Original Article

Intrauterine Insemination Experience in a Government Teaching Hospital Setup

Das Vinita¹, Pandey Amita², Agarwal Anjoo³, Mehrotra Seema⁴, Pradeep Yashodhara⁵

¹Professor and Head ^{2,4}Assistant Professor ³Associate Professor ⁵Professor
Department of Obstetrics and Gynaecology, C.S.M Medical University, Lucknow.

Abstract

Objectives: Intrauterine insemination with or without controlled ovarian hyperstimulation is a viable treatment option for male factor, cervical factor and unexplained infertility. We enumerate our 10 year experience in performing intrauterine insemination at a government teaching hospital setup. **Study Design:** Retrospective observational study. **Results:** Nine hundred eighty nine couples were observed for 3104 treatment cycles. Male factor and anovulation were the two common causes of infertility in this cohort. Out of the 232 pregnancies that occurred during the study, 34.05% resulted in live birth. Highest cycle fecundity was seen in cases of idiopathic infertility (16%) followed by male factor infertility (15%). 91.8% conceptions occurred in the 1st cycles of intrauterine insemination. **Conclusion:** In the resource deprived Indian scenario controlled ovarian hyperstimulation with intrauterine insemination is an effective, less invasive, feasible & financially acceptable modality for the treatment of sub-fertility.

Keywords: intrauterine insemination, male factor, idiopathic infertility, ovarian, hyperstimulation.

Introduction

Intrauterine insemination (IUI) with or without controlled ovarian hyperstimulation (COH) is a popular modality for treatment of sub-fertility. Although considerable discussion and debate has appeared in western literature regarding the utility of COH & IUI, lately the National Institute of Clinical Excellence (NICE), UK has revised the evidence for assessment and treatment

of infertile couples and has recommended that IUI should be offered to couples with infertility because it is as effective as IVF, less invasive and requires fewer resources¹. The rationale put forward in support of COH & IUI is that ovarian stimulation corrects subtle, unpredictable ovulatory dysfunction and there is increased probability of conception if increased density of motile spermatozoa is placed closer to multiple fertilizable oocytes. Hence, it is considered to be a viable treatment option for male factor, cervical factor and unexplained infertility². Here we attempt to enumerate our 10 year experience in performing IUI, its success rate and the stumbling blocks encountered in a government teaching hospital setup.

Methods

This is a retrospective observational study of subfertile couples undergoing COH and IUI at the infertility unit

Paper received on : 23/04/2007 accepted on : 08/02/2010

Correspondence:

Prof. Das Vinita

B-2, Sector – B

Aliganj, Lucknow – 226 024

Tel No. (Res.) 0522-2385533, 2330759

E-mail:- das_lko@yahoo.com

Table 1:
Baseline characteristics of couples undergoing IUI

Variable	No. of Couples	% of Couples
Age of Female		
< 30 years	178	18
> 30 years	811	82
Age of male partner		
< 30 years	227	23
> 30 years	762	77
Duration of Infertility		
< 5 years	227	23
5 – 10 years	386	39
> 10 years	376	38
Type of Infertility		
Primary	603	61
Secondary	386	39

Table 2:
Pregnancy outcome in patients conceived by IUI

Outcome Variable	No. of Females	% of Females
Live Birth		
• Term	79	34.05
• Preterm	7	3.02
Still Birth	1	0.43
Miscarriage	68	29.31
Ectopic pregnancy	9	3.88
Multiple pregnancy	10	4.31
Ongoing pregnancies	13	5.60
Lost to follow up	45	19.40

Table 3:
Cycle fecundity by factor causing infertility

Diagnosis	Pregnancy / Cycle	Fecundity
Male Factor	127/849	0.15
Anovulation	62/787	0.08
Idiopathic / unexplained	112/702	0.16
Tubo-peritoneal	23/392	0.06
Cervical Factor	31/256	0.12
LPD	6/92	0.06
Others	2/26	0.07

Table 4:
Cycle fecundity by attempt of IUI

No. of Attempt for IUI	Pregnancy / Cycle	Fecundity
1	56 / 989	0.057
2	59 / 722	0.082
3	53 / 601	0.088
4	45 / 470	0.096
5	12 / 192	0.063
≥ 6	7 / 130	0.054

*91.8% conceptions in first 4 cycles of IUI

in our hospital from 1995-2004. All registered couples at our centre underwent a standard investigation protocol. The infertility work up included a detailed medical and menstrual history, complete examination, confirmation of ovulation by follicular monitoring or mid-luteal serum progesterone levels, tubal patency test by hysterosalpingography, sonosalpingography or diagnostic laparoscopy and semen analysis of the male partner. Couples included in the study were the ones with male subfertility (as per WHO criteria), cervical subfertility (negative post coital test), minimal tubo-peritoneal disease (endometriosis stage I & II, minimal adnexal adhesions), anovulation and unexplained infertility. Women with bilateral tubal block, endometriosis

stage III & IV, untreated hypothyroidism and hyperprolactinemia were excluded from the study. Following eligibility criteria and informed consent, 989 subfertile couples who had undergone 3104 treatment cycles were included in this data analysis.

All the women underwent a standard treatment protocol that included ovulation induction using antiestrogens (clomiphene citrate) alone or combined with gonadotrophins. Follicular monitoring using transvaginal sonography was done from D6-8 onwards & all women were given injection Human chorionic gonadotrophin (hCG) 5000 IU for LH surge when the dominant follicle was > 18mm. IUI was performed within 36-48 hrs of hCG administration and the second IUI was repeated 24 hours after the first one in patients where the follicle did not rupture even 48 hours after hCG administration. Semen for IUI was prepared by the standard swim up technique and all patients were given progesterone for luteal phase support for 10 days following IUI.

Results:

Nine hundred eighty nine subfertile couples enrolled in the study were observed for 3104 treatment cycles. Table I shows baseline characteristic of couples registered in the study. In most of the couples both partners were >30 years of age (86%). Although the duration of infertility was not significantly different, most of the couples had primary infertility (61%). In our study 64% of the couples had multiple factors contributing towards infertility (Fig 1). On analyzing the various causes of infertility we found that male factor was the commonest and contributed to 61% of the cases of subfertility followed by anovulation which was present in 42% of the female partners. Unexplained or idiopathic infertility was seen in 28% cases. The outcome variable for suc-

Fig 1 : Causative factors for infertility

cess of IUI was occurrence of pregnancy. This was defined as delay in menses associated with presence of a positive pregnancy test or a detectable rise in serum beta hCG levels. In our set up the overall pregnancy rate per cycle was 7.47% (232/3104) and pregnancy rate per couple was 23.45% (232/989).

Subsequently, we also recorded the outcome of pregnancy in patients conceived by IUI (Table 2). Of the 232 pregnancies that occurred during the study, 34.05% resulted in live birth, 29.31% had abortion and 3.88% had ectopic pregnancy. There were 10 cases of multiple pregnancies (4.31%) all of whom were twins and 19.40% patients were lost to follow up. When we calculated cycle fecundity according to factor responsible for infertility, the highest success rate was seen with idiopathic or unexplained infertility (16%) followed by male factor infertility (15%) (Table 3). On calculating the fecundity according to the number of attempts taken for intrauterine insemination, we found that 91.8% conceptions occurred in the 1st four cycles of IUI (Table 4) which happened to be the most rewarding and hence should be performed with utmost care. Other factors affecting the cycle fecundity in our analysis were age of the female partner, number of dominant follicles on the day of hCG administration and duration of infertility.

Discussion

Controlled ovarian hyperstimulation coupled with intrauterine insemination is considered to be a popular treatment option for male factor, cervical factor and unexplained infertility. The universal preference for this method is based on the hypothesis that both these methods increase the proximity of gametes in the reproductive tract. Therefore this treatment modality is often advised before attempting more invasive therapies such as in vitro fertilization or gamete intrafallopian transfer³. In this retrospective observational study we have analyzed couples with male and female subfertility undergoing controlled ovarian hyper stimulation with intrauterine insemination.

In our setup the overall pregnancy rate per cycle was 7.47% as against 8.2% and 9.2% reported by Steures et al⁴ and Iberico et al⁵ which are comparative. Agarwal⁶ from AIIMS reported a pregnancy rate of 18% in couples with unexplained infertility undergoing COH / IUI, which is close to the 16% pregnancy rate seen in our centre in similar cases. The pregnancy rate per couple was 23.45% in our study as compared to 28.1% re-

ported by Shibahara et al⁷. The slightly decreased fecundity rates in our study can be attributed to the stumbling blocks in a government teaching hospital like ours, such as resource constraints, inertia to new technologies and difficulty in purchasing new instruments. Apart from this there are other teething problems in the initial years, multiple performers including residents performing and monitoring IUI and of course a learning curve inherent to a training hospital.

On analyzing the pregnancy outcome in couples conceived by IUI we found that there were 34% term live births and 3% preterm live births as compared to 72% term live births and 9.13% preterm live births reported by Guzick et al⁸. The miscarriage rate at our center was 29% which was higher than that reported in other studies (20.96% by Guzick et al). The multiple pregnancy rate was only 4.3% in our study as compared to 7% reported by Costello et al⁹ probably because a significant number of patients in our study with twin pregnancy miscarried. The ongoing pregnancy rate in our center was 5.6% which is comparable to the 6.7% ongoing pregnancy rate reported by Steures et al⁴.

The effectiveness of IUI is well established in couples in whom subfertility is due to male factor (Cohlen et al¹⁰) or when subfertility is unexplained. In our study too, the highest cycle fecundity was seen with unexplained infertility (16%) and male factor infertility (15%).

The timing of insemination is reported to influence the overall pregnancy rate. In our study all inseminations were performed at the time of anticipated follicular rupture i.e. within 36-48 hours of giving hCG injection which is the accepted protocol world over. Although the influence of the number of IUI performed per cycle on the overall pregnancy rate is presently a matter of debate, in our study a second IUI was performed 24 hours after the first one in all cases in the initial years. Later on a second IUI was performed only in cases where the follicle rupture was delayed by more than 48 hours after giving hCG. We did not observe any significant difference in the fecundity rates when either one or two IUIs were performed in a cycle.

In our center, the cycle fecundity by the number of attempt was 5.7% after first IUI and increased subsequently to 9.6% after the fourth IUI. Thereafter the fecundity declined sharply. Overall maximum conceptions were seen to occur in the first four cycles of IUI.

In contrast to this Khalil et al¹¹ reported highest pregnancy rate in the first treatment cycle but they too agreed that there was only a slight increase in cumulative birth rate after the fourth treatment cycle. It has now become an accepted practice to offer other assisted reproductive technologies to infertile couples when pregnancy has failed to occur within at least six well claimed intrauterine inseminations. Kerin et al¹² also observed that on an average 3.3 insemination cycle were required for each woman to become pregnant and only a few women conceived after five unsuccessful months of treatment. Contrary to this, Wiltbank¹³ reported an increase in success rate of IUI from 17% to 33% in couples with less than three and more than three attempts with IUI respectively.

Other factors influencing conception in couples undergoing COH and IUI were age of the female partner, duration of infertility and number of dominant follicles on day of hCG administration. Similar observations were made by Iberico et al⁵. They observed a three fold increase in pregnancy rate when IUI was done with dominant follicles. They also reported a lower pregnancy rate where the duration of infertility was >3 years. Ghosh et al¹⁴ reported that women with age >30 years were half as likely to become pregnant as compared to women <30 years.

Conclusion

Controlled ovarian hyperstimulation with intrauterine insemination has been shown to have a clinically significant improvement in fecundity when compared to intercourse in unmedicated cycles, especially in cases with male, unexplained, cervical factor and anovulatory infertility. Although the cost effectiveness of this therapy has not been worked out, several observational studies suggest that it is a more cost effective treatment than IVF. Considering these facts we conclude that in the resource deprived Indian scenario especially in a public enterprise dealing with masses who cannot afford expensive health care; COH with IUI definitely holds good as an effective, less invasive, feasible and financially acceptable modality for treatment of subfertility.

References

1. RCOG. The management of infertility in secondary care. (Evidence based clinical guidelines, No.3). London: RCOG Press, 1998.
2. Dodson WC and Haney AF. Controlled ovarian hyperstimulation and intrauterine insemination for treatment of infertility. *Fertil Steril* 1991;55:457-67.
3. Peterson CM, Hatasaka HH, Jones KP et al. Ovulation induction with gonadotropins and intrauterine insemination compared with invitro fertilization and no therapy – A prospective nonrandomized, cohort study and meta analysis. *Fertil Steril* 1994;62:535-44.
4. Steures P, van der Steeg JW, Mol BW et al. Prediction of an ongoing pregnancy after intrauterine insemination. *Fertil Steril* 2004;82:45-51.
5. Iberico G, Vioque J, Auza N. et al. Analysis of factors influencing pregnancy rates in homologous intrauterine insemination. *Fertil Steril* 2004;81:1308-13.
6. Agarwal S, Mittal, S. A randomized prospective trial of intrauterine insemination versus timed intercourse in superovulated cycle with clomiphene. *Indian J Med Res* 2004;120:519-22.
7. Shibahara H, Obara H, Ayustawati et al. Prediction of pregnancy by intrauterine insemination using CASA estimates and strict criteria in patients with male factor infertility. *Int J Androl* 2004;27:63-8.
8. Guzick DS, Carson SA, Coutifaris C et al. Efficacy of superovulation and intrauterine insemination in the treatment of infertility. *N Engl J Med* 1999;340:177-83.
9. Costello MF, Emerson S, Miranda T et al. Case series of a single center treatment of ovulatory infertility with clomiphene citrate and intra uterine insemination. *Aust N Z J Obstet Gynaecol* 2004;44:156-9.
10. Cohlen BJ, te Velde ER, van Kooij RJ et al. Controlled ovarian hyperstimulation and intrauterine insemination for treatment male subfertility – A controlled study. *Hum Reprod* 1998;13:1553-8.
11. Khalil MR, Rasmussen PE, Erb K et al. Homologous intrauterine insemination. An evaluation of prognostic factors based on a review of 2473 cycles. *Acta Obstet Gynecol Scand* 2001;80:74-81.
12. Kerin JF, Kirby C, Peek J et al. Improved conception rate after intrauterine insemination of washed spermatozoa from men with poor quality semen. *Lancet* 1984;1:533-5.
13. Wiltbank MC, Kosasa S, Rogers B. Treatment of infertile patients by intrauterine insemination of washed spermatozoa. *Andrologia* 1985;17:22-30.
14. Ghosh C, Buck G, Priore R et al. Follicular response and pregnancy among infertile women undergoing ovulation induction and intrauterine insemination. *Fertil Steril* 2003;80:328-35.