 cases had a positive outcome. Out of these 42 positive cases, 27 cases were from IUTPI group whereas 15 were from IUI group (Table 1).

Table 1: Distribution of cases according to IUI versus IUTPI and pregnancy outcome.

Outcome	IUI		IUTPI		Total		Z test
	No.	%	No.	%	No.	%	p-value
Positive	15	12.71	27	22.88	42	17.80	0.039
Negative	103	87.29	91	77.12	194	82.20	0.039
Total	118	100.00	118	100.00	236	100.00	

Majority (51.85% in IUTPI and 46.67% in IUI) of the pregnancies occurred in the age group of 26-30 years. Younger age of the patient was associated with better pregnancy outcome in both the groups. Interestingly, in IUTPI, 4 positive cases were beyond 36 years of age, reflecting IUTPI to be a better method in older age group too. BMI <25 was also associated with better pregnancy outcome. The pregnancy rate was higher in the BMI group <25 (25.30% in IUTPI and 15.29% in IUI) as compared to the ≥25 group (17.14% in IUTPI and 6.06% in IUI). The pregnancy rate in both the groups was higher and statistically significant in patients who had development of 2 follicles (32.65% in IUTPI and 19.15% in IUI) compared to those with 1 follicle (17.74% in IUTPI and 7.69% in IUI) (Table 2). The pregnancy rate was higher in patients with bilateral tubes patent (23.58% in IUTPI and 13.59% in IUI). It can thus be seen that the pregnancy rate with respect to various variables under study was higher in the IUTPI group compared to IUI group.

Table 2: Pregnancy rate and preovulatory follicle number.

Preovulatory follicle no	IUI			IUTPI		
	Total	Positive	Pregnancy rate (%)	Total	Positive	Pregnancy rate (%)
1	65	5	7.69	62	11	17.74
2	47	9	19.15	49	16	32.65
3	6	1	16.67	7	0	0
p-value	0.041			0.001		

Test: Chi-square test for goodness of fit.

Table 3: Various parameters and outcome.

| | IUI | | | | | IUTPI | | | | |
| | Positive (15) | | Negative (103) | | p-value | Positive (15) | | Negative (103) | | p-value |
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Duration of infertility (in yrs)	5.60	3.582	7.70	4.104	0.063	6.76	3.781	7.91	3.855	0.173
Endometrial thickness (in mm)	8.09	0.834	8.12	1.059	0.938	8.68	0.892	7.91	1.678	**0.025**
prewash sperm count (in millions/ml)	64.80	27.475	61.37	28.156	0.659	72.26	27.167	66.99	27.735	0.358
Prewash sperm motility (in %)	58.33	14.475	60.29	14.052	0.616	67.81	13.298	58.24	18.759	**0.015**

Table 4: Comparison of two methods.

| Parameters | Method | N | Mean | SD | Std. error mean | Student's T test | | |
						t value	d.f.	p-value
Patient's age (in years)	IUI	118	29.364	4.338	0.399	-1.410	234	.161
	IUTPI	118	30.212	4.906	0.452			
Husband's age (in years)	IUI	118	31.992	4.361	0.401	-.550	234	.583
	IUTPI	118	33.339	5.287	0.487			
Patient's BMI	IUI	118	23.669	1.845	0.170	.521	234	.603
	IUTPI	118	23.462	3.905	0.360			
Duration of infertility (in years)	IUI	118	7.432	4.088	0.376	-.418	234	.676
	IUTPI	118	7.648	3.853	0.355			
Prewash sperm count(in million/ml)	IUI	118	62.661	28.625	2.635	-1.550	234	.122
	IUTPI	118	68.195	26.046	2.398			
Prewash sperm motility (in %)	IUI	118	60.042	14.059	1.294	-.185	234	.853
	IUTPI	118	60.432	18.064	1.663			
Postwash sperm count (in million/ml)	IUI	118	46.127	23.775	2.189	-1.840	234	.067
	IUTPI	118	51.661	22.479	2.069			
Postwash sperm motility (in %)	IUI	118	74.746	12.754	1.174	-1.320	234	.189
	IUTPI	118	80.288	16.616	1.530			
Preovulatory follicle no. (on the day of hCG injection)	IUI	118	1.500	0.596	0.055	-.432	234	.666
	IUTPI	118	1.534	0.609	0.056			
Endometrial thickness in mm (on the day of hCG injection)	IUI	118	8.113	1.030	0.095	.143	234	.887
	IUTPI	118	8.088	1.564	0.144			
Day of menstrual cycle when inj hCG given	IUI	118	12.671	1.357	0.125	-1.910	234	.057
	IUTPI	118	13.432	2.887	0.266			

The mean duration of infertility in the positive versus negative outcome cases was 6.76±3.781 years versus 7.91±3.855years in IUTPI (p=0.173) whereas 5.60±3.582 years versus 7.70±4.104 years in IUI (p=0.063). Thus lesser duration of infertility was associated with better pregnancy outcome. The mean ET of positive outcome cases compared to negative outcome cases was 8.68±0.892mm versus 7.91±1.678mm in IUTPI (p=0.025) whereas 8.09±0.834 mm versus 8.12±1.059mm in IUI (p=0.938). Thus increased

endometrial thickness was positively associated with better pregnancy outcomes in IUTPI which was also significant statistically. Most of the pregnancies occurred when the procedures were performed between Day 12 to Day16 of the menstrual cycle. The mean prewash sperm count in positive versus negative outcome cases in IUTPI was 72.96±27.167 million/ml versus 66.99±27.735 million/ml (p=0.358) whereas in IUI it was 64.80± 27.475 million/ml v/s 61.37±28.156million/ml (p=0.659). The mean prewash sperm motility in positive v/s negative outcome cases in IUTPI was 67.81±13.298% versus 58.24±18.759% (p=0.015) whereas in IUI it was 58.33±14.475% versus 60.29±14.052% (p=0.616). Thus increased prewash sperm motility was associated with a statistically significant increase in pregnancy outcome in the IUTPI group (Table 3).

Statistical tests show that both the groups IUTPI and IUI were comparable at baseline with respect to demography and various other variables like age, BMI, infertility duration, sperm parameters, preovulatory follicle number and day of menstrual cycle when injection hCG was given (Table 4). With this baseline comparability, the pregnancy rate was calculated for the two groups. This came out to be 22.88% in IUTPI and 12.71% in IUI. The p value for the same was 0.039 which was statistically significant. Thus IUTPI was found to have better pregnancy rate as compared to IUI.

The Table 4 compares various variables in the two groups IUI and IUTPI. p-value for none of these variables was significant (p>0.05) indicating that both the groups were comparable at baseline with respect to these variables.

DISCUSSION

With the current trend of increasing infertility in population there has been more research over assisted reproductive techniques aimed to cater to need and resources of the general population. Our study has tried to compare the clinical pregnancy rate between one such less costly and less invasive newer method called IUTPI with the age old first line method of assisted reproduction IUI. Both the methods are principally similar with the exception of the volume of inseminate used (0.5 ml in IUI versus 10ml in IUTPI) and a specially designed instrument called Double Nut Bivalve Speculum (DNB) which clamps the cervix tightly, thus preventing backflow of the inseminate during the procedure in IUTPI. The pregnancy rate with IUTPI was found to be much better with a statistically significant association compared to IUI.

The volume of 10ml of inseminate in IUTPI was sufficient to fill the uterine cavity (intrauterine), pass through the interstitial part of the tubes and the ampulla (tubo), finally reaching the peritoneal cavity and the pouch of doughlas where it would be mixed with the peritoneal and follicular fluids (peritoneal). IUTPI, thus, acted as a more physiological and dynamic process where sperms retain their energy and fertilizing ability compared to conventional IUI, a passive process where sperms are placed in the uterus and left to proceed to the positions of fertilization on their own. It also increased rates of live births due to the removal of tubal plugs which might be involved in proximal tubal blockage.

The clinical pregnancy rate with IUTPI in our study was 22.88% and with IUI was 12.7%. This result corroborates with the study result of Elkholi DGEY et al who found that the overall cycle pregnancy rate of patients in IUTPI group was 14.81% compared to 9.21% in patients of IUI group.[1] Similar result was found in studies done by Mamas E et al and Mamas L et al (26.3% pregnancy rate per cycle in IUTPI).[2,3] Mamas L found a pregnancy rate of 29.4% in his study which indicated IUTPI to be a useful technique in the treatment of unexplained infertility, mild or moderate male infertility, and mild or moderate endometriosis.[4]

Young age was associated with better pregnancy outcome as found by Dinelli L et al in their study.[5] Aging is associated with progressive follicular depletion and diminished oocyte quality, which is accompanied by a reduction in the size or activity of the cohort of follicles available to respond to clomiphene citrate stimulation. This negative impact on treatment outcome may be due to the higher rate of aneuploidy found in dysmorphic oocytes.

Similarly, increase in pregnancy rate with an increase in the number of preovulatory follicles is explained by the fact that multifollicular development may result in an increased number of fertilizable oocytes and a better quality endometrium and luteal phase, thus improving fertilization and implantation rates. This finding is supported by studies done by Dinelli L et al, Yavuz A et al and Ashrafi M et al.[5-7]

Souter I et al found that higher BMI was associated with poor pregnancy outcome supporting the result of our study.[10]

Increased endometrial thickness was associated with a significant increase in the pregnancy outcome in IUTPI. Similar results were found in studies done by Dinelli L et al, Wolff EF et al and Habibzadeh V et al.[5,8,9]

Decreased duration of infertility was also associated with improved pregnancy outcome as found by Ashrafi M et al in their study.[7]

Studies done by Dinelli L et al and Yavuz A et al indicate an important role of sperm parameters in pregnancy outcome.[5,6] Sperm motility is one of the important predictors of pregnancy outcome. Live birth rates are low if the percentage of non motile sperms are greater due to the damaging effects of oxygen free radicals released from these non motile sperms, leukocytes and immature germ cells.

Thus both IUI and IUTPI, assisted reproductive techniques, can be used for infertile couples meeting the inclusion and exclusion criteria, with good pregnancy outcome. IUTPI, however, was found to be a better insemination technique over IUI. Endometrial thickness, preovulatory follicle number and prewash sperm motility significantly affected the pregnancy outcome. Various other variables like patient's age, BMI, tubal patency and duration of infertility also positively affected the treatment outcome.

CONCLUSION

IUTPI may become an attractive first line option for the treatment of infertility in couples suffering from unexplained infertility, minimal and mild endometriosis, mild male factor infertility, ovulatory dysfunctions and ejaculatory failures, particularly because of its substantial cost benefits when compared to in vitro fertilization and significantly better pregnancy rates when compared to IUI.

However, large multicentric trials are needed to establish IUTPI as a first line option for infertile patients.

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