MALE-FACTOR INFERTILITY

Subzonal Insemination (SUZI) or in Vitro Fertilization (IVF) in Microdroplets for the Treatment of Male-Factor Infertility

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Purpose: The results of subzonal insemination (SUZI) and in vitro fertilization with microdroplet insemination used in couples with male-factor infertility are presented.

Results: The total fertilization rate was 17.4% for SUZI (n = 89) and 49.3% for microdroplet IVF (n = 100). The fertilization rate for standard IVF (n = 510), not including any male-factor infertility and performed during the same period, was 73.2%. The "take-home baby rate" per started cycle and per embryo transfer (ET), respectively, was 10 and 17.6% for SUZI and 20 and 24.7% for microdrop IVF. For standard IVF these figures were 27 and 31.7%.

Conclusion: It was concluded that microdroplet IVF can be used with good results in cases of moderate male-factor infertility. The normal (2PN) fertilization rate with the SUZI technique was only 15.1%. However, despite the low fertilization rate, SUZI should be considered when dealing with severe male-factor infertility.

KEY WORDS: in vitro fertilization; male-factor; microdrop; micromanipulation; subzonal insemination.

INTRODUCTION

Since the birth of the first human after conception in vitro the clinical results of in vitro fertilization and embryo transfer (IVF-ET) have improved continuously and are nowadays close to normal conception. However, for infertile couples where the man has abnormal sperm (male-factor), the standard IVF procedure has not been very successful. Fertilization in vitro is usually compromised when an insufficient number of sperm is available. In some cases, the chances of fertilization can be increased by improving the methods of recovering motile sperm, such as Percoll density-gradient centrifugation (1). However, a more difficult problem arises when samples of apparently normal sperm fail to fertilize. Because of the multitude of causes responsible for IVF failure, male-factor IVF has been approached with a variety of methods. For example, cases of moderate sperm abnormalities may result in successful fertilization after Percoll preparation of the semen sample and IVF in microdroplets, whereas for severe male-factor cases with a very low sperm count, micromanipulation-assisted fertilization may be the only alternative to ensure that sperm will pass the zona pellucida of the oocyte.

In recent years, several micromanipulation-assisted fertilization techniques have been developed and applied in clinical practice, such as partial zona dissection (PZD) (2–6), subzonal insemination (SUZI) (7–12), and, most recently, intracytoplasmic sperm injection (ICSI) (13,14).

We incorporated micromanipulation-assisted fertilization into our IVF program in January 1992 for two groups of patients, couples who had undergone earlier standard IVF but with failed fertilization and couples in whom the men had poor semen quality (see Materials and Methods).
The aim of this paper is to report our experience of subzonal insemination (SUZI) and microdroplet IVF in cases of male-factor infertility and previously failed fertilization in a previous IVF attempt.

MATERIALS AND METHODS

Study Groups

The study included couples admitted to our IVF program between January 1992 and March 1993. The cycles were allocated to three treatment groups depending on the sperm quality or previously failed fertilization in a standard IVF procedure. Group I consisted of a total of 89 cycles in which subzonal insemination (SUZI) was performed. To be allocated to group I, the following criteria had to be fulfilled: (a) a sperm motility grade <3 (grading 1-4), and two of the following sperm parameters below the WHO criteria for normal sperm samples—total sperm count, percentage motile sperm, and percentage abnormal sperm; or (b) a sperm motility grade <3 and a sperm recovery after Percoll preparation of ~<0.5 million motile sperm. Sixteen cycles were recruited to the SUZI group (group I) due to the fact that earlier standard IVF procedures did not result in fertilization despite that the sperm recovery after Percoll preparation was above 0.5 million and the original sperm sample was considered normal according to the WHO criteria.

Group II consisted of 100 cycles in which microdroplet insemination was performed. To be allocated to this group the total number of sperm in the ejaculate had to be below the WHO criteria and the motility grade normal (grade 3 or 4). Thus, cycles could be allocated to microdroplet IVF if <0.5 million sperm were recovered after preparation and the motility was normal (grade 3 or 4). Group III consisted of 510 cycles with standard IVF. To be allocated to this group the sperm samples had to be normal according to the WHO criteria. The standard IVF group was included for comparison of the fertilization and pregnancy rates when no male infertility was present. The comparison group was treated during the same period as the other two groups. In group III, 72% had tubal infertility, 20% unexplained infertility (>3 years), and 8% endometriosis.

Thus, the criteria for allocating certain cases to group I or II were arbitrarily chosen because no absolute sperm parameters that clearly indicate when microinjection or microdroplet techniques should be applied are known. On the other hand, the criteria used for allocating cases to the SUZI treatment group are based on previous experience that severe male-factor cases very seldom fertilize in vitro. Before the introduction of the SUZI technique, both standard IVF and microdroplet IVF were avoided for severe male-factor cases. The reason for now accepting such cases and performing this study was the assumption that SUZI would result in fertilization.

Ovarian Stimulation and Oocyte Retrieval

Gonadotropin releasing hormone (GnRH) analogue (Buserelin, Hoechst, Stockholm, Sweden), at a dose of 300μg, was given as a nasal spray three times a day (900 μg/day) for 2 weeks from cycle day 21. If a menstrual bleeding occurred during the period of down-regulation, no estradiol (E2) measurements were performed since the bleeding was regarded as an indication of a sufficiently low E2 level to start gonadotropin stimulation. In those women who did not have menstrual bleeding during the 2 weeks of GnRH suppression, a blood sample was obtained for E2 measurement. If the E2 level was above 0.1 nmol/ml, the pituitary suppression with GnRH analogue was continued for another week and an ultrasound scan was carried out to exclude an ovarian cyst. If a cyst was observed, this was punctured using vaginal ultrasound guidance and the ovarian suppression was continued, as above, until an appropriate E2 level was achieved. Follicular development was stimulated with intramuscular injections (i.m.) of human menopausal gonadotropin (hMG; Pergonal, Laboratoires Serono S.A., Aubonne, Switzerland) or follicle stimulating hormone (FSH) purified from urofollitropin (Fertinorm HP, Laboratoires Serono S.A.) given as i.m. injections at a dose of 225 IU/day. On the ninth day of injections of gonadotropins, a vaginal ultrasound scan was performed. If there were at least three follicles with a mean diameter of at least 18 mm, 10,000 IU of human chorionic gonadotropin (hCG; Profasi, Laboratoires Serono S.A.) was injected 38 hr before oocyte retrieval. If the follicles did not meet this ultrasound criterion, a calculated growth rate of 2 mm/24 hr was used to predict the appropriate time for hCG injection.

Oocytes were retrieved under guidance of vaginal ultrasound as described earlier by our group (15). The aspirated follicular fluid was immediately passed to the laboratory located next door. Oocytes were identified in sterile plastic dishes (Sterilin Ltd,