Gamete intra-Fallopian transfer in male sub-fertility

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Between July 1985 and July 1987, GIFT was performed in 69 out of 255 patients (87 of 333 treatment cycles) treated because of male infertility. In this group a pregnancy rate of 30% per cycle was achieved, compared to an overall pregnancy rate of 35%. Indications for GIFT include long-standing infertility that has not responded to any other method of treatment, andrological sub-fertility and various forms of genital pathology with patent tubes. These results show that the pregnancy outcome after GIFT in couples with severe male infertility is significantly lower than that following GIFT in patients with long-standing infertility. The pregnancy rates seem, however, much higher than those achieved using intrauterine insemination. In this paper, the results of treating couples with male sub-fertility by GIFT are discussed in detail.

Key words: GIFT/male infertility/pregnancy rate

Introduction
Since the first reports appeared (Asch et al., 1982, 1985, 1986) on the successful treatment of non-tubal infertility using gamete intra-Fallopian transfer (GIFT), the method has achieved worldwide popularity.

In cases of idiopathic infertility (Templeton and Penney, 1982) pregnancy rates of 20-40% per treatment cycle have been reported (Braeckmans et al., 1986; DiGregorio et al., 1986; Formigli et al., 1986; Kobayashi et al., 1986; Nemiro and McGaughey, 1986; Molloy et al., 1986; Lim-Howe et al., 1987; Noss et al., 1987).

The aim of this paper is to discuss the success of GIFT in infertile couples whose infertility is due to a male factor. The lower limits of semen analysis will be discussed.

Materials and methods
As reported earlier, GIFT has been performed here since 1985 in cases of long-standing non-tubal infertility (Noss et al., 1987). These patients had previously failed to conceive despite intensive treatment over long periods. At least one healthy tube is a basic prerequisite for this method. Before inclusion in the gamete transfer programme documented evidence is required of a thorough investigation into the cause of infertility and of the treatment methods already tried. GIFT is considered only after failure of less invasive methods of treatment.

The established indications include long-standing infertility without genital pathology. 'Idiopathic infertility' (Templeton and Penney, 1982), treated corpus luteum insufficiency, treated hyperprolactinaemia and other causes, e.g. oligomenorrhoea, polycystic ovarian syndrome, all fall into this category. In our clinic, GIFT is also performed in a group of patients with an andrological factor. Male sub-fertility is defined in this programme as a sperm density of < 10^6 spermatozoa/ml and/or a motility of < 30% and/or < 30% normal forms. Patients whose semen quality is better than the lower limit defined above but not as good as the criteria defined by the World Health Organization (1987) are classified into the moderate andrological factor group. Following Kerin and Quinn (1987), these patients have been included in the first group of indications and not in the male factor group. Before entry into this programme, the spermiogram must have been repeated at least twice and the final andrological diagnosis confirmed with the therapy spermiogram.

Further indications for GIFT include certain types of genital pathology. In this category are patients with endometriosis, with peritubal adhesions which disturb the 'ovum pick-up mechanism' and patients following conservative surgery of uterus, tube or ovary (microsurgical tubal repair, microsurgery of ovarian cysts, etc.). The first group (long-standing infertility) will be mentioned briefly and used as a comparison. Attention will be focused on couples whose infertility is mainly due to an andrological factor.

Patients and treatment schedule
A total of 255 patients was treated with GIFT in 333 cycles between July 1, 1985 and July 23, 1987. The mean age of the women was 32.7 ± 4.6 years and the mean duration of infertility was 6.7 years.

Follicle stimulation was carried out using gonadotrophins. In women with normal menstrual cycles, the HMG or FSH therapy was started on day 3. Women with a standard body weight received standardized doses of HMG. On days 3 and 4, 4 ampoules of HMG or FSH were given. From day 5 onward, the dose was reduced to 2 ampoules daily. The exact stimulation schedule has been published earlier (Noss et al., 1987). Criteria for ovulation induction were a continuous rise in 17β-oestradiol (E2), an absolute E2 concentration of > 400 pg/ml and at least two follicles measuring > 15 mm in diameter.

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The laparoscopy was performed 36–38 h following the application of 10 000 IU HCG. A mean of 6.2 eggs were retrieved and 3.9 eggs were replaced per patient. Any supernumerary eggs were not inseminated in vitro for cryopreservation or embryo transfer.

The method of sperm washing is a modification of the swim-up technique described by Lopata et al. (1980). The sperm preparation is summarized in Tables I and II. During the GIFT procedure, 100 000 motile spermatozoa per egg were introduced into the tubal ampulla.

Patients received 5000 IU HCG on days 4 and 7 following the ovulation induction to support the luteal phase and 2500 IU HCG were given on day 10.

Results

In the group with long-standing infertility, 108 patients were treated over 121 cycles and 52 clinical pregnancies (43%) were achieved. The average age of these women was 31.7 years and the mean duration of infertility was 6.4 years. Eight of these pregnancies ended in spontaneous abortion (15.4%) and there were three ectopic pregnancies (3.8%). In this group, 13 multiple pregnancies occurred (25%). This is the highest incidence of multiple gestation among the three groups. The results are summarized in Table III.

Table IV defines andrological sub-fertility. If <800 000 progressively motile spermatozoa/ml were present after swim-up, GIFT was not performed. Men with a semen analysis of poorer quality than this were excluded from the GIFT programme.

In the group with male infertility, 69 patients have been treated in 87 cycles during the two years of the programme. The average age of the women was 33.3 years and duration of infertility, 6.8 years. In the majority of cases, the couples suffered from primary infertility. In the few cases of secondary infertility the former pregnancies were usually from a different partner.

The mean number of previous inseminations was 5.8. Most of these inseminations had been performed in unstimulated cycles.

From a total of 69 patients, 26 clinical pregnancies were achieved, giving a pregnancy rate of 30% per treatment cycle. Seven of these pregnancies spontaneously aborted (26.9%) and one pregnancy was an ectopic. In this group there have been no multiple pregnancies to date (Table V).

In cases with isolated oligozoospermia, nine pregnancies were achieved in 14 treatment cycles.

If these treatment cycles are subtracted from the total number of patients with male infertility in 55 couples (73 treatment cycles), 17 clinical pregnancies occurred (23.3%). In this subgroup there were four spontaneous abortions and one ectopic pregnancy (Table IV).

Table V shows the results achieved in cases of moderate andrological factor. As pointed out earlier, this group is not included in the category defined as male infertility, these patients being included in the group of long-standing infertility. In this group, patients with so-called genital pathology were also included. A moderate andrological factor was defined as a sperm count of 11–20 × 10⁹/ml and/or a motility of 31–40% and/or 31–40% normal morphological forms (Table V). The mean age of the women in this group was 32.9 years which is not
statistically different from the age of patients in the male factor group. The mean duration of infertility was 7.2 years. A total of 64 clinical pregnancies was achieved in 126 patients over 148 treatment cycles, which gives a pregnancy rate of 43.2% and is similar to the rate in patients with long-standing infertility. In our opinion, the moderate andrological factor therefore is not an important cause of infertility.

It is interesting that the rate of spontaneous abortions (14%) in this group is similar to that in the group of couples with long-standing infertility. There is a significantly higher risk of multiple gestations than in the andrological factor group.

A clinical study was performed in couples with a male factor below the exclusion criteria for GIFT (<800000 spermatozoa/ml). In such cases, tubal embryo transfer (TET) was attempted. The follicles were punctured transvaginally under ultrasound control; the insemination of all eggs obtained took place 2-6 h later. TET was carried out in the pronuclear or two-cell stage by means of laparoscopy. This procedure has been used in 20 patients over 20 treatment cycles. From a total of 90 inseminated oocytes, only one fertilization was achieved. On the day following follicle puncture the TET was carried out in this patient; a pregnancy did not occur.

Discussion

A total of 255 patients over 333 cycles was treated between July 1985 and July 1987 with a diagnosis of long-standing infertility, male infertility and genital pathology. A total of 118 clinical pregnancies was achieved, which is a pregnancy rate of >35% per treatment cycle. Therefore, GIFT is a highly efficient method of treating cases of non-tubal infertility. On the other hand, in-vitro fertilization with embryo transfer (IVF and ET) is only indicated in patients with tubal damage which is not correctable by means of microsurgery. If, in addition, a several andrological factor is present, IVF is not performed.

These results show clearly that the so-called andrological factor only becomes relevant below a sperm density of 10 x 10^6/ml and/or < 30% motility and/or < 30% morphologically normal spermatozoa. In couples where the husband has only a moderate andrological defect, pregnancy rates are equal to those in couples with long-standing infertility. Similarly, the rate of spontaneous abortion is low. On the other hand, the rate of multiple pregnancies is as high as in the group with long-standing infertility. In the group of patients with long-standing infertility, multiple pregnancies occur almost always in patients aged <35 years.

Kerin and Quinn (1987) showed in a prospective randomized study that a moderate andrological factor is not an important cause of infertility. It was also shown that intrauterine insemination in this group does not significantly increase the pregnancy rate. In normal menstruating women, the LH surge was monitored and pregnancy rates following normal intercourse and intrauterine insemination were compared. The difference in pregnancy rates per cycle between 4.5 and 8.8% was not statistically significant.

In couples with a severe andrological factor, a pregnancy rate of almost 30% was achieved using GIFT. Especially interesting is the absence of multiple pregnancies in this group. If we take our poor fertilization results in patients with <800000 spermatozoa into account, this may contribute to explaining the absence of multiple pregnancies. The rate of spontaneous abortion was 27% higher than in the group of patients with long-standing infertility. Allen et al. (1985) reported a spontaneous abortion rate of 26% in patients with pregnancies following intrauterine insemination.

This study shows that an isolated oligozoospermia is not an important cause of infertility, nine pregnancies in 14 treatment cycles proving this point.

If couples with oligozoospermia as the only andrological problem are excluded, a pregnancy rate of >20% can still be achieved in the male factor group using GIFT. This rate is higher than the 8.7% pregnancy rate after intrauterine insemination described by Kerin and Quinn (1987).

The most difficult problem is encountered in patients with very poor semen analysis (i.e. <800000 motile spermatozoa/ml after swim-up). In a few of these cases GIFT was performed, but no pregnancies occurred. The so-called 'in-vitro fertilization test' and tubal embryo transfer do not offer an alternative for these patients. It is not clear why in-vitro fertilization should offer a better chance than an in-vivo fertilization. The Fallopian tube is surely not worse than the test-tube as a site for fertilization.

Increasing experience has not led to a change of opinion, that couples with very poor semen analysis should be excluded from attempts at GIFT. Whether the injection of one spermatozoa into one egg (micromanipulation) will be able to help such couples remains to be further investigated.

References


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