Is intracytoplasmic morphologically selected sperm injection effective in patients with infertility related to teratozoospermia or repeated implantation failure?

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Objective: To evaluate the potential benefit of intracytoplasmic morphologically selected sperm injection (IMSI) in patients selected for either severe teratozoospermia or repeated implantation failure after conventional intracytoplasmic sperm injection (ICSI).
Design: Prospective nonrandomized observational study.
Setting: University hospital assisted reproduction unit.
Patient(s): Four hundred seventy-eight patients were enrolled to evaluate ICSI and IMSI results for two indications. The first group (T) was composed of patients with severe teratozoospermia (<10% normal spermatozoa in fresh ejaculated and selected semen, according to David classification) and no or one previous ICSI failure. In the second group (IF), patients with at least two previous failed ICSI attempts were enrolled in absence of severe male factor (>10% normal spermatozoa in fresh ejaculated semen and >20% in selected sperm).
Intervention(s): ICSI/IMSI, biologic, and clinical data collection.
Main Outcome Measure(s): Live-birth rate (LBR).
Result(s): In group T, LBR was significantly higher when IMSI procedure was used compared with ICSI (38% [50/132] vs. 20% [25/126]). However, LBR observed in group IF was not significantly different between IMSI and ICSI procedures (21% [19/90] vs. 22% [28/130]).
Conclusion(s): IMSI procedure is a valuable option for patients with severe teratozoospermia at their first or second attempts, but it does not improve pregnancy rate in patients with repeated ICSI failures in the absence of severe male factor. (Fertil Steril® 2013;100:62–8. ©2013 by American Society for Reproductive Medicine.)
Key Words: ICSI, IMSI, high-magnification spermatozoa selection, live birth rate

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Assisted reproduction technologies (ART) outcome depends on several factors, including sperm morphology. Some authors have assessed the impact of teratozoospermia on intrauterine insemination (IUI), in vitro fertilization (IVF), or intracytoplasmic sperm injection (ICSI) outcome (1–5). Although the prognostic value of teratozoospermia

on ICSI outcome remains questionable (6), it seems that head abnormalities are mainly responsible for sperm fertilization deficiency whereas flagellar abnormalities have not been shown to have any impact on fertilization (7, 8). In conventional ICSI, the choice of spermatozoon is based on its motility and its normal-looking shape under ×200 or ×400 magnification. However, minor head malformations that can negatively affect ICSI outcome (8) are not easily detected at this degree of magnification (9). Therefore, new techniques such as spermatozoa preselection by hyaluronic acid binding (10–13) or polarization microscopy (14–16) have been developed to better select optimal spermatozoa. Recently, Bartoov et al. (9) suggested performing sperm injection after selection of motile spermatozoa at a very high magnification (×6,000 to ×12,000). Publications assessing the benefit of this technique (intracytoplasmic morphologically selected sperm injection [IMSI]) reported controversial results. Some authors highlighted a positive impact of IMSI regarding clinical outcome (8, 17–19), but this conclusion was not shared by others (19–22). Many differences regarding the design and the selection of patients might explain this discrepancy between studies. Two were prospective randomized trials but included unselected patients (17, 22). Others evaluated the benefit of IMSI in patients with previous conventional ICSI implantation failure (8, 18, 19, 21) without assessing the influence of sperm abnormalities. Consequently, there is a need to identify which subgroup of patients with either severe male factor or recurrent implantation failure might benefit from the IMSI procedure.

The purpose of the present study was to evaluate the technique of sperm preselection under high magnification before classic ICSI, i.e., IMSI, in two specific subgroups: patients with repeated implantation failure after conventional ICSI in the absence of strong teratozoospermia and patients selected for male infertility related to severe teratozoospermia.

MATERIALS AND METHODS

Study Groups

In all, 478 infertile couples undergoing ART from March 2006 to December 2011 were enrolled in this feasibility study and scheduled on a voluntary basis for either IMSI or ICSI procedures as follow. All patients included in this study had an indication for ICSI. The use of IMSI was proposed to each of them. All couples provided written consents after full information on the potential benefit and risk of the IMSI procedure. It included the lack of evidence for an improved outcome owing to technical issues (time-consuming method related to sperm selection). Patient selection was based on two distinct indications. The first group (T) comprised 258 patients with severe teratozoospermia at their first or second attempt. Severe teratozoospermia was defined by the presence of <10% normal spermatozoa in fresh ejaculated semen and in selected sperm according to the David classification criteria. The second group (IF) comprised 220 couples whose infertility was related to mild male factor and who had at least two implantation failures after transfers of good-quality embryos. In this group, sperm inclusion criteria were the following: normal spermatozoa >10% in fresh ejaculated semen and >20% in selected sperm.

This study was approved by the local Ethical Committee of Jean Verdier University Hospital Center. Furthermore, each couple included in this study was asked to sign an approval consent form before enrolling in the study. Figure 1 shows the cohort flowchart of the study.

Semen Evaluation and Preparation

We used only fresh ejaculated semen. ICSI was commonly indicated for: 1) oligoasthenozoospermia as defined by the World Health Organization: i.e., sperm concentration <15 million spermatozoa/mL and/or progressive motility <30%; or 2) previous conventional IVF fertilization failure. Sperm morphology assessment was based on the David classification (23) modified by Jouannet (24), as usually performed in most French ART units, according to which all defects observed in each spermatozoon are considered together (25, 26).

Semen was prepared for microinjection with the use of a two-layer density technique (45% and 90%) of Puresperm (Nidacon International) diluted in Ferticult HEPES culture media (Fertipro). After 20 minutes of centrifugation at 300*g*, the semen pellet was washed with Ferticult HEPES media and then centrifuged for 5 minutes at 600*g*.

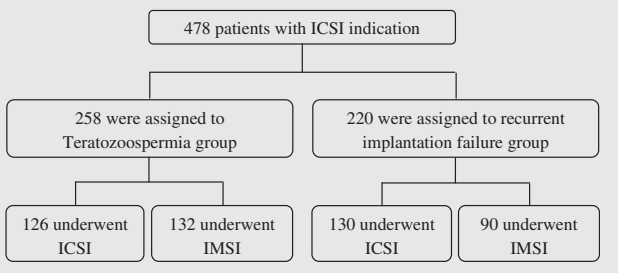
Ovarian Stimulation and Oocyte Retrieval

Ovarian stimulation was conducted according to previously described standard agonist or antagonist protocols (27, 28). Dose adjustment of gonadotrophins was performed from day 6 according to hormonal and ultrasound data. When at least three follicles measuring ≥17 mm were observed, triggering of ovulation was done by injection of 250 μg hCG (Ovitrel; Merck Serono). Transvaginal oocyte retrieval was performed 36 hours later.

ICSI and IMSI Procedures

Conventional ICSI was performed with the use of a Hoffman-contrast Nikon inverted microscope. Motile normal-looking spermatozoa were selected at ×200 magnification to be injected into a mature oocyte. In the IMSI technique, a spermatozoa preselection step was performed at ×10,000

FIGURE 1



The consort flowchart of patients through the trial.

El Khattabi. IMSI vs. ICSI in two specific indications. Fertil Steril 2013.