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Pregnancy rates in a GIFT programme are markedly affected by semen quality

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INTRODUCTION

Gamete intrafallopian transfer (GIFT) was originally described for the treatment of infertile couples in whom the female partner has patent Fallopian tubes[1]. The value of GIFT in treating normospermic couples has been reported by other groups[2-4], although we initially had poor results when applying the technique to oligospermic couples[2].

One of the main limitations of GIFT is the inability to confirm whether fertilisation occurs *in vivo* if pregnancy fails to ensue. The experience with the oligospermic cases in our GIFT programme then led us to devise a protocol whereby fertilisation could be confirmed *in vitro* and oocytes transferred at the pronuclear stage; this was termed PROST in a preliminary communication[5].

The aims of the present study were to:

(1) Outline the poor success rate of the conventional GIFT technique in treating oligospermic couples;

(2) Evaluate the usefulness of simply increasing the number of motile spermatozoa transferred in oligospermic couples, and

(3) Determine the diagnostic and therapeutic value of PROST in the treatment of couples with a male factor present, or a suspected impairment of gamete function based on results from previous treatment cycles.

MATERIALS AND METHODS

All women in this study had follicular growth stimulated by the administration of clomiphene citrate (CC; Clomid, Merrell-Dow Pharmaceuticals Inc.), human menopausal gonadotropin (hMG; Pergonal, Serono) or a combination of CC/hMG. The response to treatment was monitored daily from

day 8 of the menstrual cycle by ultrasound and the measurement of serum estradiol-17β, progesterone and luteinising hormone using radioimmunoassay. Ovulation was triggered by the occurrence of an endogenous LH surge or the administration of 10 000 IU human chorionic gonadotropin (hCG; Primogonyl, Schering) at an appropriate time[6], and oocytes collected via laparoscopy or an ultrasonically-guided transvaginal route[7].

GIFT

Four mature oocytes were replaced per patient into the Fallopian tubes at laparoscopy, using a 50 cm, 16-gauge Teflon catheter (Cook, Australia), inserted 4 cm into each tube. In the first series of patients, 100 000 motile spermatozoa were transferred per tube, but in the second series this was increased to the maximum number recovered without compromising the quality of the preparation.

Men were classified as being moderately oligospermic ($5.1–11.9 \times 10^6$ motile spermatozoa/ml) or severely oligospermic ($\leqslant 5 \times 10^6$ motile spermatozoa/ml), according to the criteria of WHO[8].

PROST

Oocytes were inseminated with 100 000 spermatozoa *in vitro* 4–6 h after the collection. If fertilisation was then underway 18 h later, as judged by the presence of two pronuclei, the patient was taken back to the operating theatre. The pronuclear oocytes were then transferred back into the Fallopian tubes as for GIFT. PROST was carried out in seven couples where the male partner had an identifiable problem (Group A) and on five couples with a suspected impairment of gamete function based on the results from previous treatment cycles (Group B). In Group A, three men were severely oligospermic, two men moderately oligospermic and two were severely oligospermic with either IgA or both IgA and IgG in the semen. In Group B, three couples had experienced fertilisation failure in an IVF programme, one had failed fertilisation of supernumerary oocytes in a GIFT programme and one had not conceived on the AID programme despite the insemination of spermatozoa from donors of proven fertility during two treatment cycles.

RESULTS

GIFT

The pregnancy rates achieved for oligospermic couples following GIFT are given in Table 1. No pregnancies were obtained in 11 couples when the usual technique of replacing 100 000 motile spermatozoa into each Fallopian tube was used. However, once increased numbers of motile spermatozoa were replaced, six out of 21 (29%) pregnancies resulted. A mean of 0.47×10^6 motile spermatozoa were transferred in the modified technique, with a range of $0.11–0.90 \times 10^6$ motile spermatozoa. Table 2 shows that there is no difference in numbers transferred between those women who conceived and those

Table 1 Pregnancy rate for oligospermic couples in a GIFT programme, when either the regular (100 000) or modified (> 100 000) number of spermatozoa are transferred

Insemination technique	*Pregnant/total patients*	(%)
Regular	0/11	(—)
Modified	6/21	(29%)

Table 2 The number of spermatozoa transferred (geometric mean ± 1) in pregnant and non-pregnant women, using the modified GIFT technique

Patients	*Spermatozoa transferred* ($\times 10^6$)
Non-pregnant	0.42 (0.37–0.49)
Pregnant	0.46 (0.43–0.51)*

*Difference not significant

who did not. Four of the six pregnancies achieved are ongoing singleton pregnancies, one was an ectopic pregnancy and one was a blighted ovum.

PROST

The total spermatozoal concentration and percentage motility in Group A were significantly lower than in Group B ($p<0.001$), as shown in Table 3. In Group A, the overall fertilisation rate of oocytes by husband's spermatozoa (20%) was significantly lower ($\chi^2=15.67$, $p<0.001$) than that for oocytes inseminated with other donor spermatozoa (86%). Furthermore, four of seven couples had no fertilisation by husband's spermatozoa. One ongoing pregnancy was achieved.

Table 3 PROST results for couples treated with a male factor present (Group A), or a suspected impairment of gamete function based on results from previous treatment cycles (Group B)

		Group	
		A	*B*
Patients			
Total number		7	5
No. fertilisation		4	2
Semen			
Total sperm ($\times 10^6$/ml)*		3.3 (0.5–5.1)	65 (41–101)
Motility (%)*		38 (33–44)	55 (52–57)
Activity		+—++	++—+++
Oocytes			
Fertilised†	H	4/39 (20%)	5/12 (42%)
	D	6/7 (86%)	3/3 (100%)
Pregnancies		1	1

* geometric mean
† by spermatozoa from either husband (H) or donor (D)

The fertilisation rate of oocytes by husband's spermatozoa in Group B was significantly higher than for Group A ($\chi^2 = 6.60$, $p < 0.01$). Two of the five couples experienced failed fertilisation and both of these had a similar result in previous IVF–ET treatment cycles. One biochemical pregnancy was diagnosed.

DISCUSSION

The present study has shown that our initial experience with GIFT in the treatment of oligospermic infertility was disappointing, and that no pregnancies were achieved when the conventional number of spermatozoa were replaced. This is in contrast to the report of Asch *et al.*[9] who showed that one out of two women with oligospermic partners became pregnant following the transfer of four oocytes and 100 000 motile spermatozoa, although the pregnancy miscarried within the first 2 months of gestation. Evidence from our IVF programme[10], in which reduced fertilisation rates are seen with oligospermic males, suggests that the proportions of spermatozoa capable of fertilising oocytes are reduced in oligospermic couples. Accordingly, a simple modification to the GIFT procedure was implemented, by which an increased number of motile spermatozoa were replaced into the Fallopian tube, and this proved particularly successful as shown in Table 1.

The diagnostic and therapeutic value of PROST was also seen, with couples being identified in which fertilisation did not take place, and pregnancies resulting from two of the transfers following the positive verification of fertilisation. It is felt that PROST should be used to complement the GIFT technique, providing a further treatment option in which fertilisation can be confirmed *in vitro* but in which the fertilised oocyte can be allowed to develop in the natural tubal environment. Future GIFT treatment cycles could then be undertaken once the fertilising ability of the spermatozoa had been confirmed by the PROST technique.

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