ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 68 . 16
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 5, Issue –3, June - 2020, Page No. : 474 - 479

Comparing pregnancy rates of one versus two intrauterine insemination (IUIs) in patients affected with male factor and unexplained infertility

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Citation this Article: Dr. Gurjar Anil, Dr. Verma Asha, Dr. Bajya Monika, Dr. Amrita, Dr. Sharma Deepali,“ Comparing pregnancy rates of one versus two intrauterine insemination (IUIs) in patients affected with male factor and unexplained infertility”, IJMSIR- June - 2020, Vol – 5, Issue -3, P. No. 474 – 479.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Infertility happens when a couple cannot conceive after 12 months of having regular unprotected intercourse. It is estimated that around 8 to 12 percent of couples worldwide experience fertility issues. The aim of our study was to compare pregnancy rates of single versus double IUI in couples having either male factor infertility or unexplained infertility. We carried out a prospective randomised study, wherein 144 patients (mild male factor infertility (n=72) and unexplained infertility (n=72)) underwent controlled ovarian hyperstimulation (COH) with letrozole followed by IUI. The patients were categorised on the basis of the cause of infertility (male factor, M; unexplained infertility, U), and were randomised into one of the following groups : Single IUI group received single insemination 34 – 40 hours post hCG injection and double IUI group received two inseminations 24 and 48 hours post hCG injection. Clinical pregnancies diagnosed by TVS were included in the final analysis. We found that the pregnancy rate irrespective of etiology of infertility with double and single IUI was 13.89% and 12.50% respectively ($p>0.05$). In patients with idiopathic infertility, pregnancy rate with both single and double IUI was 11.11%. In patients with male infertility, the pregnancy rate with double IUI (16.67%) was higher than with single IUI (13.89%). However, the difference was not statistically significant and as such Double IUI did not offer any significant advantage over a single well timed insemination in patients with male factor or unexplained infertility.

Keywords: Intrauterine Insemination, controlled ovarian hyperstimulation, male factor infertility, unexplained infertility.

Introduction

Infertility as per WHO is defined as 1 year of unprotected intercourse without conception during childbearing age and affects approximately 10% of the population. In addition to its economic costs, infertility has a major psychological impact leading to depression and anxiety symptoms.[1] The last two decades have seen many advances in the management of infertility. Intra Uterine Insemination (IUI) is a therapeutic process of placing washed spermatozoa transcervically into the uterine cavity for the treatment of infertility.[1]

IUI is believed to reduce the effect of factors such as vaginal acidity and cervical mucus hostility. Benefit is also derived from the deposition of a bolus of prepared motile, morphologically normal sperms as close to the oocytes as possible at the time of ovulation.

As initiation of pregnancy depends upon the number and quality of sperms at the site of fertilization, there is a need for assessment of optimal method of IUI. We carried out a comparative study to find out the pregnancy rates in single versus double IUI in couples having either male factor infertility or unexplained infertility.

Methods

This comparative study was carried out in Zenana Hospital, Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur during the year April 2019 - April 2020, after approval by Research Review Board of our Institute. Written informed consent by each subject was sought before the study.

The study population included all infertile couples meeting the inclusion and exclusion criteria. The inclusion Criteria for unexplained infertility cases were patients having normal semen analysis and normal hormonal assay. It included women whose endometrial biopsy for TB PCR was negative and had no obvious pathology and atleast one patent tube was present. In the couples having Male Infertility, the volume of semen was >2cc, sperm count was 5-15 million/cc, motility was around 30-50% and sperm having normal shape was about 5 to 30%.

The exclusion criteria was applied in cases where in the husband semen analysis showed semen count as <20 million, its concentration < 10 million/ml and morphology <5% normal [severe teratospermia]. Women whose Diagnostic Laparoscopy revealed moderate to severe Endometriosis, or any uterine abnormality such as fibroid uterus, congenital malformation of the uterus, Asherman's Syndrome or bilateral blocked tubes were excluded.

Eligible and Consenting Couples Were Divided into Male Factor Infertility (M) and Unexplained Infertility (U). These were then separately randomised into single and double IUI groups. In SINGLE IUI GROUP (M_1, U_1) - IUI was done 34-40 hrs after hCG injection. In DOUBLE IUI GROUP (M_2, U_2) - IUI was done twice. First in 24 hrs and second in 48 hrs after hCG injection

Controlled Ovarian Stimulation was done by giving orally tab letrozole 5 mg from day 2 – day 6 of the cycle. TVS was used to monitor follicle size and detect ovulation. It was performed from day 8 onwards on alternate days. The hCG 5000 IU was administered when the mean follicular diameter was >18-20 mm.

Semen was prepared by *swim up procedure*. To 1 volume of semen, 1.5 volumes of wash medium was added and was mixed with a sterile pipette which was then centrifuged at 1200 rpm for 10 minute and

supernatant was discarded. Pellet was resuspended with 0.6 ml of wash medium in single IUI. In double IUI 0.6 ml wash medium was used in 1st and 0.4 ml wash medium in second insemination.

Once the semen specimen was ready, IUI cannula was introduced into the uterus without applying any force and the semen specimen was slowly ejected from the syringe. The patient was advised to remain on the table for 15 minutes. The patient was prescribed vaginal micronized progesterone 200 mg BD and Tab folic acid 5 mg 1 OD for 14 days.

If patient missed a menstrual period 16–18 days after final insemination, a quantitative beta hCG was done.If it was positive, TVS was performed.Clinical pregnancies diagnosed by TVS were considered in the analysis.

Statistical Analysis

It was carried out by entering all the qualitative and quantitative data in Excel Sheet and analysed statistically. Quantitative data was summarised in the form of Mean ± SD and difference in mean of both groups were analyzed using student't' test. Qualitative data was summarized in the form of proportion and difference in proportions were analysed using Chi-Square test. The level of significance and alpha error was kept 95% and 5% respectively.

Results

In our study, we recruited a total of 144 patients. 72 patients had unexplained infertility and 72 patients had male factor infertility. The average age of patients in our study was 28.354 ± 4.354 years. The average age of patients in the positive outcome group was 26.842 ± 3.236 years while in the negative outcome group it was 28.584 ± 4.465 years.

The average BMI of the patient in our study was 23.660 ± 1.786. Pregnancy rates in patients with BMI < 25 was 15.38% and in patients with BMI > 25 was 7.5%. The average duration of infertility in our study population was 7.556 ± 4.146 years. In 81 cycles there was monofollicular development on the day of hCG injection, in 55 cycles there was development of 2 follicles and in 8 cycles there was development of 3 follicles. However, the pregnancy rate with 2 follicles (16.36%) was higher than with single follicle (11.11%) or three follicles (12.50%).

The average endometrial thickness in the positive outcome group was 8.105 ± 0.772 mm while in the negative outcome group it was 8.159 ± 1.135 mm. We found no association between endometrial thickness and IUI results (Student 't' test, 'P' value = 0.795).

In our study, there were 114 patients with primary infertility (79.17%) while 30 patients had secondary infertility (20.83%). The pregnancy rate in patients with secondary infertility (16.67%) was higher than in those with primary infertility (12.28%). The average pre-wash sperm count in our study in patients with unexplained infertility was 67.778 ± 17.108 million/ml while in patients with male factor infertility it was 16.306 ± 2.832 million/ml.

The pregnancy rate was higher in patients with male infertility (15.28%) as compared to unexplained infertility (11.11%). However the difference was not statistically significant (Chi-square test, 'P' value = 0.622).

The overall pregnancy rate with IUI in our study was 13.19%. The pregnancy rate irrespective of etiology of infertility with Double IUI (13.89%) was slightly higher than Single IUI (12.50%). However the difference was not statistically significant (Chi-square,

'P' = 1.00). In patients with idopathic infertility, pregnancy rate with both single and double IUI was 11.11%. In patients with male infertility, the pregnancy rate with double IUI (16.67%) was higher than with single IUI (13.89%). However, the difference was not statistically significant.

Table 1 : BMI and Outcome of IUI

BMI	Positive		Negative		Total	
	No.	%	No.	%	No.	%
< 25	16	15.38	88	84.62	104	100.00
> 25	3	7.50	37	92.50	40	100.00
Total	19	13.19	125	86.81	144	100.00

Table 2 : Frequency of IUI and Outcome of IUI

IUI	Positive		Negative		Total	
	No.	%	No.	%	No.	%
Double	10	13.89	62	86.11	72	100.00
Single	9	12.50	63	87.50	72	100.00
Total	19	13.19	125	86.81	144	100.00

Table 3 : Frequency of IUI and Outcome of IUI in Unexplained Infertility

IUI	Positive		Negative		Total	
	No.	%	No.	%	No.	%
Double	4	11.11	32	88.89	36	100.00
Single	4	11.11	32	88.89	36	100.00
Total	8	11.11	64	88.89	72	100.00

Table 4 : Frequency of IUI and Outcome of IUI in Male Infertility

IUI	Positive		Negative		Total	
	No.	%	No.	%	No.	%
Double	6	16.67	30	83.33	36	100.00
Single	5	13.89	31	86.11	36	100.00
Total	11	15.28	61	84.72	72	100.00

In our study we found that the pregnancy rate with double IUI as compared to single IUI was greater overall (13.89% v/s 12.50%) and in patients with male infertility (16.67% v/s 13.89%). However, the difference in pregnancy rates was not statistically significant.

Discussion

The overall pregnancy rate with IUI in our study was 13.19%. It is comparable to the pregnancy rates of other studies in which the clinical pregnancy rate ranged from 10 to 16%.

In our study, we found that the pregnancy rate with double IUI as compared to single IUI was greater overall (13.89% v/s 12.50%) and in patients with male infertility (16.67% v/s 13.89%). However, the difference in pregnancy rates was not statistically significant.

Our results are similar to those of Ransom et al (1994)[2], Karlstrom et al (2000)[3], Cantineau et al (2003)[4], Khadem and Zadah (2003)[5], Alborzi et al (2003)[6], Osuna et al (2004)[7], Rahman S (2010)[8], Tongue E (2010)[9], Bagis et al (2010)[10], Polyzos et al (2010)[11], but contrast with those of Silverberg KM et al (1992)[12], Ragni et al (1999)[13], Liu W (2006)[14] and Randall GW (2008)[15].

Possible explanations for the discrepancy of results – Silverberg et al (1992)[12] found a pregnancy rate of 50% with double IUI compared to 10.5% with single IUI. He used frozen donor semen in approximately one quarter of patients undergoing single IUI. It is generally agreed that the use of cryopreserved semen yields lower pregnancy rates than does the use of fresh semen.

Moreover, there was heterogeneity in the patient characteristic among different studies. In addition, sample size and ovulation protocols and semen preparation methods differed among the studies.

Those who advocate double IUI feel that after IUI there is retrograde colonisation of cervical mucus that may result in sustained release of sperms (Ripps et al,

1994)[16]. In ovulation cycles which use CC and hMG for COH multiple ovulations occur sequentially over a period of atleast several hours after hCG administration. The second IUI is thought to provide additional sperms to fertilize those oocytes that ovulate subsequently thereby filling the window of opportunity for IUI. However, in our study we used letrozole for ovulation induction which has a higher incidence of monofollicular development as compared to CC and Gonadotropins used in the other studies. Therefore, as there are no sequential ovulations over a period of time, the second IUI does not provide any significant benefit in cycles using letrozole for ovulation induction in conjunction with IUI.

The different pregnancy rates in our study in patients with male factor infertility (15.28%) compared to other studies (Liu et al[14] – 18.1%, Bagis et al[10] – 9.09%) may be attributed to the lack of standardisation of semen analysis and different thresholds for semen parameters for performing IUI in different studies. On the other hand, various counting chambers are used with different methodologies (eg. manual v/s computerised) to calculate these parameters. Consequently, the variation of results among centres may well be beyond acceptable, weakening the results reported by several studies.

Conclusion

Controlled Ovarian Stimulation IUI is an effective first line method of treatment in patients with mild male factor and unexplained infertility. Double IUI does not offer any overall significant advantage over a single well-timed insemination in patients with unexplained infertility. Though, a slight advantage was found by double IUI male factor infertility.

References

1. Abdelrahman M Abdelkader, John Yeh. Potential use of IUI as a basic option for infertility : A review for technology limited medical settings. Obstetrics and Gynecology International, Vol. 2009.
2. Ransom MX, Blotner MB, Bohrer M, Corsan G, Kemmann E. Does increasing frequency of intrauterine insemination improve pregnancy rates significantly during superovulation cycles? Fertility Sterility, 1994 Feb; 61(2) : 303-7.
3. Karlstrom PO, Bergh T, Lundkvist O. Addition of gonadotropin - releasing hormone agonist and/or two inseminations with husbands sperm do not improve the pregnancy rate in superovulated cycles. Acta Obstet Gynecol Scand, 2000 Jan; 79(1) : 37-42.
4. Cantineau AEP, Heineman MJ, Cohlen BJ. Single versus double intrauterine insemination in stimulated cycles for subfertile couples : a systematic review based on a cochrane review. Human Reproduction, 2003; 18(5) : 941-946.
5. Khadem N, Zadeh Z. Effect of double IUI on pregnancy rate in super ovulated cycles with clomiphene. Journal of Reproduction and Infertility, 2003; Vol. 4, Issue 4, No. 16.
6. Alborizi S, Motazedian S, Parsanezhad ME, Jannati S. Comparison of Effectiveness of Single IUI v/s Double IUI per Cycle in Infertile patients. Fertil Steril, 2003; 80 : 595 - 599.
7. Osuna C, Matorras R, Pijoan JI, Rodriguez-Escudero F. The Heterogeneity of Randomized, controlled trials of IUI. Fertil Steril, 2004; 83 : 34 - 35.

8. Rahman S, Malhotra N, Kumar S, Roy K, Agarwal A. A randomised control trial comparing the effectiveness of single versus double intrauterine insemination in unexplained infertility. Fertility Sterility, Dec 2010; Vol. 94, Issue 7 : pg 2913-2915.
9. Tongue E, Var T, Onalan G, Altinbas S, Tokmak A. Comparison of the effectiveness of single versus double intrauterine insemination with three different timing regimens. Fertility Sterility, Sep 2010; Vol. 94, Issue 4 : pg 1267-1270.
10. Bagis T, Haydardedeoglu B, Kilicag E, Cok T. Single versus double intrauterine insemination in multifollicular ovarian hyperstimulation cycles : A randomised trial. Human Reproduction, 2010; 25(7) : 1684-1690.
11. Polyzos N, Tzioras S, Marri D, Tatsioni A. Double versus single intrauterine insemination for unexplained infertility : a meta-analysis of randomised trials. Fertility Sterility, Sept 2010; Vol. 94, Issue 4 : pg 1261-1266.
12. Silverberg KM, Johnson JV, Olive DL, Burns WN, Schenken RS. A prospective, randomised trial comparing two different intrauterine insemination regimens in controlled ovarian hyperstimulation cycles. Fertility Sterility, 1992; 57(2) : 357-61.
13. Ragni G, Maggioni P, Guermandi E, Testa A, Baroni E. Efficacy of double intrauterine insemination in controlled ovarian hyperstimulation cycles. Fertility Sterility, October 1999; Vol. 72, Issue 4 : pg 619-622.
14. Liu W, Gong F, Lu OK, Chang Sha, China. Comparing the pregnancy rates of one versus two intrauterine inseminations in male factor and idiopathic infertility. Journal of Assisted Reproduction & Genetics, Feb 2006; Vol. 23, No. 2.
15. Randall Gary W, Gantt Pickens A. Double v/s Single Intrauterine Insemination Per Cycle : Use in Gonadotropin cycles and in diagnostic categories of ovulatory dysfunction and male factor infertility. Journal of Reproductive Medicine, 2008; Vol. 53, No. 3 : pp 196-202.
16. Ripps BA, Mihnas BS, Carson SA, Buster JE. IUI in fertile women delivers large numbers of sperms to the peritoneal fluid than intracervical insemination. Fertil Steril, 1994 Feb; 61(2) : 398-400.