Use of suboptimal sperm increases the risk of aneuploidy of the sex chromosomes in preimplantation blastocyst embryos

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Objective: To compare autosomal and sex chromosome aneuploidy rates of embryos derived from sperm with abnormal and normal parameters.

Design: Retrospective cohort study.

Setting: Assisted reproduction center.

Patient(s): Three thousand eight hundred thirty-five embryos generated from 629 couples undergoing IVF.

Intervention(s): None.

Main Outcome Measure(s): Incidence of aneuploidy in the trophectoderm of blastocyst embryos derived from standard IVF embryos and intracytoplasmic (ICSI) males with normal and oligozoospermic semen samples, in couples with donor eggs (mean maternal age, 25.0 years) and their own eggs (mean maternal age, 35.4 years).

Result(s): The rate of sex chromosome aneuploidy was significantly (around threefold) higher in the oligozoospermic group compared with in both control groups (standard vs. ICSI insemination). This applied whether donor (young) or own (older) eggs were used. Significant differences were seen in the oligozoospermic samples for autosomes 1, 2, 11 (own eggs), and 18 (donor eggs) compared with both control groups; however, no significant difference was seen between each of the treatment groups for the overall rate of autosomal aneuploidy. No significant differences were seen between the two control groups (normozoospermic males, standard vs. ICSI insemination) in either of the egg group types for any chromosome pairs.

Conclusion(s): Severe male factor infertility is associated with a significant increase in the occurrence of sex chromosome abnormalities in blastocyst embryos compared with in embryos derived from normal semen samples. Aneuploidy rates in embryos derived from sperm with normal parameters were not significantly different whether ICSI or standard insemination was used to achieve fertilization. These results highlight severe male factor infertility as a possible referral category for preimplantation comprehensive chromosomal screening. (Fertil Steril® 2015;104:866–72. ©2015 by American Society for Reproductive Medicine.)

Key Words: Sex chromosome, aneuploidy, ICSI, autosome

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/coatesa-male-infertility-embryo-aneuploidy/

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Studies have shown evidence of a significantly higher proportion of aneuploid sperm in the ejaculates of men with male factor infertility when compared with normal controls (1, 2). A review of the literature by Tempest and Griffin demonstrated a clear correlation between suboptimal semen parameters, principally oligozoospermia, and increased sperm aneuploidy rates for most chromosomes examined, although it
was noted that patient parameters were not always clearly defined (3). Sperm of poor quality are frequently unable to penetrate an egg, either in vivo or through standard insemination techniques in vitro, possibly leading to failure of fertilization. To overcome this barrier to conception, intracytoplasmic sperm injection (ICSI) was developed and has found widespread, worldwide use as the treatment of choice for male factor infertility (4, 5). Partly because of the increase in sperm aneuploidy associated with some infertile men, the rates of aneuploidy in the products of conception (POC) of nonviable pregnancies and the prevalence of birth defects and achievement of developmental milestones in children conceived through assisted reproduction have been studied. This has enabled the comparison of the outcomes of standard IVF, ICSI, and natural conception, and the results have been relatively reassuring (6–9). To date, however, there has not been a published study asking whether rates of aneuploidy in preimplantation blastocyst embryos are elevated in ICSI cases derived from oligozoospermic and/or normal sperm samples, controlling for any possible detrimental effect that the ICSI process itself may have on occurrence of aneuploidy.

In addition to the risk of perpetuating aneuploidy through the injection of disomic sperm, the technique of ICSI has, it has been suggested, the potential to be detrimental to embryo development in several ways (10). ICSI has been shown to compromise sperm nuclear decondensation, possibly leading to aneuploidy in the embryo (11). The ICSI process has the potential to disrupt the oocyte spindle apparatus when the ICSI needle passes through the oolemma into the center of the oocyte, possibly leading to abnormal patterns of chromosome segregation (12). Finally, the oocyte may be handled outside of the incubator for a longer period of time during ICSI compared with standard insemination, that is, during cumulus cell removal with hyaluronidase and injection of sperm. Slight temperature and pH changes during micromanipulation may increase the possibility of stress-induced aneuploidy. All of these interventions associated with the ICSI technique have the potential to impair chromosome segregation in the egg and subsequently the cleaving embryo.

If the genetic component of sperm is the predominant risk factor for aneuploidy in the blastocyst embryo, one may expect that aneuploidy would be the most prevalent in embryos derived from the sperm of more severely oligozoospermic males (as the potential for sperm aneuploidy appears to be directly correlated with the severity of abnormalities in semen parameters). Conversely, if the ICSI process itself induces aneuploidy, one would expect that all ICSI treatments would show an increase in embryo aneuploidy as compared with standard insemination cycles, regardless of sperm quality.

Testing the ploidy status of preimplantation embryos via trophectoderm (TE) biopsy and comprehensive chromosomal screening (CCS) is now a routine practice in many IVF centers throughout the world. Pregnancy rates per cycle are increased in older female age groups by identifying chromosomally abnormal embryos and selecting known euploid embryos for uterine transfer (13–15). The objective of this study was therefore to test the hypothesis that aneuploidy frequency (sex chromosome or autosome) in human embryos increases, either as a result of injection of suboptimal sperm or as a result of the ICSI procedure itself.

**MATERIALS AND METHODS**

Between August 2010 and March 2015, 629 couples underwent IVF using either ICSI or standard insemination. A total of 3,835 embryos resulting from these cycles were tested for aneuploidy by TE biopsy followed by CCS using array comparative genomic hybridization (aCGH) in a single tertiary fertility center.

All male patients underwent semen analysis before the IVF cycle commenced and again on the day of the oocyte retrieval to determine whether ICSI or standard insemination would be used to achieve fertilization. The parameters measured included sperm density/ml, forward progression, speed of progression, percent normal forms (16), and anti-sperm antibody binding. Patient history was also taken into account when deciding which method of insemination was to be used on the retrieval day. Reasons for performing ICSI on the day of egg collection were as follows: decreased sperm concentration, motility, and/or morphology; use of frozen sperm; many years of unexplained infertility without a pregnancy; or previous poor fertilization using standard insemination in an earlier IVF cycle. Those included in the study had their embryos biopsied at the blastocyst stage at their request to assess the chromosomal status before transfer to the uterus. Indications for CCS included advanced reproductive age of the female patient, history of repeated pregnancy losses, history of failed IVF cycles, history of previous aneuploid pregnancy, diminished ovarian reserve, or patient request.

Controlled ovarian stimulation protocols for these IVF cycles were carried out as described elsewhere (17). On completion of the retrieval procedure, oocytes were placed in Quinns Advantage Fertilization Medium (Origio) supplemented with 5% human serum albumin (HSA; Irvine Scientific) under oil (Ovoil, Vitrolife), and ICSI or standard insemination was carried out 4 hours after retrieval.

For standard insemination, 15,000 sperm were placed with each cumulus-oocyte complex on the day of oocyte retrieval. The ICSI procedure was performed on all mature eggs as described elsewhere (12). Once all eggs had been either inseminated or injected, they were returned to the incubator for overnight culture. All embryos were moved to Quinns Advantage Cleavage Medium (Sage, Origio) supplemented with 10% HSA from days 1 to 3 and subsequently moved to Quinns Advantage Blastocyst Medium (Sage, Origio) supplemented with 10% HSA from days 3 to 6.

All embryos to be biopsied were hatched on day 3 postretrieval with a Hamilton Thorne laser by making a small opening and then left in culture until day 5 or 6 of development. Embryos were considered suitable for biopsy on day 5 when at least 10% of the TE was protruding from the breach in the zona pellucida made on day 3. All embryos that had not fully expanded by day 5 were cultured until day 6 and biopsied before noon if they had reached full expansion by that time. Embryos were only biopsied if there was a visible inner cell mass (ICM) and multicelled TE protruding from
the zona pellucida. Embryos that grew to an expanded blasto-
cyst stage had 3–8 TE cells excised using a Hamilton Thorne
laser with an 800-μm pulse. The biopsied cells were placed in
nonstick wash buffer in microfuge tubes and labeled accord-
ingly with an appropriate embryo number. Biopsied embryos
were then vitrified and stored for future use. Biopsied cells
were sent to Reprogenetics Laboratory Los Angeles for anal-
ysis using aCGH (Illumina). Aneuploidy in embryos was
determined through the use of BlueFuseMulti software (Illu-
mina) for ratio analysis in which per-chromosome Cy3/Cy5
ratios were interpreted as chromosome gains or losses.
Smoothing algorithms during data analysis incorporated the
generation of green lines drawn automatically based on the
result of the aneuploidy calling algorithm and classified
each whole chromosome as either “copy number neutral” or
showing evidence of gain or loss by estimating the probability
of each outcome. The software then automatically selected the
most likely status for each chromosome through the genera-
tion of a horizontal green line. When a chromosome was
determined to be copy number neutral, the green line was
drawn across the chromosome at zero on the log2 ratio scale.
Where a chromosome was determined to have an abnormal
copy number, the green line was drawn across the chromo-
some at the level of the median log2 ratio of the set of probes
that map to the chromosome. Euploid embryos were kept in
storage for future use.

For the purposes of testing the hypothesis that it is the ef-
fect of compromised semen parameters that increases the
aneuploidy rate, patients were divided into two treatment
groups: the first underwent ICSI with normal semen parame-
ters (>19 × 106/mL, >30% gross normal morphology, >30%
motility; 16). The second underwent ICSI, but male patients
were diagnosed with severe oligozoospermia (<6 × 106/mL
sperm).

Any possible effect of the ICSI procedure itself was con-
rolled for by comparing rates of aneuploidy in embryos
derived from the control group using standard insemination
with normal sperm (15,000 motile sperm placed with intact
cumulus-oocyte complexes on the day of retrieval) and ICSI
with normal sperm. Finally, to control for maternal age, the
groups were further subdivided into “own eggs” and “donor
groups.” Within each group the mean maternal age was near
identical (that is, 35.5, 35.3 and 35.3 years, respectively
within the own eggs group, and 24.9, 24.9 and 25.0, respec-
tively within the donor eggs group). Thus, six groups were
examined in total, and differences in aneuploidy rates for
these chromosomes in turn, the aneuploidy levels in the oligo-
zoospermic males, namely, chromosomes 1, 2, and
11 (own eggs) and chromosome 18 (donor eggs). For each of
these chromosomes in turn, the aneuploidy levels in the oligo-
zoospermic samples were chromosome 1, 7% (compared
with 2.3% and 1.5%; P = .01); chromosome 2, 6.0% (compared
with 2.0% and 1.7%; P = .006); chromosome 11, 4.4%
(compared with 0.8% and 1.8%; P = .03); and chromosome
18, 4.7% (compared with 1.0% and 1.3%; P = .02). Other au-
tosomes showed greater aneuploidy levels in ICSI males but not
at the level of statistical significance (threshold P < .05).

DISCUSSION
The current study is, to the best of our knowledge, the first to
determine aneuploidy rates of all 23 chromosome pairs assess-
ing the effect of sperm quality and method of insemination in
resultant blastocyst-stage embryos. By subdividing our patient
population, we determined that severe male factor infertility
appears to be a risk factor for increased sex chromosome aneu-
ploidy. Given that sex chromosome aneuploidy was signifi-
cantly elevated in both the own egg and donor egg popula-
tions, we provide evidence that the observed effect is
independent of maternal age. Moreover, as no significant
increase was seen for any of the chromosomes in either of
the ICSI with normal sperm groups, the most plausible expla-
nation for our observations was suboptimal genetic quality
of the sperm (probably increased sperm aneuploidy) rather
than any effect of the procedure itself. In humans, the majority
results are summarized in Table 1. Each chromosome pair
is considered individually, and the data set is broken down
into couples who used their own eggs and couples who used
donor eggs. In both groups, standard IVF is compared with
ICSI with normal semen parameters and ICSI with oligozo-
spermia. For both the own eggs and donor eggs categories,
the mean maternal age was near identical within the three
groups, that is, 35.5, 35.3, and 35.3, respectively, for the group
using their own eggs, and 24.9, 25.0, and 25.0 for the group
using donor eggs. The greatest number of cycles used ICSI
with normal sperm (262 and 222, respectively), with standard
insemination the next most common (77 and 25 cycles,
respectively) and ICSI with oligozoospermia constituting 31
and 12 cycles, respectively. Corresponding numbers of em-
byros ranged from 85 to 1,743 depending on the group.
When standard insemination was compared with ICSI with
normal sperm, no significant difference was seen, either
when considering overall aneuploidy, overall autosomal
aneuploidy, sex chromosome aneuploidy, or aneuploidy of
any individual chromosome. In both the own egg and donor
egg groups, the sex chromosome aneuploidy was significantly
greater in the oligospermic patient group than in the other two
groups. That is, it was 6.1% in the oligozoospermic males
compared with 2.1% and 1.7% in the two normal semen cate-
gories (P = .006) for the group using their own eggs and 5.9% in
the oligozoospermic males compared with 2.0% and 1.4% in
the two normal semen categories (P = .04) for the group using
donor eggs. Severe oligozoospermia thus perpetuates a three-
fold increase in TE aneuploidy regardless of maternal age.

There was no significant increase in overall aneuploidy as
a result of ICSI with oligozoospermic males, nor in the overall
rate of autosomal aneuploidy. Three individual autosomes,
however, did show significantly increased levels of aneuploidy
in the oligozoospermic males, namely, chromosomes 1, 2, and
11 (own eggs) and chromosome 18 (donor eggs). For each of
these chromosomes in turn, the aneuploidy levels in the oligo-
zoospermic samples were chromosome 1, 7% (compared
with 2.3% and 1.5%; P = .01); chromosome 2, 6.0% (compared
with 2.0% and 1.7%; P = .006); chromosome 11, 4.4%
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18, 4.7% (compared with 1.0% and 1.3%; P = .02). Other au-
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at the level of statistical significance (threshold P < .05).

RESULTS
Our results are summarized in Table 1. Each chromosome pair
is considered individually, and the data set is broken down

independent of maternal age. Moreover, as no signifi-
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within the own eggs group, and 24.9, 24.9 and 25.0, respec-
tively within the donor eggs group). Thus, six groups were
examined in total, and differences in aneuploidy rates for
each chromosome pair were evaluated by Kruskal–Wallis
one-way analysis of variance on ranks, followed by
multiple-comparison tests to stratify significant treatment
differences if indicated (significance set at P ≤ .05).

Institutional Review Board approval was obtained for re-
view of patient charts and laboratory data for this study. The
study was also approved by the University of Kent Local
Research and Ethics Committee.
### Table 1

Patient data followed by collective and individual levels of aneuploidy (including percentages) for each patient group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group using their own eggs</th>
<th>Group using donor eggs</th>
<th>Total number</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Standard IVF</td>
<td>ICSI, normal sperm</td>
<td>ICSI oligozoospermia</td>
<td>Standard IVF</td>
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<tr>
<td>Mean maternal age (y)</td>
<td>35.5</td>
<td>35.3</td>
<td>35.3</td>
<td>24.9</td>
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<tr>
<td>No. of cycles</td>
<td>77</td>
<td>262</td>
<td>31</td>
<td>25</td>
</tr>
<tr>
<td>No. of embryos</td>
<td>385</td>
<td>1,300</td>
<td>114</td>
<td>208</td>
</tr>
<tr>
<td>Embryos for biopsy, mean</td>
<td>5</td>
<td>5</td>
<td>3.7</td>
<td>8</td>
</tr>
<tr>
<td>Total aneuploidy (%/embryo)</td>
<td>158 (41)</td>
<td>477 (37)</td>
<td>53 (46)</td>
<td>44 (21)</td>
</tr>
<tr>
<td>Total with autosomal aneuploidy (%/embryo)</td>
<td>155 (40)</td>
<td>466 (39)</td>
<td>51 (45)</td>
<td>42 (20)</td>
</tr>
<tr>
<td>Total (%) with sex chromosome aneuploidy</td>
<td>8 (2.1)</td>
<td>22 (1.6)</td>
<td>7 (6.1)*</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Individual aneuploidies</td>
<td>XXX</td>
<td>XO x12</td>
<td>XO x5</td>
<td>XO x2</td>
</tr>
<tr>
<td></td>
<td>OY x3</td>
<td>OYY</td>
<td>XY</td>
<td>OY x2</td>
</tr>
<tr>
<td></td>
<td>OYY</td>
<td>XXX x4</td>
<td>XXX</td>
<td>XXX x9</td>
</tr>
<tr>
<td></td>
<td>XYY</td>
<td>XXX x2</td>
<td>XYY x2</td>
<td>NS</td>
</tr>
<tr>
<td>Individual autosomal aneuploidies %</td>
<td>1</td>
<td>2.3</td>
<td>1.5</td>
<td>7.0*</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2.0</td>
<td>1.7</td>
<td>6.0*</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1.6</td>
<td>1.5</td>
<td>0.9</td>
</tr>
<tr>
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<td>4</td>
<td>1.0</td>
<td>1.9</td>
<td>4.4</td>
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<tr>
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<td>1.8</td>
<td>4.4*</td>
</tr>
<tr>
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<td>4.9</td>
<td>3.9</td>
<td>2.6</td>
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<td>7.5</td>
<td>7.0</td>
<td>5.3</td>
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<td>17</td>
<td>1.6</td>
<td>1.2</td>
<td>1.8</td>
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<td>22</td>
<td>3.9</td>
<td>5.8</td>
<td>7.0</td>
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</tbody>
</table>

Note: NS = not significant.
* Significantly greater in ICSI with oligozoospermia group (own eggs).
** Significantly greater in ICSI with oligozoospermia group (donor eggs).

of aneuploidies are maternal in origin. In the sex chromosomes, however, while 47,XXX is 5% paternal in origin, 47,XY is 50% paternal in origin and 100% of 47,YYY cases are paternally derived. For 45,XO, 75% of cases indicate that the remaining sex chromosome is maternal in origin, suggesting that the error arose on paternal meiosis (18, 19). If increased sperm aneuploidy is indeed the underlying cause of our observations, we would expect the effect to be seen predominantly in the sex chromosomes rather than in the autosomes and to observe proportionally fewer 47,XXX and 45,OY conceptuses; this is the case. In our results (Table 1), only one 47,XXX and one 45,OY (out of 12 in total) were observed. In addition to the sex chromosomes, the autosomes that showed a significant increase in the oligozoospermic group were chromosomes 1, 2, and 11 in the group using their own eggs. Among spontaneous abortions, the larger chromosomes (up to chromosome 12) have greater paternal contributions to trisomy (18, 19), and it is noteworthy that all these autosomes fall into this category (including three of the largest four). In the donor egg group, none of the autosomes apart from chromosome 18 showed elevated levels of aneuploidy for the oligozoospermic males. As a smaller chromosome, 18 is predominantly (96%) maternally derived (18, 19), so increased sperm disomy is unlikely to be the cause. The result may of course be a statistical anomaly; however, one possible explanation is that trisomy 18 is the only autosomal aneuploidy of which we are aware that arises predominantly in maternal meiosis II. Human eggs only complete meiosis II after fertilization, so perhaps a (genetically) suboptimal sperm may impair subsequent segregation of maternal chromosome 18 more than any other. Some of these questions could be addressed in future studies by a molecular analysis of the phase and parent of origin of the aneuploidy; the ability to do this has recently been reported using single nucleotide polymorphism microarrays (20, 21). Such an approach is not trivial, however, as it would require taking and sampling parental DNA. This is not currently routine for ethical, logistical, and cost reasons; however, if new approaches such as karyomapping were implemented (22, 23), it might become so in the future. Through the use of four control groups, we observed that only the sex chromosomes showed an increase and in only the severe oligozoospermia group for both donor and own eggs. We therefore feel that this provides sufficiently compelling data on its own that it is the presence of compromised semen parameters that led to the effect that we observed. In any event, it is very unlikely that patients or clinicians (the groups that these data will affect most) will pay a great deal of attention to whether or not the abnormalities are paternally derived. Moreover, when we presented these preliminary results to the Pacific Coast Reproductive Society recently, 62% of 700 participants said that they would change their practice as a consequence of our findings. A further consideration is that we have sampled only a few cells from the TE, assuming the ploidy status to be representative of the rest of the embryo. Confined placental mosaicism (where cells derived from the TE differ in ploidy status compared with those derived from the ICM) is nonetheless a well-described phenomenon (18, 24), with the errors of meiotic origin most likely leading to adverse clinical outcomes. Implementation of an approach that can distinguish not only parent but also phase of origin of the aneuploidy (20, 21) would ultimately allow us to select against those embryos that arose as a result of fertilization with an aneuploid sperm.

Since the implementation of ICSI over 20 years ago, IVF babies born using both ICSI and standard insemination techniques have been followed closely to assess rates of major birth defects compared with spontaneously conceived babies. There appears to be an equal, modest increase in major birth defects with IVF-derived offspring compared with naturally conceived offspring, whether ICSI or standard insemination are used to achieve fertilization in vitro (25). This suggests that the complex IVF process as a whole, or an intrinsic aberration in the infertile population, is responsible for this increase, rather than the insemination method used. Indeed, follow-up of babies conceived via ICSI and standard insemination thus far has been relatively reassuring in that there appears to be no difference in cognitive or motor development, pubertal development, or major birth defects between standard insemination and ICSI-derived offspring (6, 26–28).

Bonduelle et al. found that sex chromosome aneuploidies were elevated in children conceived via ICSI, although the numbers of affected individuals were small (29). The control group of IVF-conceived offspring in their second report contained only 2/1,000 individuals affected with a sex chromosome aneuploidy as compared with 6/1,000 for ICSI-conceived individuals. These studies only considered ICSI versus standard insemination with no consideration of the role of the sperm quality.

Aneuploidy frequency in spontaneously aborted conceptuses conceived via ICSI compared with standard insemination has been examined with varying conclusions. Bonduelle et al. reported an increase in sex chromosome abnormalities and de novo chromosomal aberrations in pregnancies derived from ICSI with suboptimal sperm parameters as compared with standard insemination–conceived pregnancies (29). Lathi and Milki also observed a marked increase in overall aneuploidy frequency in POC from ICSI patients compared with those derived from standard insemination (76% ICSI vs. 41% IVF; P<.01). Kushnir and Frattarelli observed similar overall rates of aneuploidy in POC between standard insemination and ICSI, although a small increase in sex chromosome abnormalities in the ICSI group was found (8, 9). Again, these studies did not consider sperm quality in their analysis.

The frequency of occurrence of sex chromosome abnormalities in live-born offspring varies with the type of aneuploidy. Males with Klinefelter syndrome (47,XXY) occur in one in 500 (0.2%) live births (30) compared with in three in 199 (1.5%) blastocyst embryos derived from oligozoospermic sperm in this study. The prevalence of newborns with Turner syndrome is 32/10,000 (0.03%) and 176/100,000 for fetuses at amniocentesis (0.18%) (31). In the present study, the rate of blastocyst embryos with monosomy X from the oligozoospermic group was 3.5%.

In one of the few studies analyzing aneuploidy rates of ICSI versus standard insemination–derived embryos, Munne
et al. found that ICSI embryos did not show an increase in aneuploidy rates compared with embryos created using standard insemination, unless the parents had a balanced chromosomal abnormality (32). However, in that report, embryos were biopsied on day 3 and analyzed using fluorescence in situ hybridization (FISH) for chromosomes X, Y, 13, 16, 18, and 21. Only a subset of the karyotype was therefore analyzed, and the use of FISH for determining aneuploidy in human embryos has come under considerable scrutiny owing to its limitations for chromosomal screening of preimplantation embryos.

Since studies have shown that oligozoospermic sperm samples have an elevated proportion of aneuploid sperm, one suggested clinical solution has been to screen the sperm of these patients using FISH to determine aneuploidy frequency before ICSI. One of the limitations of the present study was that only one semen parameter (sperm concentration) was considered for analysis. Further studies might ask whether any other specific semen parameters (apart from oligozoospermia) have an impact on blastocyst aneuploidy. Indeed, for the most part, studies have focused on oligozoospermia, and Tempest et al. (33) suggested that the sperm concentration was more likely to be correlated to the levels of sperm disomy than motility or morphology. A more recent study showed that men with poor sperm morphology who had repeated pregnancy loss had a higher occurrence of sex chromosome and autosome aneuploidy in their sperm than those with normal morphology (34). These men also showed a higher rate of sperm aneuploidy with chromosomes 18, 13, and 21. The clinical value of testing sperm samples with FISH to assess the proportion of aneuploid sperm may only be useful in helping to direct patients toward CCS testing of embryos if they had otherwise not been inclined to do so.

In the results presented here, we analyzed aneuploidy rates of embryos based on sperm density. We controlled for any effect that the ICSI process might have on aneuploidy frequency by separately analyzing data of embryos created from normal sperm using ICSI and standard insemination techniques. Our study advances the current knowledge base in providing strong evidence that it is the quality of the sperm that may be the underlying cause that could lead to the slight increase in rates of anomalies associated with ICSI (specifically sex chromosomal aneuploidy) and not the consequence of the ICSI procedure itself. Our study also suggests that, at least in terms of the risk of aneuploidy, the ICSI procedure using sperm with normal parameters is no more risky in creating aneuploid embryos than standard insemination.

With the current findings and past studies in mind, patients presenting with severe oligozoospermia should be counseled regarding the possible slight increased risk of sex chromosome aneuploidy and offered CCS for preimplantation genetic screening before ET, if available.

REFERENCES


