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RESEARCH ARTICLE

Rise of the dawn - single versus double intrauterine insemination in controlled hyperstimulated cycle in infertile couples

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ABSTRACT

Objective: To compare the efficacy of single and double intrauterine insemination for pregnancy rates in infertile couples. **Methods**: This retrospective study was conducted in tertiary care hospital from January 2015 - December 2020. Patient were given ovulation induction treatment with clomiphene citrate 100mg OD or letrozole 5mg OD daily from day 2 or 3 for 5 days along with inj FSH 75IU (highly purified) was given deep IM on day 5 and day 7. In case of single IUI, it was performed after 36 hours and for double IUI, it was performed after 36 hours and 48 hours after the intramuscular trigger of hCG. **Results**: Total 250 patients were included in the study, 150 (60%) in single IUI and 100 (40%) in double IUI group. In single IUI group, 24 out of 150 patients conceived (success rate 16%). In double IUI group, out of 100 patients, 21 patients conceived (success rate 21%). There was no statistically significant difference between the two groups. **Conclusion**: The outcome of double IUI does not give significant benefit compared to single IUI. This increases the stress and disbursement of the couple without actually improving the outcome.

Keywords: Ovulation induction, sperm preparation, unexplained infertility, male infertility.

Infertility is a critical component of reproductive health, which can lead to distress, depression, discrimination and ostracism in a couple. Male factor infertility affects almost 30% - 50% of infertile couples worldwide.[1] Men with idiopathic oligospermia, asthenospermia or teratospermia, medical treatment may improve semen quality parameters. It is unclear whether such a clinical practice may indeed improve fertility in general.[2] The management of patients with unexplained infertility [3], and it is a generally preferred treatment for mild male factor infertility, ovulatory dysfunction, cervical factor infertility and endometriosis [4]. The rationale for double insemination is to create the opportunity for a longer fertilization period as follicle rupture may occur over a wide interval ~22–48 hours after hCG administration in OH/IUI cycles.[5]

There are different modalities to overcome this issue, IUI being one of it. This procedure is simple, noninvasive and cheap. The rationale for performing IUI is to overcome problems of vaginal acidic pH, cervical mucus hostility, deposit adequately good number of highly motile and morphologically normal sperm in uterus around the time of ovulation.

The success depends on prognostic factors like duration of infertility, follicle number, female age, number of sperm inseminated, progressive motile sperm count, sperm morphology, endometrial thickness. Two further important factors that could be associated with success rates are the timing and frequency of insemination.

Aims & objectives: To compare the efficacy of single and double intrauterine insemination for pregnancy rates in

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infertile couples.

Materials and methods

This retrospective study was conducted in Smt. Kashibai Navale Medical College and General Hospital from January 2015 - December 2020. Infertile couples walking into the infertility OPD willing for participation in study after fulfilling the inclusion criteria were included in the study. The sample size was 250 couples.

All couples were counselled and evaluated after taking consent. History taking physical examination and investigations were carried out. All females had undergone routine investigations including complete blood counts, blood grouping, blood sugar levels, HIV, HBsAg, ultrasonography of abdomen and pelvis, FSH and LH and prolactin on day2/3, hysterosalpingography /laparoscopy, thyroid profile. All male partners had undergone semen analysis after abstinence of 3 - 5 days.

Ovulation induction protocol: Patient were given ovulation induction treatment with clomiphene citrate 100mg OD or letrozole 5mg OD daily from day 2 or 3 for 5 days along with it inj FSH 75IU (highly purified) was given deep IM on day 5 & day 7. Patient was advised follow up for transvaginal sonography - follicular monitoring from day 10 onwards. Inj hCG 5000 IU was given deep intramuscular when follicles reach 18-20mm in size. In case of single IUI, it was performed after 36 hours & for double IUI, it was performed after 36 hours & 48 hours after the intramuscular trigger of hCG.

Semen preparation: Couple was instructed to abstain for 3 - 5 days before semen collection. Semen was collected in sterile container & kept for liquefaction for about 25 min. Simultaneously 5ml medium is kept in incubator for 30 min. Process of sperm preparation was done by swim up technique. 2ml medium was added to 2ml of semen. Then centrifugation done at 1500rpm. Supernatant discarded & again 2ml of medium is added slowly without disturbing previously formed pellet. Again, centrifugation done at 1500 rpm & supernatant removed. Remaining mixture along with pellet is incubated at 45 min. Then superficial 2 ml sample which contain healthy motile sperm formed from swim up technique are collected for the procedure.

Inclusion criteria -

• Female age 20-35 years.

• Male age 25-40 years.

• Day 3 FSH <10 mIU/ml.

• A fully screened female with no other anatomical or tubal defect.

• Couples in whom male partner has a sperm count more than 10 million /ml.

Exclusion criteria -

• Couples in whom male partner has a sperm count less than 10 million /ml.

• Couples in whom female partner has abnormal tubal function and uterine abnormality.

• Couples who have already undergone 4 cycles of IUI including single and repeat IUI.

Statistical analysis - The data collected was tabulated in SPSS. Descriptive statistics like numbers & percentages were enumerated for all categorical variables & all statistical analysis were performed using the SPSS statistical package, version 17.0.

Results

Total 250 patients were included in the study, 150 (60%) in single IUI and 100 (40%) in double IUI group. In single IUI group, 24 out of 150 patients conceived (success rate 16%). In double IUI group, out of 100 patients, 21 patients conceived (success rate 21%). There was no statistically significant difference between the two groups according to age of both male and female partners, the duration of infertility, type of infertility, pre-wash sperm count as p value >0.05.

Table 1: Age of male and the outcome

	Single IUI				Double IUI				Single IUI		Double IUI		
Age group (years)	Pregnant		Non-Pregnant		Pregnant		Non-Pregnant		Total		Total		P-value [Single vs Double IUI]
Males	n	%	n	%	n	%	n	%	n	%	n	%	
25 – 30	16	21.0	60	79.0	15	22.0	53	78.0	76	100.0	68	100.0	0.883^{NS}
31 – 35	8	18.2	36	81.8	6	21.4	22	78.6	44	100.0	28	100.0	0.734^{NS}
36 – 40	0	0.0	30	100.0	0	0.0	4	100.0	30	100.0	4	100.0	--
Total	24	16.0	126	84.0	21	21.0	79	79.0	150	100.0	100	100.0	0.313^{NS}
P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.													

Age of the male partners varied between 25 to 40 years. The pregnancy rate is higher in double IUI in all the age groups, 22.05% versus 21.05% in 25-30 years, 15.90% versus 21.42% in 31-35 years (table 1). Incidence of successful outcome (pregnancy) did not differ significantly across various age group of males (p value >0.05 for all).

Female age in the study group varied from 20 to 35 years. Pregnancy rate has been found to be more in double IUI in age group of 31 to 35 years 25% versus 13.3% in single IUI (table 2). Incidence of successful outcome (pregnancy) did not differ significantly across various age group of females (p value > 0.05 for all).

Similarly, duration of fertility showed a greater number of pregnancies with double IUI versus single IUI, for less than 5 years 21.21% versus 18.51% & 14.28% of double IUI versus 7.69% of single IUI for more than 10 years of infertility (table 3). Incidence of successful outcome (pregnancy) did not differ significantly across various groups of duration of infertility (p value > 0.05 for all).

Table 2: Age of female and the outcome

	Single IUI				Double IUI				Single IUI		Double IUI		
Age group (years)	Pregnant		Non-Pregnant		Pregnant		Non-Pregnant		Total		Total		P-value [Single vs Double IUI]
Females	n	%	n	%	n	%	n	%	n	%	n	%	
25 – 30	11	15.3	61	84.7	12	20.0	48	80.0	72	100.0	60	100.0	0.476^{NS}
31 – 35	9	18.8	39	81.2	5	20.8	19	79.2	48	100.0	24	100.0	0.833^{NS}
36 – 40	4	13.3	26	86.7	4	25.0	12	75.0	30	100.0	16	100.0	0.421^{NS}
Total	24	16.0	126	84.0	21	21.0	79	79.0	150	100.0	100	100.0	0.313^{NS}

P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.

Table 3: Duration of infertility and the outcome

	Single IUI				Double IUI				Single IUI		Double IUI		
Duration of infertility (years)	Pregnant		Non-Pregnant		Pregnant		Non-Pregnant		Total		Total		P-value [Single vs Double IUI]
	n	%	n	%	n	%	n	%	n	%	n	%	
≤5	15	18.5	66	81.5	14	21.2	52	78.8	81	100.0	66	100.0	0.683^{NS}
6 – 10	6	20.0	24	80.0	6	22.2	21	77.8	30	100.0	27	100.0	0.999^{NS}
>10	3	7.7	36	92.3	1	14.3	6	85.7	39	100.0	7	100.0	0.496^{NS}
Total	24	16.0	126	84.0	21	21.0	79	79.0	150	100.0	100	100.0	0.313^{NS}

P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.

Table 4: Type of infertility and the outcome

	Single IUI				Double IUI				Single IUI		Double IUI		
Type of infertility	Pregnant		Non-Pregnant		Pregnant		Non-Pregnant		Total		Total		P-value [Single vs Double IUI]
	n	%	n	%	n	%	n	%	n	%	n	%	
Primary infertility	12	18.5	53	81.5	7	21.9	25	78.1	65	100.0	32	100.0	0.690^{NS}
Secondary infertility	12	14.1	73	85.9	14	20.6	54	79.4	85	100.0	68	100.0	0.290^{NS}
Total	24	16.0	126	84.0	21	21.0	79	79.0	150	100.0	100	100.0	0.313^{NS}

P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.

When type of fertility was considered primary and secondary infertility showed a greater number of pregnancies with double IUI versus single IUI. Primary infertility with single IUI had 18.46% of pregnancy versus 21.87% of double IUI & secondary infertility had 14.11% pregnancy rate of single IUI versus 20.58% of double IUI (table 4). Incidence of successful outcome (pregnancy) did not differ significantly between group of cases with primary infertility and group of cases with secondary infertility (p value >0.05 for all).

Prewash sperm count of less than 50 million/ml showed 18.84% pregnancies in single IUI versus 20.45% in double IUI & for sperm count of more than 50 million/ml the pregnancies were 13.58% for single IUI versus 21.42% for double IUI (table 5). Incidence of successful outcome (pregnancy) did not differ significantly between group of cases with prewash sperm count below 50 million and group of cases with pre wash sperm count above 50 million (p value >0.05 for all).

Table 5: Prewash sperm count and the outcome

	Single IUI				Double IUI				Single IUI		Double IUI		
Pre wash sperm count (million)	Pregnant		Non-Pregnant		Pregnant		Non-Pregnant		Total		Total		P-value [Single vs Double IUI]
	n	%	n	%	n	%	n	%	n	%	n	%	
≤50	13	18.8	56	81.2	9	20.4	35	79.6	69	100.0	44	100.0	0.833^{NS}
>50	11	13.6	70	86.4	12	21.4	44	78.6	81	100.0	56	100.0	0.227^{NS}
Total	24	16.0	126	84.0	21	21.0	79	79.0	150	100.0	100	100.0	0.313^{NS}

P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS – Statistically non-significant.

Discussion

It has always been a matter of discussion whether to perform single or double IUI. Double IUI gives us an additional opportunity of well timed insemination of good quality sperms.

There are a few studies which conclude that double IUI is superior to single IUI overall, especially when comparing gonadotropins containing ovarian stimulation protocols including the ovulatory dysfunction and male factor diagnostic categories [6]. In 2003, Cantineau et al identified six studies involving 1785 women in the Cochrane database [7]. The results of five studies that reported pregnancy rate per couple showed a significant effect of using double intrauterine insemination.

Data from Society for Assisted Reproductive technology and the American Society for Reproductive Medicine, 1998 has stated age to be a significant factor affecting IUI [8]. According to study by Matheiu and colleagues two factors are of poor prognosis, i.e. duration of infertility >3 years (p = 0.01) and husband's age (p = 0.03) [9]. Our study has not found any significant difference in fertility rate in male in age groups. There is significant decline in fertility after 36-40 years of age. This decline in female fertility has been suggested to be a result of decreased oocyte quality by Navot et al [10]. Reduced uterine receptivity has been suggested as a cause of this decline of fertility by Cano et al [11].

Table 6: Comparison of various studies to our study

Studies	Single IUI	Double IUI
Randall GW, et al[13]	11%	16.2%
Sorouri, et al[14]	11.7%	13.4%
Zarek, et al[15]	16.4%	13.6%
Our study	16%	21%

There is significant decline in fertility after 30 years and significantly better pregnancy rate has been resulted by double IUI in higher age group of 31 to 35 years. A study by Tomlimson MJ and colleagues, duration of infertility did not appear to affect pregnancy rate significantly unless it had continued for more than 22 months [12].

In this study, double IUI has given better pregnancy rate 21% than single IUI 16%. The difference is not statistically significant ($p > 0.05$).

Conclusion

Double IUI has no statistically significant advantage over single IUI. There seems to be a trend towards better outcomes with an increase in frequency of IUI per treatment cycle when the cause of infertility is an isolated male factor. Small studies can be found that support double IUI, the overwhelming majority of the existing medical literature on this topic shows no benefit of double IUI compared with a single IUI. However, larger studies are required to determine if double IUI can give better results.

Conflict of interest: None. **Disclaimer:** Nil.

References

1. Lipshultz LI, Howards SS, Niederberger CS. Infertility in the Male. 4th ed. Cambridge: Cambridge University Press; 2009.
2. Willets AE, Corbo JM, Brown JN. Clomiphene for the treatment of male infertility. Reprod Sci. 2013 Jul; 20(7): 739-44.
3. Verhulst SM, Cohlen BJ, Hughes E, TeVelde E, Heineman MJ. Intra-uterine insemination for unexplained subfertility, Cochrane Database Syst Rev. 2006; 18: CD001838.
4. Duran HE, Morshedi M, Kruger T, Oehninger S. Intrauterine insemination: a systematic review on determinants of success, Hum Reprod Update. 2002; 8: 373-84.
5. Testart J, Frydman R. Minimum time lapse between luteinizing hormone surge or human chorionic gonadotropin administration and follicular rupture. Fertil Steril. 1982; 37: 50-3.
6. Cano F, Simon C, Remohi J, Pellicer A. Effect of aging on female reproductive system: evidence foe role of uterine senescence in the decline in female fecundity. Fertil Steril.1995; 64: 584-9.
7. Rakic L, Kostova E, Cohlen BJ, Cantineau AE. Cochrane Database Syst Rev. 2021 Jul 14; 7(7): CD003854.
8. Society for Assisted Reproductive technology and the American Society for Reproductive Medicine. Assisted reproductive technology in the United States: 1998 American Society for reproductive Medicine/Society for Assisted Reproductive technology registry. Fertility and Sterility. 2002; 77:18-31.
9. Mathieu C, Ecochard R, Bied V, Lornage J, Czyba JC. Cumulative conception rate following intrauterine artificial insemination with husband's spermatozoa; influence of husband's age. Hum Reprod. 1995;10:1090-7.
10. Navot D, Goldstein N, Mor Joset S, Simon A, Relou A, Birkenfeld A. Multiple pregnancies: risk factors and prognostic variables during induction of ovulation with human menopausal gonadotropins. Hum Reprod. 1995; 6: 1152-5.
11. Cano F, Simon C, Remohi J, Pellicer A. Effect of aging on the female reproductive system: evidence for a role of uterine senescence in the decline in female fecundity. Fertility and Sterility. 1995; 64: 584.
12. Tomlimson MJ, Arthur AJB, Thompson KA, Kasraie JL, Bentick B. Prognostic indicators for intrauterine insemination (IUI): Statistical model for IUI success. Hum Reprod. 1996; 11(9):1892-6.
13. Randall GW, Gantt PA. Double vs single intrauterine insemination per cycle: use in gonadotropin cycles and diagnostic categories of ovulatory dysfunction and male factor infertility. J Reprod Med. March 2008; 53(3): 196-202.
14. Zahiri Sorouri Z, Rashid Shomali R, Pourmarzi D. Single versus double intrauterine insemination in controlled ovarian hyperstimulation cycles: A randomised trial. Arch Iran Med.2016;19(7): 465-469.
15. Zarek SM, Hill MJ, De Cherney AH, Osheroff JE, Levens ED. Single-donor and double-donor intrauterine insemination cycles: does double intrauterine insemination increase clinical pregnancy rates? Fertil Steril. 2014; 102: 739-43.

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