Journal of India Vol. 51 No. 6 November-December 2001 Pg 120-123

Donor Insemination Using Cryopreserved Semen and Factors Affecting It's Success Rate

Himanshu Roy, Shanti Roy, Sharika Roy, Shipra Roy

Institute for Research in Human Reproduction, Kamkarbagh, Patna 800020

Summary

AIMS: To find out the success rate of donor insemination with cryopreserved semen and factors affecting it

Methods: A retrospective study of 290 patients undergoing 603 cycles of donor insemination with cryopreserved semen done between Dec. 97 and Mar. 2000. Patients were given Clomiphene citrate for follicular stimulation. Ovulation was timed with 5,000 I.U. of H.C.G. when follicle size was 18 to 21mm. Single intrauterine insemination was done about 36 hrs. later.

Result: There were 51 clinical pregnancies giving a rate of 17.58% pregnancies per patient and 8.45% pregnancy per cycle. Cumulative pregnancy rate after 5th cycle was 37.98%. The patients who conceived were younger than the patients who did not conceive. Odds ratio for getting pregnant was favourable if 35 years of age. Most of the women who did conceive, did so in the first four cycles. There were greater number of follicles in the cycle in which the patient conceived.

Conclusion: The chances of success of I.U.I. with cryopreserved donor insemination is related more to the age of women than to the duration of infertility. It is also related to no. of mature pre ovulatory follicles present. More research is needed to increase the success rate of this kind of infertility treatment. Patient usually present at a very late age and follow up is poor due to social stigma.

Introduction

Donor insemination though being a late development in contemporary gynaecological practice is not unknown in Hindu mythology. Donor insemination has been in practice in various forms. The main drawbacks in A.I.D. (Artificial Insemination with Donor semen) are the danger of S.T.D.s with fresh semen, the low success rate with insemination using intravaginal insemination or intra uterine insemination using unprepared semen. These types of practices are very rampant in small cities, semi urban and rural areas and even in few cities. Use of cryopreserved washed semen for A.I.D. answers all these problems but it is alleged to give very poor results. The various factors which can affect the success of donor insemination are age of patient (Shenfield et al 1993), duration of infertility, number of preovulatory follicles (Pittot et al 1990), method of stimulation (Hashen et al 1986), no. of motile spermatozoa inseminated (Wong et al 1985), no. of insemination per cycle (Khalifa et al 1989), method of timing of insemination, route of insemination, previous fertility of the recipient, irregularity of menstrual cycle, cervical score at time of insemination, cryopreservation technique and seasonal variations. This study has been done to find out the success rate of A.I.D. using thawed cryopreserved semen and influence of factors such as age of recipient, duration of infertility, gravidity of the women, number of cycles, dose of Clomiphene and number of follicles before giving H.C.G. (Table - I).

Table – I
Overview of Factors Affecting the Success Rate

	Conceived	Not conceived	Difference	p –value
Mean age	26.81 (+/- 0.52)	28.64 (+/- 0.35)	1.83	0.01
Duration of infertility	9 (+/- 0.59)	9.85 (+/- 0.33)	0.85	0.23
No. of Cycles	1.76 (+/- 0.14)	2.15 (+/- 0.1)	0.39	0.08
No. of Follicles	2.12	1.92	0.2	0.13
Dose of C.C. (Tab/day)	1.56	1.7	0.14	0.09

Material and Methods

290 women came for donor insemination in our institute from 1-12-1997 to 31-03-2000 and 603 cycles of I.U.I. was done using cryopreserved semen. Detailed history was taken. V.D.R.L. of both partners was done. Blood grouping and Rh typing of recipient couple was done. The only prerequisite was at least one patent tube on H.S.G. Other investigations like diagnostic laparoscopy, Ser. Prolactin and T.S.H. were done if required. Follicular stimulation was done with C.C. 50 mg from 2nd to 6th day of the cycle. Dosage of C.C. was increased in cases of inadequate follicular response. Follicular monitoring was started from the 10th day of the cycle using 5 MHz transvaginal probe. 5,000 I.U. of H.C.G. was given I.M. when the size of the leading follicle reached 18 – 24 mm. I.U.I. was done only once, 36 hours after H.C.G. injection. Written consent was taken from the couple. Cryopreserved semen was used after matching the blood group, height and colour of donor with recipient's husband and thawing and checking the number of motile spermatozoa. Insemination was done with specimens having more than 5 million motile sperms/ml. I.U.I. was done in lithotomy position without using any sedation or anaesthesia. Patients were allowed to rest for half an hour on the table and then discharged. Ampicillin capsules 250 mg was given 4 times a day for 5 days, luteal support with progesterone was given in selected cases. No limitation of activity was advised after the patients were discharged. Follow up was done with Ser H.C.G., 14 days after insemination or with T.V.S. 25 days post insemination.

Result

51 out of 290 women achieved pregnancy after donor insemination in 609 cycles. The age of patient who conceived was distributed from 19 to 36 years, maximum no. (i.e. 50%) belonging to 25-29 years of age group and the mean age was 26.81 (S.E.M. +/-0.52) years. The mean age of 239 patients who did not conceive was 28.64 (S.E .M. +/- 0.33) yr. The range of age was 20 to 42 yr. In this group too maximum numbers of patients (36.82%) were in of age group 25-29 yr. (Table – II). The difference between the mean age of patients who conceived and those who did not was 1.83 yr.with a p value of 0.01. Thus, the paients who were successful in achieving pregnancy were of significantly younger age group than the patients who failed to do so. The odds ratio for achieving pregnancy for women less than 35 years of age was 11.11 compared to women older than 35 years of age.

Table II
Age Distribution

Age group	Conceived	Not conceived
<20	1	2
20-24	9	47
25-29	25	88
30-34	15	61
35-39	1	35
>40	0	7

The mean duration of infertility was 9 (S.E.M. +/-0.59) yrs with range of 2 to 18 yr, in the patients who conceived. In the patients who did not conceive, the mean duration of infertility was slightly higher being 0.98 (S.E.M. +/- 0.33) yr, with a range of 1 to 25 yr. Thus, the difference of 0.85 yr. Between these two group is insignificant, p value being 0.23.

27 out of 51 i.e. 52.94% paients conceived in the first cycle, 27.45% in 2nd, 11.76% in 3rd, 5.88% in 4th and 1.96% (n=1) in 5th cycle of IUI with a mean of 1.76 (S.E.M. +/- 0.14) cycles for a total of 90 cycles. A mean of 2.15 (S.E.M. +/-0.1) cycles were done per patient in women who failed to get pregnant. The difference from group of patients who did conceive was 0.39 with a p value of 0.08 which is slightly short of significance.

Table – III
Relationship between age and No. of cycles to conceive

No. of cycles to conceive	Mean age
1	26.5
2	27.4
3	27.33
4	26.66
5	25

If we study the correlation of mean age to no. of cycles (Table – III) to conceive we find that patients who conceived in 1st cycle had a mean age of 26.5 yrs. While those who conceived in 2nd cycle 27.4 yrs., 3rd cycle 27.33 yrs., 4th cycle 26.66 yrs and in 5th cycle 25 yrs. There is a positive correlation (r = 0.02) between these two parameters but the strength of correlation is not strong.

On comparing the duration of infertility to no. of cycles taken to conceive (Table – IV), we find that the mean duration of infertity in patient who conceived in the 1st cycle was 9.15 yr., 2nd cycle 8.23 years, 3rd cycle 10.17 yr., 4th cycle 7.5 yrs while in the patient who conceived in 5th cycle was 8 years. Again, the correlation coefficient is positive (r = 0.02) but the strength of association was not very strong.

Table – IV
Correlation of duration of infertility to No. of cycles to conceive

No. of cycles to conceive	Mean duration of infertility
1	9.15
2	8.23
3	10.17
4	7.5
5	8

If we study the dose of Clomiphene Citrate (50 mg tab.), we find that the mean dose in patients who conceived was 1.56 tab./day (S.E.M +/- 0.08). In the same patients, the mean dose of CC in ultimate conception cycles was 1.54 tab while in earlier cycles it was 1.51 tab. In the patients who did not conceive, the mean dose was 1.74 (S.E.M +/- 0.02) tab/day.

Thus, the patients who conceived had used lesser amount of CC but the difference did not reach to significant value (p = 0.79).

The Number of follicles before giving ovulatory dose of CC in patients who conceived ranged from 1 to 5 with a mean of 2.12. The mean no. of follicles in patient who did not conceive was 1.92, the difference being 0.2 from patients who conceived, the difference between these two being insignificant (p = 0.13). If we analyse the patients who conceived we find that the mean no. of follicles in earlier cycles was 1.74 and in the final conception cycle was 2.46. The difference in these two groups was 0.006 which is a significant difference.

In ultimate conception cycle, the correlation coefficient between dose of CC and number of follicles was 0.1 and in the same patients in the earlier cycles it was 0.14. Thus, even though the dose of CC and no. of follicles were positively correlated, there was no significant difference between the correlation coefficient of the ultimate conception cycle and earlier non conception cycles in women who conceived.

251 of the total 290 patients had primary infertility and 39 were having secondary infertility. Among the patients who conceived, 93.75% had primary and 6.35% had secondary infertility. In patients who failed to conceive, 84.8% were cases of primary and 15.2% were of secondary infertility. So, the odds ratio to conceive for patients having primary infertility was 2.69.

Finally on doing the life table analysis (Table V) which takes into consideration the patients lost to follow up, the pregnancy rate per cycle for 1st, 2nd, 3rd, 4th and 5th cycle is 9.31, 8.43, 7.69, and 4.76 percent respectively with cumulative pregnancy rate being 9.31, 17.74, 25.53, 33.22 and 37.98 pregnancy per cycle after 5th cycle.

Discussion

Thus after performing 609 cycles of I.U.I. in 290 patients, 51 became pregnant, 230 were lost to follow up and 9 failed to conceive. Cumulative pregnancy rate at end of 5th cycle was 37.98% and did not increase further

Table V
Life Table Analysis

Cycle No.	No. of Patients	Conceived	Lost to follow up	Pregnancy/Cycle	Cumulative Pregnancy Rate
1	290	27	97	9.31	9.31
2	166	14	75	8.43	17.74
3.	77	6	32	7.79	25.53
4	39	3	15	7.69	33.22
5	21	1	11	4.76	37.98

Table – VI
Comparison with Other Studies

Author	No. of Patients	No. of cycles	Pregnancy Rate/Cycle	Cumulative Pregnancy Rate
Centola 1990	99	113	6	15.2
Shenfield 1993	443	2998		40
Lashen, 1999	38	89	9	21
Present, 2000	290	609	8.45	3[illegible]8

with more cycles. Pregnancy rate at the end of 5 cycles of treatment was 8.45% per cycle.

The success rate was significantly related to the age of women. Younger women had better chances of achieving pregnancy. It was also significantly related to the number of mature follicles present before giving ovulatory dose of H.C.G. Success rate was not directly related to duration of infertility or dose of C.C.

A reasonable success rate can be achieved in donor insemination programme if a standardised protocol is used for intra uterine insemination of cryopreserved semen (Table–VI). The success rate might be increased if early resort to follicular stimulation is used with the help of H.M.G. or F.S.H. but it has got the disadvantages of increasing the cost, risk of multiple pregnancies and ovarian hyperstimulation syndrome.

Due to the stigma attached to donor insemination, couples present at a very late stage when the prognosis for success might be compromised. A particular problem faced by us is large number of patients being lost to follow-up. Many patients after getting pregnant do not report back to the place where insemination was originally done. The taboo associated with donor insemination can be broken by awareness compaigns. It will also help in recruiting better donors for the programme. F.O.G.S.I. should also come out with clear guidelines and consent forms for this kind of treatment because the legislation has got a lot of grey area regarding the legality of child borne out of A.I.D.

References

1. Centola GM, Mattox JH, Raubertas RF. Fertil Steril; 54(6): 1089, 1990.
2. Khalifa Y, Redgment CJ, Tsirigotis M, Grudzinskas JG, Craft IL. Hum Reprod., 10(1):153, 1995.
3. Lashen H, Atnan M, Kennedy V. Human Reproduction; 14(8): 1983, 1999.
4. Pittrot RU, Shaker A, Dean N, Bekir JS, Campbell S, Tan SL. J Assist Reprod Genet, 13(4): 310, 1996.
5. Shenfield F, Doyle P, Valentine A, Steele SJ, Tan SL. Human Reproduction; 8(1): 60, 1993.
6. Wong AW, Ho PC, Kwan M, Ma HK. Int J Fertil. 34(1): 25, 1989.