Isolated teratozoospermia does not affect in vitro fertilization outcome and is not an indication for intracytoplasmic sperm injection

Brian Robert Keegan, M.D., Ph.D., Sara Barton, M.D., Xavier Sanchez, B.S., Alan S. Berkeley, M.D., Lewis C. Krey, Ph.D., and Jamie Grifo, M.D., Ph.D.

NYU Fertility Center, New York University School of Medicine, New York, New York

Objective: To reevaluate clinical management of isolated teratozoospermia, in couples initiating IVF.
Design: Retrospective analysis of fertility indices in 535 cycles.
Setting: A large, university-based fertility center.
Patient(s): Consecutive couples (n = 495) who had a semen analysis using Kruger/Tyberberg strict criteria at our center within 12 months before undergoing their first and/or second IVF cycle in 2002–2004 with >2 million postwash, motile sperm on the day of egg retrieval.
Intervention(s): Eggs were fertilized either by conventional IVF or ICSI. Semen analysis and gamete/embryo manipulation was standardized in all cases.
Main Outcome Measure(s): Fertilization, fertilization failure, pregnancy, and live birth rates.
Result(s): There was no statistical difference in fertilization, fertilization failure, pregnancy, and live birth rates in the first or second IVF cycle when comparing couples with isolated teratozoospermia (<5% normal morphology) to those with a normal semen analysis. Furthermore, no improvement in these outcomes was noted when ICSI was used to treat these teratozoospermic couples.
Conclusion(s): Because isolated teratozoospermia generally does not impact on the major indices of IVF, these patients need not be subjected to the unnecessary cost and potential risks of ICSI. Future studies, however, should focus on different sperm morphologic and biochemical parameters to determine if they are important for clinical management in IVF. (Fertil Steril® 2007;88:1583–8. ©2007 by American Society for Reproductive Medicine.)

Key Words: Teratozoospermia, sperm morphology, Kruger/Tygerberg strict criteria, intracytoplasmic sperm injection (ICSI), fertilization, fertilization failure, in vitro fertilization (IVF)

Semen analysis, namely the determination of sperm count, sperm concentration, percent motile sperm, and percent normal sperm morphology, provides valuable information for clinical management and is easy and inexpensive to obtain; as such, it is routinely part of the initial evaluation of couples with a history of infertility (1). This information continues to be useful when couples approach IVF after failing less invasive methods of fertility treatment. Guidelines have been developed for IVF with low sperm count and poor motility (2); however, appropriate counseling for teratozoospermia, poor morphology, has been more controversial. In 1986, Kruger et al. (3) published a novel system to analyze sperm morphology and correlated it with the likelihood of fertilization in IVF. Subsequent publications (1, 4–8) refined and modified this system, leading to the Strict Kruger/Tygerberg criteria, which showed severely reduced fertilization rates and an increased incidence of failed fertilization in individuals with <5% normal sperm morphology (5, 9–13).

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Reprint requests: Brian Robert Keegan, M.D., Ph.D., NYU Fertility Center, New York University School of Medicine, 660 First Avenue, 5th Floor, New York, New York 10016 (FAX: 212-263-0059; E-mail: brian.keegan@med.nyu.edu).

Laboratory techniques such as high insemination concentrations of sperm (14) and intracytoplasmic sperm injection (ICSI) (15) were developed to treat various causes of poor fertilization in IVF; thus, they were investigated as potential treatments for teratozoospermia. Several studies validated the use of these procedures by showing an improvement in fertilization rate and a decrease in fertilization failure rate (16–18). Thus, at the time of their publication, these investigators recommended high insemination concentrations (19–22) and subsequently ICSI (16, 23, 24) for the treatment of teratozoospermia in IVF. Other studies, however, suggested that the difference in fertilization rate was small, and that there was no impact on other prognostic end points such as pregnancy and live birth rates (25–27). Therefore, ambiguity remained about the optimal clinical management of these patients.

In addition to conflicting data surrounding the use of ICSI in teratozoospermia, there are other factors to consider. Two obvious issues are ICSI's cost (28) and invasiveness to the gametes (23). Moreover, recent studies have reported an increase in sex chromosomal anomalies in ICSI offspring, although they are exceedingly rare (29). After considering all of these factors, it has been suggested that ICSI be used judiciously, and restricted to cases where success at conventional IVF insemination seems unlikely or has already failed (28).

Concurrent with the development of this micromanipulation technique, there also has been other changes in IVF protocols, including those used for ovarian stimulation, egg and embryo manipulation, semen preparation, and embryo culture, which have led to an improvement in IVF outcomes (30, 31). Considering these advances and the uncertain role that morphology plays in IVF, we felt it was critical to reevaluate the affects of isolated teratozoospermia on IVF. In addition, recognizing the potential concerns regarding ICSI, we felt it was necessary to determine if there was any therapeutic benefit to this procedure. These clinical questions were evaluated with a retrospective analysis of recently completed IVF cycles at our fertility center.

MATERIALS AND METHODS

Experimental Design

The New York University School of Medicine institutional review board approved this retrospective study (IRB #H-05162). Couples (n = 495) were selected who experienced their first and/or second IVF cycle between January 1, 2002 and December 21, 2004, with at least one oocyte retrieved per cycle, semen analysis performed at our facility within 12 months of IVF date, and >2 million motile, postwash sperm on the day of IVF (motility counts below this are uniformly referred for ICSI, and therefore, were not eligible for this study).

A total of 535 consecutive IVF cycles were evaluated that met the above selection criteria; in 518 of these cycles conventional insemination or ICSI was performed, whereas in the remaining 17 cycles both insemination procedures were used to inseminate the eggs. The 518 cycles were divided into the following four groups: group 1 (n = 214): normal sperm morphology (≥5% normal sperm morphology at semen analysis with >2 million motile postwash sperm) and conventional insemination; group 2 (n = 240): isolated teratozoospermia (<5% normal sperm morphology at semen analysis with >2 million motile postwash sperm) and conventional insemination; group 3 (n = 17): normal sperm morphology (≥5% normal sperm morphology at semen analysis with >2 million motile postwash sperm) and ICSI; and group 4 (n = 47): isolated teratozoospermia (<5% normal sperm morphology at semen analysis with >2 million motile postwash sperm) and ICSI. Within these groups the following outcomes were analyzed: fertilization, fertilization failure, clinical pregnancy, and live birth rates, as well as the average female age, average male age, percent with previous cycles, mean number of embryos retrieved, and percent of day 5 transfers. Fertilization rate was defined as the number of zygotes with two pronuclei and two polar bodies 16–18 hours after insemination divided by the number of oocytes retrieved. A fertilization failure was defined as no fertilized eggs in a cycle when at least one oocyte was retrieved. A clinical pregnancy was defined as the presence of an intrauterine gestational sac(s) with fetal heartbeat activity at 28–35 days postretrieval.

Statistical Analysis

The rates of fertilization, fertilization failure, pregnancy, live birth, previous cycle, and embryo transfer date were compared between groups using chi-square analyses. Female age, male age, and the number of embryos generated per cycle were compared between groups using Student's *t* test. Power and statistical significance were calculated using standard statistical methods for sample size (www.statpages.org).

Sperm/Semen Analysis and Manipulation

Semen samples were collected by masturbation 3–5 days after the last ejaculation on the days of semen analysis and egg retrieval for IVF. In both procedures semen volume, concentration, and motility were determined using standard World Health Organization (1) criteria. After semen samples were allowed to liquefy for at least 30 minutes before analysis, the ejaculate volume was determined by pipeting and sperm concentration and motility were determined by placing a 5-μL drop of the sample on a Makler chamber (MidAtlantic Diagnostics, Inc., Mount Laurel, NJ). In this standardized procedure, at least 200 sperm were counted on two separate chambers and the results were averaged. When processing the semen specimens for IVF these calculations were repeated after the motile sperm concentration was enriched using Isolate gradient (Irvine Scientific, Santa Ana, CA) or swim-up protocols. Each Makler chamber was cleaned and examined daily for physical damage; low (<20 million/mL) and normal (>20 million/mL) washed-sperm control specimens were prepared in-house and tested daily before clinical use.

Sperm morphology was assessed in the initial semen analysis using the Kruger/Tygerberg Strict Criteria as outlined by the World Health Organization (1) in 1999. Briefly, 10–20 μL of semen depending on the total count was placed on a precleaned slide and stained using the Diff Quik staining protocol (Dade Diagnostics, Miami, FL). Two technologists analyzed at least 200 sperm cells under 1,000× oil immersion magnification and the values were averaged. Spermatozoa were determined to be normal if they had oval shaped heads (4–5.5 μm long × 2.5–3.5 μm wide), cylindrical midpieces (7–8 μm long × 1 μm wide), intact uncoiled tails (45–50 μm long × 0.5 μm wide), narrow terminal segments (4–6 μm), and no duplicate segments. Quality control procedures for morphology assessment included a weekly determination of intertechnician coefficient of variation of <10% using discarded semen samples. In addition, the stain was checked daily for crossover contamination and changed weekly.

IVF Protocols

To stimulate production of multiple follicles, most patients received either purified and/or recombinant gonadotropins; GnRH agonists and/or antagonists were used to suppress endogenous gonadotropin secretion. Patients who had three or more follicles that were at least 17 mm in diameter were