CLINICAL ASSISTED REPRODUCTION

An Open Multicenter Study to Compare the Efficacy of Intraperitoneal Insemination and Intrauterine Insemination Following Multiple Follicular Development as Treatment for Unexplained Infertility

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Purpose: This multicenter study was carried out to compare the efficacy of intrauterine insemination (IUI) and intraperitoneal insemination (IPI) associated with multiple follicular development as treatment for unexplained infertility.

Method: A total of 205 couples completed the trial. Sixty-seven couples underwent treatment with IPI (group A) and 138 couples underwent treatment with IUI (group B).

Results: Clinical pregnancy was obtained in 23 couples in group A (pregnancy rate: 34.3%) and in 36 couples in group B (pregnancy rate: 26.1%). No significant difference was observed between group A and group B. As for the evolution of pregnancies and the incidence of twin pregnancies, no significant difference was observed between the two groups.

Conclusions: Because IUI and IPI allow us to obtain the same results and IPI is more invasive than IUI, the latter technique can be considered the method of choice and IPI should be used when IUI is difficult to perform, as in the presence of a tight cervical canal.

KEY WORDS: intraperitoneal insemination; intrauterine insemination; multicenter study; multiple follicular development; unexplained infertility.

INTRODUCTION

For many years artificial insemination has been performed mainly depositing the semen in the vagina and/or in the cervix (1). These techniques have been replaced by sperm deposition in upper tracts of the female reproductive organs (2-4). Intrauterine insemination (IUI) simply requires injection of a small amount of prepared sperm into the uterine cavity by using a thin catheter passed through the cervix (2). Otherwise, intraperitoneal insemination (IPI) is performed by injection of prepared sperm directly in the pouch of Douglas by culdocentesis (3, 4).

Since both IUI and IPI require the same sperm preparation and are performed after induction of multiple follicular development (MFD), differences in the pregnancy rate obtained with the two techniques should depend only on the site of sperm deposition.

Until now, few studies (5-9) have been performed to compare the results obtained with the two techniques. These studies considered a small sample size or few consecutive cycles for each couple, while it has been
reported that repeated cycles of induction of MFD associated with insemination allow reaching a pregnancy rate that is comparable to that with major techniques (10).

The aim of this study was to compare the efficacy of IPI with that of IUI as treatment for unexplained infertility in a multicenter trial.

MATERIALS AND METHODS

Patients

The study population was defined by the inclusion and exclusion criteria described below to select a homogeneous group of infertile patients.

The inclusion criteria were as follows:

1. Female age ≤ 40 years.
2. Duration of infertility ≥ 2 years.
3. Diagnosis of unexplained infertility [progesterone > 8 ng/ml (conversion factor to SI units is 3.180) for at least 10 days and prolactin < 15 ng/ml in the luteal phase of the cycle, postcoital test adequate, bilateral tubal patency, and no pelvic pathology; sperm analysis with a sperm concentration > 20×10^6/ml, progressive motility > 25%, total motility > 50%, and normal morphology > 50%].

The exclusion criteria were as follows.

1. Clinically relevant systemic disease.
2. Treatment for infertility in the previous 6 months.

All couples gave fully informed consent to participate in the study, for which local ethical committee approval was obtained.

Study Design

This clinical trial was an open, comparative study conducted at four centers. Each center enrolled 60 couples. All couples were assigned to one of the following two treatment groups: group A, three consecutive cycles of multiple follicular development followed by IPI; and group B, three consecutive cycles of multiple follicular development followed by IUI. The fertility centers that participated in the study could randomly assign the couples to one of the two groups or perform the techniques customarily used at that center.

Multiple Follicular Development

Multiple follicular development (MFD) was obtained by administering follicle-stimulating hormone (FSH; Metropin, Serono, Rome, Italy), starting with a daily dose of 2 ampoules from the third day of the cycle. During treatment with exogenous gonadotropins, pelvic ultrasonography, to determine the number and diameter of ovarian follicles, and blood samples for estradiol (E2) rapid assay (Medical System, Genova, Italy) were obtained every other day until the mean diameter of the dominant follicles reached 10 mm and E2 plasma levels reached 100 pg/ml (conversion factor to SI units for E2 is 3.671). Thereafter both examinations were performed daily. The dose of FSH was adjusted according to ultrasound picture and endocrine monitoring. The treatment was discontinued when E2 plasma levels reached 600–1800 pg/ml and there were at least two follicles with a mean diameter ≥ 14 mm. Human chorionic gonadotropin (hCG, Profasi; Serono, Rome, Italy; 10,000 IU) was administered 24–36 hr after the last injection of FSH.

The administration of a GnRH analogue, starting on day 1 of the menstrual cycle, was optional.

IUI or IPI was performed 30–36 hr after hCG administration.

The cycles were canceled if no follicles were found and/or the E2 level was ≤ 50 pg/ml after 50 ampoules of FSH, ovarian cysts ≥ 35 mm in diameter were found by ultrasound, or there was the risk of severe hyperstimulation syndrome.

Progesterone luteal support was not used in any of the patients.

Sperm Preparation

Sperm was prepared by the conventional layering technique for both IUI and IPI. Approximately 1.0 ml of medium was layered onto 1 ml of sperm and the specimen was incubated at 37°C for 60 min. At the end of the incubation period, the uppermost layer of the medium, containing motile spermatozoa, was collected. If the semen sample was too viscous, it was diluted 1:5 with medium and centrifuged for 5 min before performing the layering.

Insemination Techniques

IUI. The female partner was in the lithotomy position. The cervix was exposed with a vaginal speculum and cleaned with normal saline. The sperm suspension was drawn into a Kramer de la Fontaine catheter