

Intra-Uterine Insemination for Treatment of Male Infertility

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Summary

The aim of this prospective randomized controlled study was to determine the possible role of ovulation induction with intrauterine insemination (IUI) in the treatment of male infertility. A total of 50 patients were randomized to receive ovulation induction with or without IUI. All patients had ovarian hyperstimulation with clomiphene citrate. Ovulation was induced using human chorionic gonadotrophin and timed intercourse (TI) was advised 24-48 h later or IUI was effected 36-48 h later. Pregnancy rates after three cycles were significantly higher in the IUI group (16%) compared to 4% in TI group. However no pregnancy occurred in patients, having sperm count < 10 million/ml. Ovulation induction with clomiphene citrate with IUI is an effective treatment for male infertility due to moderate degree of oligospermia.

Introduction

Artificial insemination of husband's semen (AIH) has been used in the treatment of infertile couples for more than 200 years. The first documented use of AIH was in 1770 by John Hunter (Acosta and Kruger, 1996). The term AIH covers a wide range of techniques. The semen can be placed intra-vaginally, intra-cervically, intra-uterine, intra-tubal or directly intra-peritoneal. Most studies refer to intra-uterine insemination (IUI) which seems to be a standardized technique. The rationale for artificial insemination is the increase in gamete density at the site of fertilization. (Allen et al, 1985). The theoretical advantage of IUI over intravaginal techniques may be due to increasing number of sperms arriving at the fertilization site as a consequence of bypassing of the cervical mucous barrier. The increasing use of IUI in male infertility is mainly the result of the refinement of

techniques for preparation of washed motile spermatozoa as are used in in-vitro fertilization (IVF) procedures. Washing procedures seem to be necessary to remove prostaglandins, infectious agents, antigenic proteins and defective spermatozoa. Though IUI may have beneficial effect on the number of functional sperms at the site of fertilization, yet its role remains controversial. (Ho et al 1992; Yovich, & Matson 1998). The present study summarizes results of 68 intra-uterine inseminations with husband's sperms performed in 25 patients.

Materials & Methods

The study was carried out at Naval Hospital INHS Asvini from November 1996 to June 1998. Infertile couples undergoing treatment for idiopathic oligospermia were selected for the study. In selected patients no cause of infertility was detected in female

partner on standard investigations – hysterosalpingography (HSG), ovulation studies, hormonal profile and laparoscopy. Patients were randomized in two groups – control groups and IUI group. Procedure of ovulation induction and follicular monitoring was similar in both the groups. Timed coitus was advised in control group and IUI was done in study group. Minimum 3 cycles of treatment were planned for each group. Semen analysis was done after abstinence for 3 days. Values were compared with standard values laid down by WHO manual 1992. Sperm concentration less than 20 million was considered as oligospermia and motility less than 50% was taken as asthenospermia. Patients having count less than 5 million per ml. were excluded from the study.

After selection of patients all the female partners in control as well as IUI group underwent ovarian hyperstimulation with clomiphene citrate and human chorionic gonadotrophin (hCG). Clomiphene citrate 50 mg was given orally from 5th to 9th day of cycle. Daily follicular study was done from tenth day onwards. When follicle reached >18mm, the patient was given hCG 10,000 IU and IUI was done 36 hours later.

Sperm preparation

The semen sample was collected after 3 days of abstinence in a wide mouth polypropylene container. Method of collection was by masturbation. Samples were examined for sperm concentration, motility and morphology. Makler counting chamber was used in all cases for the counting. Monopercoll gradient separation technique was used in all cases. One ml 80% percoll was placed in 10 ml sterile conical tube. It was then carefully layered with 1ml liquefied semen. The gradient was then

gently stirred at semen percoll interface leaving 0.5 ml of the bottom end of the tube undisturbed. It was then centrifuged at 1000 r.p.m. for 30 minutes all the motile spermatozoa travel through the gradient and reach the bottom by forming a pellet, while the debris remain in the upper layer. Supernatant was then removed by carefully skimming the surface with sterile pipette leaving 0.1 ml at the bottom of the tube. Then 0.5ml. of Earl's medium was added to allow slight resuspension. The pellet was then carefully transferred to a clean sterile centrifuge tube, washed and resuspended with 0.5 ml of Earl's media. Prepared samples were evaluated for sperm concentration, percentage motility and percentage morphology. After examination 0.5 ml of the sample was inseminated into the uterus using Makler intra-uterine insemination canula.

Results

Both the groups were well matched. (Table I). There was no statistical difference in sperm concentration, percentage motility and percentage of normal morphology between the two groups in the initial semen samples (Table I). After preparation with mono-percoll technique sperm count got reduced but there was significant increase in percentage of motile and morphologically normal spermatozoa (Table II). Pregnancy rates of 4% and 16% per patient and 1.4% and 5.8% per cycle were obtained in control group and IUI group respectively (Table III). Initial sperm concentration was found to be directly proportional to pregnancy rate. No pregnancy was obtained in patients where sperm count was less than 10 million/ml. In patients where sperm count was more than 10 million/ml., one pregnancy was obtained in control group compared to 4 pregnancies in IUI group (Table IV).

Table-I Showing demographic data

	Control Group	Study Group (IUI Group)
No. of patients	25	25
Age of the patients in years (mean)		
Male	31	30.8
Female	27	26.2
Duration of infertility in months (mean)	40	37
No. of cycles	70	68

Table II Showing semen parameters in control group and study group (before and after preparation).

Semen parameters	Control Group	Study Group	
		Initial sample	After preparation
Sperm concentration In million	12.64±6.17	11.84±5.92	4.96±1.70
Percentage motility	43.75±14.87	42.80±14.23	71.88±2.38
Percentage normal Morphology	40.91±6.91	39.98±5.92	63.29±4.67

Table III Pregnancy rates achieved in control and IUI groups.

Group	No. of patients Rate/patients	Pregnancies rate/cycle	Pregnancy	No. of cycles	Pregnancy
Control Group	25	1	4%	70	1.4%
IUI Group	25	4	16%	68	5.8%

Table IV – Effect of initial sperm concentration on pregnancy rate.

Sperm Concentration in million/ml	Control group Pregnancy/no of patients	IUI group Pregnancy/no of patients
Less than 10	Nil/6	Nil/7
10-20	01/19	04/18

Discussion

At present the conflicting claims are often made regarding the efficacy and merits of different methods of assisted reproduction including IUI. Nevertheless all the clinicians working in the field of human reproduction have to admit that there is still a need for simple, inexpensive, acceptable and effective treatment for infertility. The treatment with IUI can be of great value for the patients who cannot afford highly expensive and aggressive assisted reproductive techniques (GIFT, IVF, ZIFT, SIFT etc).

In this study, we used ovarian stimulation protocol with clomiphene in all the patients. Clomiphene is a cheap drug and is readily available. Only monopercoll density gradient technique was used for sperm preparation in all the patients because it is known to be associated with higher pregnancy rates. (Shailka 1995, Pardo, 1988). We obtained 16% pregnancy rate in patients undergoing IUI for three cycles compared to 4% in control group. However the results of other workers are not consistent with this. Controlled prospective cross over study by Velde et al (1989) showed no advantage with IUI over timed coitus. Shaler et al (1995) obtained pregnancy rate of 5.4% per patient and 1.12% per cycle using clomiphene ovarian stimulation with IUI. Comhair et al (1995) obtained 17% pregnancy rate in 4 cycles. However very high pregnancy rates varying between 38% to 48% has been obtained by some workers using GnRh and hMG protocols (Check et al, 1995, Rammer & Friedrich, 1998). Comparing our results with the results obtained by others is not a easy task because of marked differences in the pregnancies obtained in their studies. This could be due to use of different sperm preparation technique and different ovarian hyperstimulation protocols. However our results are comparable with some of the workers who did not use hMG for ovarian hyperstimulation (Shalev 1995; Pratap Kumar et al 1996). The pregnancy rates were directly proportional to the

degree of oligospermia. In severe degree of oligospermia (sperm count < 10 million) no pregnancy was obtained in either of the two groups. All the pregnancies in the control group and in the IUI group occurred when count was > 10 million/ml. Shalev 1995) also did not obtain any pregnancy in patients with severe oligospermia.

It can be concluded that IUI is a simple procedure effective in treatment of moderate degree of oligospermia. An adequate trial with IUI should be given in these patients before recommending highly expensive treatment like in vitro fertilization or sperm micromanipulation.

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