Attitudes about genetic risk of couples undergoing in-vitro fertilization

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Many couples undergoing in-vitro fertilization (IVF) are at a higher risk of having a child with a genetic abnormality. In a sample of 55 consecutive couples starting IVF, only 33% had no genetic risk factor. The most common genetic risks were advanced maternal age and possible abnormalities associated with severe male infertility. Despite education on these risks, 71% of couples had no interest in receiving formal genetic counselling. Only 14% of couples at risk would consider using a gamete donor to avoid transmitting a genetic disorder to a child. The triple test to screen for fetal abnormalities was acceptable to 82% of couples, but only 47% planned to have amniocentesis or chorionic villi sampling. Couples were significantly more likely to opt for prenatal testing if they would consider terminating a pregnancy should the fetus have a severe genetic abnormality (P < 0.01). Roman Catholic couples tended to have more conservative attitudes about pregnancy termination. Socio-economic status and whether the infertility factor was male or female were not predictors of a couple’s attitudes.

Key words: genetic counselling/genetic risk/in-vitro fertilization/prenatal diagnosis

Introduction

Couples attempting conception by in-vitro fertilization (IVF) often have genetic risk factors that could lead to birth defects or health problems in their children. Many women who use assisted reproductive technology are over age 35, either because of years spent attempting to get pregnant, or because of choices to delay childbearing. Advanced maternal age increases the risk of aneuploidy in offspring (Jorde et al., 1995). Advanced paternal age also may contribute to genetic risk for offspring, although genetic counselling and prenatal diagnosis are usually not advised until the male partner is over age 55.

Although the rate of genetic abnormalities in children conceived through conventional IVF does not appear significantly elevated (MRC Working Party on Children Conceived through IVF, 1990), the advent of intracytoplasmic sperm injection (ICSI) to treat severe male infertility has raised new fears about producing a cohort of impaired children (Meschede et al., 1995; Persson et al., 1996). It has become increasingly clear that impaired spermatogenesis is associated with a higher than normal rate of genetic abnormalities in a man’s somatic cells (Wilkins-Haug et al., 1997). Men who are azoospermic have an 8–15% rate of abnormal karyotypes (Wilkins-Haug et al., 1997). For men whose sperm counts are less than 10×10⁶/ml, rates of abnormalities are around 6%. Micro-deletions of the Y chromosome have also been diagnosed in 10–15% of men with severe infertility (Pryor et al., 1997). A son conceived through ICSI would inherit his father’s Y chromosome mutation, and therefore also his impaired fertility.

Mutations in the cystic fibrosis CF gene have also been observed in infertile men. In one recent series of 127 men with decreased sperm quality, 14% of those with azoospermia and 18% of those with oligozoospermia had mutations in at least one copy of the CF gene, suggesting that it has a role in spermatogenesis (van der Ven et al., 1996). Some CF mutations produce the bilateral congenital absence of the vas deferens (CBAVD) syndrome (Chillon et al., 1995). Spermatozoa retrieved from the epididymides of men with CBAVD can be used with high success in ICSI (Schlegel et al., 1995). Even if the female partner has no detectable CF mutation, the couple has about one chance in 80 of conceiving a child who will have cystic fibrosis (Persson et al., 1996). The probability that a son born to a man with CBAVD will have the syndrome himself depends on the exact combination of mutations that have led to the condition, some apparently extraneous to the CF gene (Chillon et al., 1995).

Despite increased genetic abnormalities in men with impaired spermatogenesis, the rate of birth defects among children conceived through ICSI does not appear to exceed that of the general population (Tournaye et al., 1995; Palermo et al., 1996). The sperm injection procedure itself does not seem to cause genetic damage (Meschede et al., 1995). However, problems such as male infertility will not be evident for many years. Many centres karyotype all men with oligozoospermia or azoospermia of unknown aetiology (Wilkins-Haug et al., 1997), and offer genetic counselling and prenatal diagnosis to all couples undergoing ICSI.

Little information, however, has been available regarding the attitudes of couples themselves about taking genetic risks. A recent pilot study from our programme suggested that couples choosing ICSI for severe male infertility have a very strong desire for genetic children and have little concern about genetic risk factors (Schover et al., 1997). The current study reports on structured interview data from a larger and more diverse sample of couples undergoing IVF.

Materials and methods

Fifty-five consecutive married couples scheduled to begin IVF during the 5 months between February and July, 1997, underwent an
hour-long semi-structured interview with an experienced, clinical psychologist. An interview including both partners was a required part of our programme. Couples were told that the purpose of the interview was to assess their current ability to cope emotionally with their infertility treatment, to make sure both partners were comfortable with their choice of treatment, and to familiarize them with the psychological support services available. Because the interview is part of our normal clinical services and no identifying data are reported here, no Institutional Review Board approval was sought.

Genetic counselling before proceeding with IVF was mandatory for couples in which the husband had CBAVD, and offered to couples with idiopathic severe male infertility or other known genetic risk factors. For couples with advanced maternal age, genetic counselling was not routinely offered, but risks of aneuploidy were discussed. We assumed that those who became pregnant and chose to have prenatal diagnostic testing would have genetic counselling at that time.

Each partner’s age and reproductive history was available from the medical record. The psychologist asked about religious practice and rated the family’s occupational status taking into account both spouses’ occupations as professional (physicians, doctoral level scientists, business executives, attorneys, etc.), white collar (engineers, teachers, small business owners, sales representatives, etc.), or blue collar (clerks, secretaries, factory workers, construction workers, etc.). Psychological questionnaires were not administered, but the interview included a series of standardized open-ended questions about motivations for infertility treatment, psychological adjustment of each spouse (including a lifetime history and current assessment of substance abuse, affective, and anxiety disorders by DSM–IV criteria), and the degree of conflict and intimacy in the marital relationship.

Other attitudes assessed in the interview included ethical or religious concerns about IVF and cryopreserving embryos, whether IVF was a financial burden, and what options to treat infertility the couple would consider next if IVF failed. Each couple was also asked the questions about genetic issues and prenatal diagnosis listed in Table I. Responses were recorded in a multiple-choice format. The answer recorded reflected the consensus the spouses reached within the interview. If they disagreed and were unsure how they would reconcile their views, a response of ‘unsure’ was used.

Statistical analyses were performed using Stats+ (StatSoft Inc., Tulsa, OK, USA). Procedures included \( \chi^2 \) tests, Fisher’s exact test, and Pearson’s product-moment correlations.

Results

Background information
Out of 55 consecutive couples undergoing IVF during the period of data collection, 92% were Caucasian, and 4% each were African-American or Asian-American. The psychologist rated socio-economic status as professional for nine couples (17%), white collar for 31 (56%), and blue collar for 15 (27%). IVF was considered financially burdensome by 22 couples (40%). A total of 49% of couples were Roman Catholic, 34% were Protestant and 17% identified with other or no religious denomination. Thirty-nine wives (71%) and 42 husbands (76%) had no prior children. The psychologist identified a history of psychological distress or problems in 18 wives (33%) and eight husbands (15%). Marital conflict was seen in 10 couples (18%).

Medical variables
Eighteen couples (33%) had male factor infertility, 29 (53%) had female factor infertility, and 11 couples (20%) had factors in both partners or idiopathic infertility. Five wives (9%) had a prior elective abortion and 13 (24%) had a prior miscarriage or ectopic pregnancy. Six couples (11%) were unsure whether they would agree to cryopreserve embryos, whereas all others planned to do so. All but four couples (7%) welcomed the idea of twins conceived through IVF. After a brief discussion about the medical risks of triplet pregnancies, 28% of couples said they would probably or definitely use selective reduction in that situation. Because our programme typically replaces a maximum of three embryos, selective reduction for higher-order multiple pregnancy was not discussed. If IVF failed, 18 couples (32%) planned to try adoption, 11 (20%) were considering gamete donation, 13 (24%) would stop trying to have a child, and 13 (24%) were unsure what they would do next.

Genetic risk factors
Eighteen couples (33%) had no increased risk factors for having a genetically abnormal child. Seven (12%) had either CBAVD or idiopathic severe male infertility. In 22 couples (40%) the wife was age 35 or older. In eight couples (15%) another genetic risk factor was present (for example repeated miscarriages, Huntington’s disease in a spouse’s parent, or risk of an inherited cancer syndrome from family history). Table II details the percentage of couples intending to use genetic counselling, use the triple test, or have invasive prenatal diagnosis (amniocentesis or CVS) within each of these risk groups. Couples without any genetic risk were asked if they would use invasive prenatal diagnosis if it were medically recommended for some reason (for example, a positive triple test). For 37 couples who carried some genetic risk, only seven (19%) would ever consider using a gamete donor to avoid having a child with a genetic abnormality. Demographic factors such as religion, socio-economic status, financial strain of IVF, or gender of the spouse with an identified infertility problem, were not predictive of intention to use genetic counselling or prenatal diagnostic testing.

Attitudes about terminating an affected pregnancy
Couples’ attitudes to terminating a pregnancy if prenatal diagnostic testing disclosed a genetic abnormality are detailed in Table III. Couples who intended to use prenatal diagnostic testing were also more willing to consider pregnancy termination in the event of an abnormality such as Down’s syndrome, which can cause moderate to severe mental retardation; \( \chi^2 \) analyses found significant associations with attitudes about termination, both for intention to use the triple test \( [\chi^2 (4) = 13.35, P = 0.01] \) and for invasive prenatal testing \( [\chi^2 (4) = 11.98, P = 0.02] \). Attitudes about pregnancy termination were not significantly associated with socio-economic status, but there was a trend \( (P = 0.06) \) for Roman Catholic couples (62%) to be more likely than others (37%) to reject terminating a pregnancy in the event of a trisomy such as Down’s syndrome.

Discussion
These interviews confirm our earlier data (Schover et al., 1997), suggesting that couples utilizing IVF have a strong
Table I. Questions asked on genetic risk and prenatal diagnostic testing

<table>
<thead>
<tr>
<th>Question</th>
<th>Response format</th>
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<tbody>
<tr>
<td>If you do become pregnant, how likely would you be to have a screening test in your second trimester that measures three chemicals in the mother’s blood to assess risk for neural tube defects or Down’s syndrome?</td>
<td>Definitely would have the test/Probably would have the test/Unsure/Probably would not have the test/Definitely would not have the test</td>
</tr>
<tr>
<td>Amniocentesis and chorionic villi sampling (CVS) are procedures that take a sample of fetal cells from the amniotic fluid or placenta to check for genetic abnormalities. The sample is gathered by a needle through the mother’s abdomen, or cervix. These tests are offered routinely to women over 35, or if a known genetic risk is present. If you do become pregnant, how likely would you be to have amniocentesis or CVS?</td>
<td>Definitely would have the test/Probably would have the test/Unsure/Probably would not have the test/Definitely would not have the test</td>
</tr>
<tr>
<td>We have a genetic clinic available, with a medical geneticist and genetic counsellors who can help you evaluate genetic risks for your child. How likely are you to have genetic diagnosis and counselling as part of your infertility treatment?</td>
<td>Have already had genetic counselling/Definitely plan to have genetic counselling/Probably will have genetic counselling/Definitely will not have genetic counselling</td>
</tr>
<tr>
<td>(Asked only if a genetic risk factor was present): How likely would you be to use a sperm or egg donor to avoid having a child with a genetic problem?</td>
<td>Definitely would use a gamete donor/Probably would use a gamete donor/Definitely would not use a gamete donor</td>
</tr>
<tr>
<td>We do not like to see triplet pregnancies because of the risk of miscarriage, having premature or low birth weight babies, and also the stress on families of raising triplets. If you were carrying a triplet pregnancy and were offered the option of selective reduction down to twins, how likely would you be to use selective reduction (knowing it carries about a 5% risk of complete miscarriage)?</td>
<td>Definitely would terminate/Probably would terminate/Unsure/Probably would not terminate/Definitely would not terminate</td>
</tr>
<tr>
<td>There is no evidence that IVF increases the risk of birth defects or genetic problems in offspring. Such problems only occur in 3–4% of all births. If you were carrying a pregnancy, however, and were told your fetus had a genetic problem, for example Down’s syndrome, that could cause moderate to severe mental retardation, how likely would you be to terminate the pregnancy?</td>
<td>Definitely would terminate/Probably would terminate/Unsure/Probably would not terminate/Definitely would not terminate</td>
</tr>
<tr>
<td>If you were carrying a pregnancy and were told the fetus had a genetic condition that would cause chronic illness in childhood, and probably lead to a shortened life expectancy, for example, cystic fibrosis, how likely would you be to terminate the pregnancy?</td>
<td>Definitely would terminate/Probably would terminate/Unsure/Probably would not terminate/Definitely would not terminate</td>
</tr>
<tr>
<td>If you were carrying a pregnancy and were told your child would have a future problem with infertility, similar to what you have experienced, how likely would you be to terminate the pregnancy?</td>
<td>Definitely would terminate/ Probably would terminate/Unsure/ Probably would not terminate/ Definitely would not terminate</td>
</tr>
</tbody>
</table>

Table II. Genetic risk factors and uptake of prenatal diagnostic testing

<table>
<thead>
<tr>
<th>Genetic risk factor</th>
<th>Probably/definitely will have genetic counselling (%)</th>
<th>Probably/definitely will have triple test (%)</th>
<th>Probably/definitely will have amniocentesis or CVS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age ≥35 years (n = 22)</td>
<td>32</td>
<td>91</td>
<td>68</td>
</tr>
<tr>
<td>Severe male factor or CBAVD (n = 7)</td>
<td>57</td>
<td>86</td>
<td>43</td>
</tr>
<tr>
<td>Other genetic risk factor (n = 8)</td>
<td>29</td>
<td>86</td>
<td>38</td>
</tr>
<tr>
<td>No genetic risk factor (n = 18)</td>
<td>0</td>
<td>67</td>
<td>28</td>
</tr>
<tr>
<td>CVS = chorionic villous sampling.</td>
<td>CBAVD = bilateral congenital absence of the vas deferens.</td>
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</table>

Table III. Probability of terminating a pregnancy given various fetal abnormalities (n = 53)^

<table>
<thead>
<tr>
<th>Probability of terminating a pregnancy</th>
<th>In the event of condition causing mental retardation (%)</th>
<th>In the event of major genetic illness (%)</th>
<th>In the event of child’s future infertility (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely yes</td>
<td>11</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Probably yes</td>
<td>23</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Unsure</td>
<td>17</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Probably no</td>
<td>21</td>
<td>30</td>
<td>2</td>
</tr>
<tr>
<td>Definitely no</td>
<td>28</td>
<td>42</td>
<td>96</td>
</tr>
</tbody>
</table>

^Two couples did not complete this final section of the interview.
need to conceive a mutual genetic child. Formal genetic counselling preparatory to IVF was only considered useful by couples facing a very clearly defined genetic risk, such as a mutation of the CF gene in the husband. Concerns about the cost of genetic testing and about insurance coverage were voiced by a number of couples. Although a high percentage of couples intended to use prenatal screening by maternal blood test, few planned to use invasive testing by amniocentesis or CVS. Even the very small risk of miscarriage entailed in invasive prenatal testing can be a deterrent once a precious IVF pregnancy is established, although neither childlessness nor previous pregnancy loss influenced couples’ decisions about prenatal diagnosis.

Although the structured interview is a mandatory part of our IVF programme, we present it as a service to the couple rather than as a screening process. It seems unlikely that couples would have perceived that they needed to supply a ‘right’ answer to these questions about their attitudes to genetic risk or prenatal diagnosis.

As surveys of couples without infertility have suggested (Evans et al., 1993), the motivation for prenatal testing was typically for reassurance, and pregnancy termination was anticipated to be unlikely unless a genetic abnormality would impose a very burdensome condition. When given the example of Down’s syndrome, a number of couples stated that the range of mental retardation in Down’s syndrome children was not severe enough to make them choose termination. Previous research also suggests that fewer couples use prenatal diagnosis or actually choose to terminate an affected pregnancy than those who indicated they intended to do so when surveyed ahead of time (Wertz et al., 1992; Adam et al., 1993; Evans et al., 1993).

Despite their own experiences with infertility, couples undergoing ICSI were not very concerned about conceiving a son who might face infertility in his turn. Almost all couples at risk of transmitting genetic male infertility spontaneously remarked that by the time their infant would become an adult, not only IVF/ICSI but even more sophisticated treatments would be available to enable him to have offspring. Couples who faced possible late-onset genetic disorders such as Huntington’s disease or familial cancer syndromes typically used similar patterns of reasoning, anticipating that cures such as gene therapy would be available to prevent their children from suffering.

The reluctance of couples in our sample to consider gamete donation as an option to avoid transmitting a genetic disorder is very similar to findings from a recent survey of 245 carriers of recessive genetic disorders (Snowdon and Green, 1997). In that study, respondents clearly preferred the options of using prenatal diagnosis, or if possible, preimplantation genetic diagnosis to preclude the necessity of considering pregnancy termination, rather than forgoing the possibility of having their own genetic child. Neither the out-of-pocket cost nor the technical difficulties of preimplantation diagnosis were addressed in the information given to participants however.

The bioethicist Cynthia Cohen (1996) recently suggested that infertile couples do not give adequate consideration to genetic risks because of their desperation to have a child. She believes health professionals have a responsibility not only to inform couples using assisted reproductive technology about the risks of having children with disabilities, but to refuse to use these treatments if there is a risk of producing a child with a poor quality of life. We must anticipate, however, that couples and health professionals will weigh these risks quite differently. What are the ethical boundaries of a health professional’s role as gatekeeper? Do providers of assisted reproductive technology have the right, much less the responsibility, to prevent the birth of a disabled child? If so, how severe a disability should preclude providing assisted reproductive technology?

It is certainly possible that the couple willing to take a risk will have regrets once a genetically abnormal child is born. As health professionals we must continue to offer guidance to couples and make sure they have the clearest understanding possible of genetic risks to their offspring. Future research should focus on methods of genetic counselling that can help couples more accurately to anticipate their future emotional reaction to a child born with a genetic abnormality. Research suggests that objective statistics about risk have far less influence on couples’ reproductive decisions than does their subjective perception of the risk and burden of having a child with a specific disorder (Beeson and Golbus, 1985; Frets et al., 1990). Exposing couples to live or videotaped accounts from parents and children who have coped with a particular genetic problem may have more emotional impact than simply providing risk estimates. After such a presentation, the couples could be asked to imagine together how they would cope with the financial, social, and emotional practicalities of caring for an ill or impaired child. Thus, despite couples’ reluctance to consider counselling, a session with a genetic counsellor or mental health professional remains an important aspect of preparation for IVF when genetic risks are present.

References


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