DOI: 10.36347/sjams.2017.v05i02.052

Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2017; 5(2D):566-569 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com

Original Research Article

A Study of Predictive Factors Affecting Outcome of Intrauterine Tuboperitoneal Insemination

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Abstract: 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 factors predicting the treatment outcome of a new assisted reproductive technique, intrauterine tuboperitoneal insemination (IUTPI) in the treatment of infertile patients. 118 cases, after applying both inclusion and exclusion criteria were enrolled in the study. Patients were given clomiphene citrate for ovarian stimulation followed by injection human chorionic gonadotropin for triggering ovulation. Insemination was then performed with washed husband's sperm after about 36-40 hours, using 10ml of inseminate. The patient was then called after 2 weeks for urine pregnancy test which, if positive was considered as clinical pregnancy. Out of 118 cases, 27 cases were positive. The pregnancy rate was 22.88%. Endometrial thickness, preovulatory follicle number, prewash sperm motility and post wash sperm motility significantly affected the pregnancy outcome. Factors like patient's age, BMI<25, bilateral patent tubes and decreased duration of infertility also positively affected the outcome. IUTPI may, thus, become an attractive first line option for infertile couples, considering cost benefits over in vitro fertilization and significantly better pregnancy rate over intrauterine insemination. A knowledge of predictive factors may be of help to offer and counsel patients regarding success of treatment outcome in IUTPI.
Keywords: Intrauterine tuboperitoneal insemination, clinical pregnancy rate, infertility

INTRODUCTION

Infertility is defined as one year of unprotected intercourse without conception during child bearing age. It affects 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 tuboperitoneal 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 assess various predictive factors affecting pregnancy outcome in IUTPI.

MATERIALS AND METHODS

The present study was a prospective study conducted in the Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from February 2016. A total of 118 infertile patients were taken. 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 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 hyper stimulation syndrome(OHSS).

A two layer gradient technique was used for sperm preparation. Insemination with washed husband's sperm was performed about 36-40 hours after HCG administration. The patient was asked to lie down in

supine position with head end low. IUTPI with 10 ml of inseminate was performed using DNB speculum. This speculum clamped the cervix tightly preventing the back flow of inseminate. The patient remained lying in the same position for 15 minutes and then sent back home. The patient was then called after 2 weeks for urine pregnancy test which, if positive was considered as clinical pregnancy. The clinical pregnancy rate was calculated using Z test. Software used was SPSS 18.0. P value <0.05 was taken as significant.

RESULTS

118 cases attending the infertility clinic, after applying both inclusion and exclusion criteria were enrolled in the present study. Out of these 118 cases, 27 cases had a positive outcome. The mean value of various variables affecting the treatment outcome according to the distribution of cases has been depicted in Table-1. Majority (51.85%) of the pregnancies occurred in the age group of 26-30 years. The mean age of patients in positive outcome group was 30.37±4.924 years compared to 30.16±4.927 years in the negative outcome group (p=0.849). Younger age of the patient was associated with better pregnancy outcome. Interestingly, 4 cases were positive even beyond 36 years of age, reflecting IUTPI to be an effective 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%) as compared to the ≥25 group (17.14%), though the difference was not statistically significant (p=0.495).

The pregnancy rate was higher and statistically significant in patients who had development of 2 follicles (32.65%) compared to those with monofollicular development (17.74%), p=0.001. The pregnancy rate was higher in patients with bilateral tubes patent (23.58%) compared to those with only one tube patent (16.67%), though the difference was not significant statistically, p=0.731. The mean duration of infertility in the positive v/s negative outcome cases was 6.76±3.781years v/s 7.91±3.855years (p=0.173). 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 v/s 7.91±1.678mm (p=0.025). Thus increased endometrial thickness was positively associated with better pregnancy outcome which was also significant statistically.

Most of the pregnancies occurred when the procedures were performed between Day12 to Day16 of the menstrual cycle. The mean prewash sperm count in positive v/s negative outcome cases was 72.96±27.167 million/ml v/s 66.99±27.735 million/ml (p=0.358). The mean post wash sperm count in positive v/s negative outcome cases was 52.70±23.131million/ml v/s 51.35±22.404million/ml (p=0.785). The mean prewash sperm motility in positive v/s negative outcome cases was 67.81±13.298% v/s 58.24±18.759% (p=0.015) whereas the mean post wash sperm motility in positive v/s negative cases was 86.44±11.281% v/s 78.46±17.534% (p=0.028). Thus increased prewash sperm motility and post wash sperm motility was associated with a statistically significant increase in pregnancy outcome in IUTPI. The pregnancy rate for IUTPI was 22.88% in our study. The mean value of variables according to the treatment outcome is shown in Table2. Table 3 shows the pregnancy rate with the number of preovulatory follicles on the day of HCG injection, which is an important factor affecting the treatment outcome.

Table-1:Mean values of various variables according to their distribution in the study

Parameters	Mean
Patient's age (in years)	30.212
Husband's age (in years)	33.339
Patient's BMI	23.462
Duration of infertility (in years)	7.648
Prewash sperm count(in million/ml)	68.195
Prewash sperm motility (in %)	60.432
Postwash sperm count (in million/ml)	51.661
Postwash sperm motility (in %)	80.288
Preovulatory follicle no. (on the day of hCG injection)	1.534
Endometrial thickness in mm (on the day of hCG injection)	8.088
Day of menstrual cycle when inj hCG given	13.432

Table-2: Mean values of various variables according to the outcome

Variables	IUTPI				
	Positive (15)		Negative (103)		p-value
	Mean	SD	Mean	SD	
Patient's Age (in yrs)	30.37	4.9247	30.16	4.927	0.849
Duration of Infertility (in yrs)	6.76	3.781	7.91	3.855	0.173
Endometrial Thickness (in mm)	8.68	0.892	7.91	1.678	0.025
Prewash Sperm Count (in million/ml)	72.26	27.167	66.99	27.735	0.358
Prewash Sperm Motility (in %)	67.81	13.298	58.24	18.759	**0.015**
Postwash Sperm Count (in million/ml)	52.70	23.131	51.35	22.404	0.785
Postwash Sperm Motility (in %)	86.44	11.281	78.46	17.534	**0.028**

Table- 3: Preovulatory follicle number and the pregnancy outcome

Preovulatory Follicle Number	IUTPI		
	Total	Positive	Pregnancy Rate (%)
1	62	11	17.74
2	49	16	32.65
3	7	0	0
p-value	**0.001**		

Test : Chi-square test for goodness of fit

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. There are few unambiguous determinants of success that the clinician should be aware of to be able to provide couples with appropriate counseling. Our study has tried to predict various factors affecting the positive outcome of this newer method, IUTPI. The volume of inseminate used was 10ml. A specially designed instrument called Double Nut Bivalve Speculum (DNB) which clamps the cervix tightly was used which prevented backflow of the inseminate during the procedure in IUTPI. The pregnancy rate with IUTPI was found to be significantly higher as compared to pregnancy rates of other assisted reproductive methods in various studies.

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, acts 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 increases rates of live births due to the removal of tubal plugs which may be involved in proximal tubal blockage.

The clinical pregnancy rate with IUTPI in our study was 22.88%. This result corroborates with the study result of Elkholi DGEY *et al.;* [1] 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. Similar result was found in studies done by Mamas E *et al.;* [2] and Mamas L *et al.;* [3] (26.3% pregnancy rate per cycle in IUTPI). Mamas L [4] 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.

Young age was associated with better pregnancy outcome as found by Dinelli L *et al.;* [5] in their study. 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.;* [5], Yavuz A *et al.;* [6] and Ashrafi M *et al.;* [7].

Souter I *et al.;* [10] found that higher BMI was associated with poor pregnancy outcome supporting the result of our study. 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.;* [5], Wolff EF *et al.;* [8] and Habibzadeh V *et al.;* [9]. Decreased duration of infertility was also associated with improved pregnancy

outcome as found by Ashrafi M *et al.;* [7] in their study. Studies done by Dinelli L *et al.;* [5] and Yavuz A *et al.;* [6] indicate an important role of sperm parameters in pregnancy outcome. Sperm motility is one of the important predictors of pregnancy outcome. Live birth rates are low if the percentage of non-motile sperms is greater due to the damaging effects of oxygen free radicals released from these non-motile sperms, leukocytes and immature germ cells.

Thus IUTPI was found to be a newer assisted reproductive option with significantly improved pregnancy rate and cost benefits. Endometrial thickness, preovulatory follicle number, prewash sperm motility and post wash 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. Endometrial thickness, prewash sperm motility and prewash sperm counts significantly affect the positive outcome in IUTPI. Factors like patient's age, BMI and preovulatory follicle number also positively affect the treatment outcome. Thus, these predictive factors must be taken into consideration before offering and counseling patients about treatment outcome in patients undergoing IUTPI as a method of assisted reproductive technique.

CONFLICTS OF INTEREST: None

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