Growth and reproductive function of children conceived by intra-cytoplasmic sperm injection

Claudia Mau Kai, MD

This PhD dissertation was accepted by the Faculty of Health Sciences of the University of Copenhagen, and defended on October 26, 2007.

Official opponents: Birthe Høgh, Thue Erik Bryndorf, and Niels Thomas Hertel.

Tutors: Niels E. Skakkebæk, Anders Juul, and Anne Loft

Correspondence: Claudia Mau Kai, Solbakken 7, 2830 Virum, Denmark.

E-mail: claudia_mau@hotmail.com

Dan Med Bull 2007;54:382

ABSTRACT

This study was performed at the University Department of Growth and Reproduction GR and the Fertility Clinic, Rigshospitalet, Copenhagen.

Increasing infertility worldwide has led to the development of in vitro fertilisation (IVF) and intra cytoplasmic sperm injection (ICSI). The first children conceived by these methods were born in 1978 and 1992, respectively.

It seems that the growth of children conceived by ICSI is comparable to naturally conceived (NC) children. However, serum levels of Insulin-like growth factor I (IGF-I) have not previously been studied in these children and data on the fecundity of adults conceived by ICSI are not yet available. Basal reproductive hormones around three months of age reflect the pituitary-testicular axis, which is transiently active at this age and assumed to be predictive of adult reproductive function.

The Y-chromosome has a structure with palindromic repeats; azoospermia factor (AZF) a, -b and -c, and smaller palindromes within the AZFc region that may lead to partial deletions (e.g. gr/gr, b2/b3). The clinical consequences of partial AZFc deletions are not clear and the prevalence of transmissions is currently unknown.

Birth data and obstetric history from pregnancies were obtained from medical records. The children were examined at the age of 3, 18 and 36 months and at 5 years of age. At 3 months of age and at 5 years of age a blood sample was obtained from approximately 60% of the children and their fathers. Data on paternal sperm parameters were collected.

Anthropometrical measurements showed no significant differences between ICSI children and controls. However, infants conceived by ICSI had subtle differences in target height attainment and serum IGF-I levels compared to NC infants.

Serum testosterone levels were significantly reduced (27%) and the LH/testosterone ratio was significantly higher (60%) in boys conceived by ICSI compared to NC boys. This points towards an impairment of Leydig cell function in boys conceived by ICSI using sperm from oligozoospermic men.

In the ICSI/IVF group 0.4% had a complete AZFc deletion, 2.7% a gr/gr deletion and 4.2% a b2/b3 deletion. The prevalence of the b2/b3 was significantly greater than that in the fertile group. All partial AZFc deletions were transmitted to the male offspring. Our findings suggest that gr/gr and b2/b3 deletions might represent a genetic risk factor for male infertility.

The increasing use of ICSI may result in the propagation of spermatogenic failure in the population and contribute to decreasing fertility rates. Further systematic follow-up of these children throughout life and their offspring is important in order to ensure the safety of this reproductive technique.