INAHTA Briefs

Issue 2002/71

Title Intracytoplasmic Sperm Injection

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Reference SMM Report No. 3/2002. ISBN 82-14-02763-2

Aim

To evaluate the risk of developmental defects in children conceived by intracytoplasmic sperm injection (ICSI), an in vitro fertilization (IVF) method that enables fertilization in spite of severely compromised semen characteristics.

Methods

A systematic review was undertaken of literature reporting the outcome of ICSI pregnancies. Publications were identified by searches in MEDLINE, EMBASE, and Cochrane. International birth defects monitoring networks were contacted in an attempt to identify relevant data published as reports. Studies were critically assessed and systematized according to the presence of a relevant control group (children conceived by conventional IVF and/or naturally conceived children), and five clinical outcomes: i) birth defects, ii) growth disturbances, iii) neurological developmental disturbances, iv) chromosomal abnormalities, and v) transmission of subfertility to male offspring. In total, 30 studies with acceptable and fair quality were found to fulfill the inclusion criteria. Two reports providing new data were also included. Data on major birth defects from studies and reports comparing children conceived by ICSI versus conventional IVF were pooled and subjected to a meta-analysis.

Results and conclusions

No meta-analyses or randomized controlled studies were identified, and all studies were classified either as cohort studies or case series. Of these, 13 studies were rated as acceptable quality, having adequate and well-defined control groups, whereas 17 studies were rated as fair quality due to weak or undefined control groups.

Birth defects were the most frequently reported outcome. Two reports and seven cohort studies of acceptable quality were included in the meta-analysis of birth defects. Overall, the risk for birth defects was 1.13 (95% confidence interval: 1.00-1.29, p=0.06). Studies that met our criteria were fairly homogenous (test for heterogeneity p=0.35). Separate meta-analysis on specific categories of malformations did not show any increased risk after ICSI.

Parents with chromosomal abnormalities or other genetic defects may transfer their defects to their offspring via ICSI. Sons of infertile males with Y chromosome microdeletions will inherit the same abnormality and therefore probably be infertile. With regard to the other outcomes, the number of accepted studies are few and heterogeneous, which makes the findings uncertain.

In conclusion, there is a small increased risk for major birth defects in offspring resulting from ICSI used to treat severe male infertility. However, this increase is not significant. Currently, there is little evidence of an increased risk for other health problems.

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