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SHORT COMMUNICATION

SZEGED, HUNGARY

The Incidence of Major Birth Defects Following In Vitro Fertilization

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***Purpose*:** To evaluate the risk of congenital malformations in newborns delivered after IVF-ET in comparison with matched controls from spontaneous pregnancies.
***Methods*:** A total of 12,920 deliveries were subjected to retrospective analysis. A total of 301 neonates were evaluated. The incidence of major birth defects was compared with controls matched with regard to age, gravidity, parity, and previous obstetric outcome after spontaneous pregnancies.
***Results*:** The incidence of major congenital abnormalities was not significantly higher ($p > 0.05$) among the cases (1.90%) than among the controls (1.15%).
***Conclusions*:** The risk of major birth defects following IVF-ET is comparable with that of spontaneously conceived, matched pregnancies.

KEY WORDS: IVF-ET; major birth defects; matched control.

INTRODUCTION

The rate of birth defects following in vitro fertilization embryo transfer (IVF-ET) varies from 3.4 to 9.0% (1–4) in the literature. The comparison of ICSI and IVF children taking part in an identical follow-up study did not show any increased risk of major malformations in the ICSI group (4). Control selection (national or clinical control) from a different population (3) creates the problem of differences in screening methods, management of pregnancy, and perinatal care between cases and controls (1,2). In both cases, only stratification procedures reveal the influence of assisted reproductive technology (ART) on the incidence of birth defects (1,2).

METHODS

We performed a retrospective study from January 1, 1995 to December 31, 2001. The IVF-ET group comprised 188 neonates from singleton, 74 from twin, and 39 from triplet pregnancies. We collected controls matched regarding maternal age, previous parity, and gravidity. Triplets were analyzed in the crude distribution (data not given in the table). Congenital malformations were diagnosed by the same experienced neonatologist, on the basis of physical examination, chest, abdominal or skull X-ray, and ultrasonography (cardiac, abdominal, head, etc.) according to International Code of Diagnosis (ICD) criteria. Birth defects were classified as major congenital malformations (e.g. congenital heart defects, gastrointestinal malformations, genitourinary tract malformations, bone malformations, etc.) or as minor anomalies (e.g. hypertelorism, low-set ears, etc.). Babies with major congenital or structural malformations were admitted to the Neonatal Intensive Care Unit (NICU) for further observation and treatment.

Comparison modification was unnecessary as we used a matched control group. Consequently, the effect of IVF-ET on the birth per se can be evaluated. Statistical analysis was performed with the SPSS program (5).

RESULTS

The incidence of major congenital abnormalities (ICD-9) was not significantly higher ($p > 0.05$) among the cases ($n = 5$, 1.90%) than among the controls ($n = 3$, 1.15%) (Table I). The 39 triplets exhibited no major malformations. The prevalence was lower than reported by others (1,3), and significantly lower than that in Western Australia (9.0%) (3).

Birth defects were diagnosed 4 weeks after delivery, in contrast with the 1-year follow-up by Hansen (3). The longer follow-up could not explain the difference: the prevalence of all types of congenital abnormalities in Hungary is 4% at delivery and 8% by 25 years of age (6). When the analysis included pregnancies terminated because of fetal abnormalities detected prenatally (+2 cases during the 6-year period vs. +1.0% in the Hungarian national database control) (6), the statistical relation (2.67% vs. 2.25%, $p > 0.05$) was unchanged. The rate of major birth defects was comparable with the clinical average (1.90% vs. 2.20%, $p > 0.05$).

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Table I. Distribution of Major Congenital Defects

Type of congenital anomalies	IVF-ET group ($n = 262$)			Matched control group ($n = 262$)		
	Singleton ($n = 188$)	Twin ($n = 74$)	Total ($n = 262$)	Singleton ($n = 188$)	Twin ($n = 74$)	Total ($n = 262$)
Cardiovascular	1	1	2	1		1
Chromosomal	1		1			
Gastrointestinal	1		1		1	1
Other	1		1		1	1
Total	4	1	5[a]	1	2	3[b]

[a] 1.9% of the total number of IVF-ET neonates.
[b] 1.1% of the total number of matched control group neonates.

CONCLUSION

The matching procedure for establishment of a control group will clearly most closely reflect the relative risk of the ART method. Differences in absolute risk of congenital abnormalities can be influenced by maternal age, certain maternal diseases, medications, toxic habits, enviromental toxic effects and population variation. The different prenatal screening methods applied (e.g., nuchal translucency, chorion biopsy) and national guiding principles concerning prenatally detected malformations can also significantly modify the perinatal outcome concerning congenital anomalies. Therefore, it is very important to collect safety data prospectively as assisted reproductive technology has been showing a dramatic increase worldwide in infertility therapy.

Use of matched controls to evaluate the perinatal effects of IVF-ET on the incidence of major birth defects demonstrate that the risk because of the method itself is minimal.

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