Outcome of Pregnancies Derived from Assisted Reproductive Technologies: IVF versus ICSI

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Purpose: To compare the course and outcome of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) pregnancies.

Methods: A retrospective study was conducted in a university-affiliated IVF unit with 200 patients who conceived in 1996–1997, 100 with ICSI and 100 with IVF. Data were retrieved from our prospectively created computerized database. In addition, all patients were interviewed by telephone, and the interviewing physician completed a detailed questionnaire. Findings for the IVF and ICSI pregnancies were compared. The main outcome measures were maternal age, implantation rate, early pregnancy complications, clinical abortion rate, multiple pregnancy delivery rate, gestational age at delivery, mode of delivery, and birth weight.

Results: In all, 238 children were born, including 104 singleton infants (45 IVF, 59 ICSI), 49 twin pairs (28 IVF, 21 ICSI), and 12 triplet sets (3 IVF, 9 ICSI). Statistically significant differences between the ICSI and IVF groups were noted for maternal age (31.3 ± 4.4 vs. 33.4 ± 4.8 , respectively, $P < 0.005$) and clinical abortion rate (11% vs. 24%, respectively, $P < 0.05$).

Conclusions: ICSI pregnancies in our series were characterized by a lower clinical abortion rate than IVF pregnancies, probably because of the mean younger age of the ICSI group.

KEY WORDS: Intracytoplasmic sperm injection; in vitro fertilization; pregnancy outcome; abortion.

INTRODUCTION

In recent years, intracytoplasmic sperm injection (ICSI) has gained tremendous popularity in assisted reproductive technology (ART) units throughout the

world (1, 2). The ICSI procedure currently is being used to solve two main problems: severe male factor infertility and fertilization failure or low fertilization in previous standard in vitro fertilization (IVF) procedures. However, because ICSI involves no natural selection of sperm and circumvents most of the known fertilization stages, concerns have been raised regarding its effect on embryo quality and pregnancy outcome. The aim of this study was to compare the course and outcome of IVF- and ICSI- derived pregnancies achieved within the same time frame in our ART unit.

MATERIALS AND METHODS

Data on patients in our ART unit (both IVF and ICSI cycles) who achieved a clinical pregnancy during the years 1996–1997 were retrieved from our computerized database. All patients also were interviewed by telephone, and the interviewing physician completed a detailed questionnaire. The main outcome measures were maternal age, implantation rate, early pregnancy complications, clinical abortion rate, multiple pregnancy delivery rate, gestational age at delivery, mode of delivery, and birth weight. Findings for the IVF and ICSI pregnancies were compared.

Gestational age was calculated from the day of oocyte retrieval, defined as two completed gestational weeks. Clinical pregnancy was defined as the presence of a gestational sac by transvaginal ultrasonography in association with rising β -human chorionic gonadotropin (hCG) levels. A clinical abortion was defined as an abortion occurring after the detection of an intrauterine sac on transvaginal ultrasound examination. Cases in which both ICSI and standard IVF were applied on sibling oocytes during the same cycle and both kinds of embryos were transferred were excluded from the current analysis, as were frozen–thawed embryo cycles and donor egg cycles.

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The ovarian stimulation protocol, ultrasound, and hormonal surveillance methods, hCG timing, oocyte retrieval technique, and embryo culture methods were similar in both the IVF and ICSI cycles. These details and the laboratory technique for standard IVF and our methodology for ICSI have all been previously described (3). ICSI was carried out whenever the couple fulfilled one of the following criteria: (i) poor semen characteristics (< 5 million total motile sperm in the ejaculate before processing); or (ii) $< 30\%$ fertilization rate in a previous standard IVF cycle. Cases of ICSI using epididymal or testicular spermatozoa were excluded. Embryo morphology was graded before embryo transfer. Cleaving embryos were selected for transfer or freezing on the basis of their morphological score. All embryos were left in culture until the embryo transfer day.

Written informed consent was obtained from all couples before treatment. Values are given as mean $\pm$ SD. For statistical analysis, Student's *t*-test and χ^2 analysis were used as appropriate.

RESULTS

Two hundred consecutive pregnancies were considered for the current analysis, 100 IVF and 100 ICSI (Table I). In all, 238 children were born, including 104 singleton infants (45 IVF, 59 ICSI), 49 twin pairs (28 IVF, 21 ICSI), and 12 triplet sets (3 IVF, 9 ICSI). The women who underwent ICSI were significantly younger than those in the IVF group (31.3 ± 4.4 vs. 33.4 ± 4.8 years, respectively, $P < 0.005$). Two extrauterine pregnancies and one heterotopic pregnancy occurred in the IVF group and one heterotopic pregnancy in the ICSI group. Interestingly, a lower clinical abortion rate was detected for the ICSI- than for the IVF-derived pregnancies (11% vs. 24%, $P < 0.05$, respectively). There was no difference in the

implantation rate between the groups in those pregnancies that ended with clinical abortions (1.1 ± 0.4 vs. 1.1 ± 0.5 , respectively).

The mean singleton term birth weight was 3188 ± 464 g for the IVF group and 3300 ± 350 g for the ICSI group. The average gestational age at delivery for the twin pairs was 35.2 ± 3.2 weeks in the IVF group and 34.6 ± 4.2 weeks in the ICSI group; mean twin birth weight was 2231 ± 525 and 2034 ± 612 g, respectively. The cesarean section rate were high in both groups (45% and 39%, respectively). None of these differences were statistically significant.

DISCUSSION

Although an earlier report demonstrated that sperm microinjection does not increase the incidence of embryos with chromosomal abnormalities (4), it is well known that the frequency of chromosomal abnormalities is high in preimplantation embryos, and that most abnormal embryos are lost before pregnancy is clinically recognized (5). During the ICSI procedure the oocytes are exposed to hyaluronidase, intense light, and fluctuations in temperature, and they are subjected to the creation of an artificial breach in the zona pellucida and oolemma, which may increase the risk of toxin and debris introduction into the perivitelline space and ooplasm. All these factors can affect the ultimate outcome of ICSI-derived pregnancies.

At the same time, the present study indicates that if all these barricades are bypassed successfully, ICSI pregnancies are associated with a significantly lower clinical abortion rate than IVF pregnancies (11% vs. 24%, $P < 0.05$). This finding probably can be attributed to the younger age of the ICSI group and especially the lack of other infertility cofactors (such as uterine malformations, prior operative procedures that involved cervical dilatation, and a history of pelvic infection) in the vast majority of them.

It should be noted, however, that earlier studies have found conflicting results. Our team previously has demonstrated that IVF embryos are characterized by a higher morphological score than ICSI embryos, leading to a higher clinical pregnancy rate and a lower preclinical (chemical) abortion rate (3). We suggested that these results could be explained by a high incidence of abnormal embryos resulting from the "forced fertilization" nature of the ICSI procedure. In ICSI, fertilization can be achieved with the aid of spermatozoa that never could have been used before in infertility treatments and abnormal oocytes might be fertilized.

Table I. Pertinent Clinical Data for the IVF and ICSI Pregnancies

	IVF (<i>n</i> = 100)	ICSI (<i>n</i> = 100)	<i>P</i> value
Maternal age (years) ^a	33.4 ± 4.8	31.3 ± 4.4	$<0.005^*$
Abortion rate (%)	24	11	$<0.05^{**}$
No. of singleton deliveries	45	59	NS ^{**}
No. of twin deliveries	28	21	NS ^{**}
No. of triplet deliveries	3	9	NS ^{**}

^a Values for maternal age are mean $\pm$ SD.

* Student's *t* test.

** χ^2 test.

Similar clinical abortion rates were reported by Palermo et al. (6), Govaerts and colleagues (7) (11% in ICSI and 15% in IVF), as well as by Coulam et al. (8) (18% and 21%, respectively). Govaerts et al. (7) also noted a significantly higher mean birth weight (2488 vs. 2281 g) and gestational age at birth (36.5 vs. 35.5 weeks, respectively) in the twin pregnancies in the ICSI group, whereas we found no such difference. These discrepancies may imply that infertile populations differ in different countries and that large-cohort studies (or meta-analyses) are needed to answer these questions.

In conclusion, according to our findings, ICSI-derived pregnancies are characterized by a lower clinical abortion rate than IVF-derived pregnancies. This finding is probably related mainly to the lack of other fertility problems in the majority of these women.

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