Single versus double insemination: a retrospective audit of pregnancy rates with two treatment protocols in donor insemination


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Our objective was to evaluate the effect of a change in treatment protocols, suggested following an inspection visit by the regulatory authority, from single to double inseminations during donor insemination treatment cycles. We therefore conducted a retrospective audit of pregnancy rates in the reproductive medicine clinic of a major teaching hospital. All patients were treated for male factor infertility by donor insemination, without ovulation induction with gonadotrophins between October 1992 and December 1995. The main outcome measures were cumulative conception and live birth rates. During the study period 250 patients underwent treatment and 650 single insemination and 277 double insemination treatment cycles were undertaken. The pregnancy rate per cycle was 0.054 and 0.119 for single and double insemination respectively. After six cycles the cumulative pregnancy rates were 0.28 and 0.47 and the take-home baby rates were 0.25 and 0.37 for single and double inseminations respectively. The change in practice from single to double insemination resulted in a doubling of the pregnancy rate per treatment cycle. Cumulative pregnancy rates after two treatment cycles of double insemination were comparable with those achieved after six cycles of single insemination. These results have significant implications for both patients and purchasers.

Key words: donor insemination/outcomes/treatment protocols

Introduction

Male factor infertility affects between 25 and 50% of infertile couples (Hull et al., 1985; Howards, 1995). For some azoospermic men donor insemination (DI) is the only treatment option available. For other men with severe oligo-, terato-, or asthenozoospermia, it is frequently the only realistic option, despite recent advances in in-vitro fertilization techniques, because it is relatively affordable. For many patients even this relatively inexpensive fertility treatment is not provided by the UK National Health Service and has to be self-funded. DI is a well-established and widely used method of assisted reproduction. Despite this there is very little published research specifically directed at the best methods of performing treatment (Cooke, 1993). Variables that might affect outcome include timing of insemination, route of insemination, number of spermatozoon inseminated and the number of inseminations, as well as factors influencing the fecundity of the woman. DI treatment centres in the UK are regulated by the Human Fertility and Embryology Authority (HFEA) and are subjected to an annual inspection. Following an annual inspection it was suggested that our unit switch from single to double insemination, despite the paucity of published data to support such a switch. This has provided us with the opportunity to review the effect of a single change in practice on treatment outcome. This audit examines the effect on treatment outcome on switching from single to double insemination and discusses the financial implications of the switch.

Materials and methods

All women who had received treatment on our programme were included with the exception of those treated with gonadotrophins to induce ovulation. All patients had tubal patency confirmed by either hysterosalpingography or laparoscopy and ovulation confirmed by mid-luteal phase progesterone before commencing treatment. If required, due to anovulation, clomiphene citrate was used to induce ovulation.

Ovulation was predicted by identifying the luteinizing hormone (LH) mid-cycle surge using urinary dipsticks (Clearplan, Unipath Ltd, Bedford, UK). Testing on a daily basis was commenced 4 days before predicted ovulation, on the basis of menstrual history. For single inseminations the semen was thawed by standing it on the bench for 20–60 min. An aliquot was taken to count the number of motile spermatozoa, and if this was inadequate, another straw or ampoule would be defrosted. At least $5\times10^6$ motile spermatozoa were used per insemination. Data from the French sperm banks (CECOS) show that pregnancy rates increase with the number of motile spermatozoa inseminated: $5\times10^6$ motile spermatozoa per insemination gave pregnancy rates of 13%, while $<5\times10^6$ reduced this to 7% (Fédération CECOS, 1993). Intracervical insemination was performed using a Wallace artificial insemination catheter (Simcare Ltd, Lancing, West Sussex, UK). Intracervical insemination was performed in preference to intrauterine insemination because it is simpler, easy to perform and avoids the need for sophisticated preparation of the semen. All semen was obtained from other HFEA-licensed centres and thus met specific criteria for post-thaw motility.

Records of the patients were examined and pregnancy outcomes noted. These data are readily available as it is a statutory requirement that treatment centres notify the HFEA of treatment outcome. Other criteria examined were age, whether primary or secondary infertility, the reason for DI, whether clomiphene was used to treat anovulation, the total number of cycles performed and the number of the cycle which resulted in pregnancy.
Pregnancy rates were calculated both as crude rates per cycle and by life-table analysis. In addition, successful pregnancy rates were calculated independently of pregnancy rates as the taking home of a baby is the endpoint of most meaning to both patients and purchasers alike. Comparison of the other features of the two treatment groups was by the unpaired t-test and $\chi^2$-test.

**Results**

Over a period of 6 years 927 treatment cycles were carried out on 250 women. In the single insemination group, 158 women were treated with 650 cycles of DI. There were 36 pregnancies, resulting in 32 live births. This gave a pregnancy rate of 5.5% and a ‘take-home baby rate’ (THBR) of 4.9% per cycle. Ninety-two women were treated in the double insemination group. They received 277 cycles of treatment with 33 pregnancies (27 live births). The pregnancy rate and THBR in the double insemination group were 11.9 and 9.8% per cycle respectively. Cumulative conception rates and cumulative THBR are shown in Figure 1a and b. There were no significant differences between the groups in any other respect (Table I).

**Discussion**

This study represents the largest series of donor insemination treatments specifically comparing single and double intracervical insemination. The switch from single to double intracervical insemination resulted in a doubling of the pregnancy rate and cumulative conception rates, and THBR previously achieved over six cycles of treatment were observed following the second treatment cycle. Centola et al. (1990) in a prospective study of 99 patients over 213 treatment cycles demonstrated an increase in monthly fecundability from 0.062 to 0.21. Why they were able to achieve such a significant increase is unclear. Similarly, in their study of methods of timing insemination, Brook et al. (1994) found that reducing the number of inseminations from two to one reduced the pregnancy rate by half. On the other hand Byrd et al. (1990), in a study comparing intrauterine versus intracervical insemination, found no significant difference but it is impossible to know how many cycles they examined, as there were many comparisons made in this study, and each group had small numbers. Lincoln et al. (1994) also contend that one insemination is as efficacious as two. They carried out a retrospective analysis of 869 treatment cycles in 167 women. However, in that study there was no discussion as to the similarity or otherwise of the two groups of patients, or of the semen parameters used.

Several studies have examined pregnancy rates following single or double intrauterine insemination (IUI) per cycle. How relevant these observations are to this study is unclear, as according to one author, spermatozoa are distributed differently by IUI rather than intracervical insemination (Ripps et al., 1994). In that study it was demonstrated that greater numbers of spermatozoa reached the tubes and peritoneal cavity following IUI. In one prospective randomized study looking at single versus double IUI of partners’ fresh semen combined with ovarian stimulation, Silverberg et al. (1992) demonstrated a significant difference with pregnancy rates of 8.7 and 52.2% for single and double IUI respectively. This study only examined a small group of women ($n = 31$) undergoing 49 cycles and the pregnancy rates achieved are not representative of the results generally achieved with IUI and ovarian stimulation. On the other hand, Ransom et al. (1994), in a larger, prospective randomized study found no significant difference in pregnancy rates (11 and 14%) between single or double IUI of partners’ thawed semen in ovarian stimulation cycles. This is borne out by the retrospective study of Khalifa et al. (1995) looking at the use of cryopreserved donor semen in ovarian stimulation cycles. The pregnancy
rates they observed were 22 and 25% for single and double IUI respectively.

Ombelet et al. (1995) undertook a randomized, cross-over study of single versus double IUI of partners’ fresh semen in cycles stimulated with either clomiphene citrate or in combination with human menopausal gonadotrophins (HMG). Interestingly where clomiphene was used alone there was no difference in pregnancy rates, while in cycles where clomiphene was combined with HMG there was a significant improvement in pregnancy rates in the double IUI group. It would thus appear that there is as yet no clear consensus on the best insemination regime and a large prospective randomized study is needed to resolve this question.

Performing double insemination increased our success rates but the mechanism is not obvious. Merely increasing the total number of spermatozoa inseminated per cycle is unlikely to be a major factor as cryopreserved spermatozoa do not survive >24 h in the female reproductive tract (Hogerzeil et al., 1991). Corrigan et al. (1994) reduced the volume of semen per insemination from 0.5 to 0.25 ml in two insemination cycles without apparently affecting pregnancy rates. The scheduling of inseminations is also undoubtedly of importance but may not explain our findings. Hogerzeil et al. (1991) found that daily insemination was more effective than alternate day inseminations. The timing of insemination may be more important than the frequency, as Brook et al. (1994) concluded that it is necessary to inseminate within 24 hours of ovulation, to ensure the semen is put into good mucus. However, another group demonstrated that the highest pregnancy rates were achieved when insemination was undertaken 24–48 hours after detection of the LH surge (Matthews et al., 1979). Whichever is correct, it appears that it is not just the number of motile spermatozoa that affects pregnancy rates, but also the period of time over which they are inseminated. Assuming this to be the case, and given that we do not know exactly when the woman will ovulate, despite detecting the LH surge, two inseminations on the day of and on the day following the LH surge ensure that live spermatozoa are present in the female reproductive tract at the time of ovulation, thus maximizing the chances of conception. Even utilizing pelvic ultrasound it would not be possible to determine precisely the time of ovulation. Another variable is the method by which the LH surge is detected. In their paper looking at the use of home ovulation kits versus laboratory testing, Anderson et al. (1996) found no difference between single or double insemination but demonstrated a significant difference in pregnancy rates between home and laboratory testers (3.4 versus 12.7%). It is interesting to note that the present series of patients, who home-tested for the LH surge, achieved a pregnancy rate of 11.9%.

Provision of assisted conception on the UK National Health Service is inconsistent. For patients and purchasing authorities treatment cost and success rates are of critical importance. Estimating the current cost of a DI treatment cycle nationally to be £285, the cost per baby born, following double insemination, at current prices is therefore £2924, which is in agreement with recently published data on the cost of a DI pregnancy (Ryan and Donaldson, 1996). We estimate that single insemination would cost ~£70 less per cycle but, as a consequence of the lower cycle fecundity, the cost per live birth is £4266. The difference in cost (~£1300) would fund four additional treatment cycles. Whilst the economic implications of the change in practice can be easily identified the emotional impact on the patient is less easy to measure. Nevertheless the likelihood is that a greater chance of success and fewer failures before success are beneficial.

The switch from single to double inseminations has resulted in improved pregnancy outcomes. This change has undoubtedly proved to be beneficial and has important financial and emotional implications.

References

Received on January 16, 1997; accepted on April 21, 1997