Perinatal outcome in multiple pregnancies - spontaneous gestation versus

M. Gojnic, K. Jeremic, V. Boskovic, A. Fazlagic, A. Stefanovic, M. Pervulov

Institute of Gynecology and Obstetrics, Clinical Center of Serbia, Belgrade (Serbia and Montenegro)

Summary

The purpose of this investigation was to determine if twin pregnancies induced by in vitro fertilization (IVF) are under greater risk of negative perinatal outcome than "spontaneous" twin pregnancies. The study included 240 patients with gemellar pregnancies. Each patient with a gemellar IVF pregnancy (120) was assigned to a pregnant woman with appropriate age, education and parity from the "spontaneous" group as a control. Pregnancies were followed clinically, with laboratory analyses and ultrasonography.

Key words: In vitro fertilization; Gemellar pregnancy.

Introduction

Because of more liberal and widespread methods of assisted reproduction, the incidence of twin and other multi-fetal gestations is increasing and they are thought to include more than 3% of all pregnancies [1]. Considering that perinatal and maternal morbidity and mortality are more common in multiple than single gestations, we can expect increasing maternal-fetal pathology with the increasing number of gemellar pregnancies. The main risk for the neonate in twin pregnancies is prematurity, with an incidence that has not changed for the last 20 years, followed by growth retardation [2]. For twins, perinatal mortality ranges from 47-120 out of 1,000 births, with the greatest risk for the second twin. Studies on the role of assisted reproduction in the rate of perinatal morbidity and mortality of gemellar pregnancies are insufficient. There is the question of an additional burden for these twin pregnancies in relation to "spontaneous" pregnancies.

Materials and Methods

Two hundred and forty pregnant women who delivered gemellar pregnancies were analyzed together with, all the data on the course of the pregnancy. All pregnant patients with incomplete data on the course of pregnancy were excluded from the study, as well as patients without adequate control after the IVF procedure. Statistical evaluation of differences between groups was performed by the Z test, Student's t-test and HI quadrant test with Jets correction.

Results

The average age of the patients in the in vitro fertilization (IVF) group was 34.57 ± 4.55 (range 28 to 43 years). Women with a secondary education 47.5% (57/120) and nullipara 95% (114/120) prevailed. The average duration of gestation in the IVF group was 35.79 ± 3.51 weeks which was a little shorter than in the controls 36.72 ± 2.76 weeks. The gestational age in the two groups is presented in Table 1.

Table 1. — *Duration of pregnancy.*

Weeks of gestation	IVF (%) n = 120	Controls (%) n = 120	Significance
≤ 27	5.00	0	NS
28-32	17.5	12.5	NS
33-37	27.5	25.0	NS
≥ 38	50.0	62.5	NS

NS: not significant.

Of the IVF and control pregnancies, respectively, 62.5% and 55% ended operatively, and the percentage of urgent operations was 28% in the first group compared to 25% in the second. The most common indication for cesarean in the IVF group was twin pregnancy after IVF and the condition after sterility.

Besides these maternal complications (Table 2), in the IVF group there was a case with placenta previa centralis, and one case of postpartum hysterectomy because of uterine atonia and extensive hemorrhage with hemorrhagic shock after surgical delivery at term.

Table 2. — *Maternal complications.*

Maternal complications	IVF (%) n = 120	Controls (%) n = 120	Significance
PIH	39 (32.5)	27 (22.5)	NS
GDM	12 (10.0)	21 (17.5)	NS
Thrombocytopenia	12 (10.0)	9 (7.5)	NS
Cerclage	57 (47.5)	39 (32.5)	NS
PPROM	24 (20.0)	27 (22.5)	NS
PROM	15 (12.5)	9 (7.5)	NS

PIH: pregnancy induced hypertension; GDM: gestative diabetes mellitus; PPROM: premature preterm rupture of membranes.

Revised manuscript accepted for publication December 6, 2004

Embryo reduction was performed in the IVF group in 18 cases (one embryo in each case) and all interventions ended without complications.

The only chromosomopathy was Down's syndrome in a male embryo with multiple anomalies that died in the uterus before planned feticide in the 28th week of gestation. A case of congenital malformation, i.e. lips and split palate, in the control group was recorded in a female neonate and it was successfully corrected postnatally.

Invasive diagnostic procedures were applied in 75% (90/120) of pregnant patients in the IVF group and 57.5% (49/120) in the control group. The most common prenatal invasive diagnostic procedure in the first group was chorionic villi biopsy (53.33%) and in the control group genetic amniocentesis (78.26%).

The average body weight of A twins (first-born) in the IVF group was 2393.75 ± 587.53 g in relation to 2563.75 ± 628.18 in the controls and for B twins (second-born) in the first group was 2259.74 ± 633.07 and in the controls 2581.81 ± 629.21 g (Table 4).

Both twins most frequently had head presentation in both groups; 32.5% (39/120) in the IVF and 47.6% (57/120) in the control group. According to frequency, the next combination in the IVF group was head-pelvis 12.5% (15/120) and in the control group pelvis-pelvis 12.5% (15/120).

The Apgar score determined at the fifth minute showed better neonate adaptation, i.e. with better corrections in all live birth categories in the control group.

The average Apgar score in the first minute for A twins in the IVF group was 6.825 ± 2.0240 vs 7.20 ± 2.388 in the control group, while for B twins there was a bigger difference between groups 6.475 ± 2.501 in relation to controls 7.625 ± 1.943 (Table 5).

Neonatal mortality in the IVF group was 15/240, while in controls it was lower (6/240). Neonatal morbidity and mortality are shown in Table 6.

Table 3. — *Fetal pathology.*

Fetal pathology	IVF n = 240	Controls n = 240	Difference significance
IFD	9	0	NS
Chromosomopathy	3	0	NS
IUGR	18	18	NS
Congenital malformations	3	3	NS
Total	33	21	NS

IFD: intrauterine fetal death; IUGR: intrauterine growth retardation.

Table 4. — *Body weight of twins A and B according to groups.*

Body weight (g)	IVF (%) A twins	Control (%) A twins	Difference in significance (A)	IVF (%) B twins	Control (%) B twins	Difference in significance (B)
< 1999	27 (22.5)	18 (15)	NS	45 (37.5)	18 (15)	$p < 0.05$, $t = 2.28$
2000-2499	24 (20)	30 (25)	NS	24 (20)	33 (27.5)	NS
2500-2999	48 (40)	42 (35)	NS	42 (35)	36 (30)	NS
> 3000	21(17.5)	30 (25)	NS	9 (7.5)	33 (27.5)	$p < 0.05$, $t = 2.35$
Total	120	120		120	120	

Table 5. — *Apgar score in the 1st minute.*

Apgar score	IVF (%) A twins	Control (%) A twins	Difference in significance (A)	IVF (%) B twins	Control (%) B twins	Difference in significance (B)
0	3 (2.5)	0 (0)	NS	6 (5)	0 (00)	NS
1-3	9 (7.5)	12 (10)	NS	12 (10)	9 (7.50)	NS
4-7	48 (40)	33 (27.5)	NS	51 (42.5)	24 (20.0)	$p < 0.05$, $t = 2.170$
8-10	60 (50)	75 (62.5)	NS	51 (42.5)	87 (72.5)	$p < 0.01$, $t = 2.714$
Total	120	120		120	120	

Table 6. — *Neonatal morbidity and mortality.*

Complications	IVF (%) n = 80	Control (%) n = 80	Difference in significance
RDS	45 (18.75)	27 (11.25)	NS
Asphyxia	54 (22.50)	36 (15.00)	NS
Hyperbilirubinemia	27 (11.25)	12 (5.00)	NS
Sepsis	9 (3.75)	3 (1.25)	NS
Diffuse hemorrhage	6 (2.50)	3 (1.25)	NS
IVH	27 (11.25)	15 (6.22)	NS
Anemia	24 (10.0)	18 (11.25)	NS
Bronchopneumonia	9 (3.75)	3 (1.25)	NS
Mortality	15/240	6/240	NS

RDS: respiratory distress syndrome.

Discussion

Most studies dealing with perinatal outcomes of multifetal pregnancies, including twin pregnancies, were limited by a long period of sample collecting, control group problems, different protocols in pregnancy management and outcome, and small samples [1, 5].

Our results (Table 1) show the average gestational age as 35.79 ± 3.50 weeks in the IVF group and a longer gestational period in the control group 36.72 ± 2.766, which is closer to other authors' results, i.e. the 37th week of gestation [3].

In more than 50% of cases in both groups, delivery ended surgically (61.5% vs 55%) with 28% urgent surgical deliveries in the IVF and 45% in the control group, which is not statistically significant. Some studies show as much as 61.5% of elective surgical endings in twins in an IVF group in relation to 35.1% in a control group [4]. Our research showed that the most common way of pregnancy termination in gemellar pregnancies was elective cesarean regardless of the way the pregnancy was conceived.

IVF twin pregnancies do not have a greater risk of maternal complications (Table 2) in pregnancy induced hypertension (PIH), gestative diabetes, thrombocytopenia, anemia, premature preterm rupture of membranes and need for cerclage than control pregnancies. No cases of maternal mortality in the sample matched with the literature [4].

Fetal pathology was present with 13.25% in the IVF group, i.e. nine cases of intrauterine death, one chromosomopathy, three congenital malformations and 18 cases of intrauterine growth retardation (IUGR), which does not differ significantly from the incidence of these categories in the control group with 8.75% (Table 3).

We found body weight under 1,999 g in 37.5% of cases

in the B twins of the IVF group and only 15% in the control group, which was statistically significant ($p < 0.05$). Almost one-third of the B twins in the control group (27.5%) weighed more than 3,000 g and only 7.5% in the IVF group ($p < 0.05$; Table 4). More detailed analysis points to smaller body weight and lower Apgar score of B twins in the IVF group, consequently with greater risks for B twins [2].

B twins in the IVF group had Apgar scores from 4-7 in 42.5% of cases (Table 5), with a statistical significance ($p < 0.05$). The control group B twins had a high Apgar score in 72.5% of cases in relation to 42.5%, which was statistically significant ($p < 0.01$) and matches the literature data [4].

In one-third of the neonates in the IVF group asphyxia occurred (22.50%), while in the control group there were 15% of cases ($p > 0.05$). Moreover, other parameters of neonatal morbidity did not show any statistical significance between groups (respiratory distress syndrome, intraventricular hemorrhage, intracranial hemorrhage, sepsis, bronchopneumonia, anemia, hyperbilirubinemia). Neonatal mortality was 15/240 in the IVF group and 6/240 in the control group, and was related mostly to B twins in both groups (Table 6).

Conclusion

IVF twin pregnancies equalized according to age, education and parity of the mother did not have greater risk of maternal complications during pregnancy than "spontaneous" twin pregnancies. Fetal and neonatal morbidity and mortality were no different than for the standard twin population, although there was a greater proportion of cases of B twins with lower body weight (under 1,999 g) and Apgar score less than 7.

References

[1] Malone F.D., D'Alton M.E.: "Multiple gestation: Clinical characteristics and management". In Creasy R.K., Resnik R. (eds.): "Maternal-Fetal Medicine", 4th ed., Philadelphia C., W.B. Saunders, 1999.

[2] Alvarez M., Berkowitz R.L.: "Multifetal gestation". *Clin. Obstet. Gynecol.*, 1990, *33*, 79.

[3] Minakami H., Sato I.: "Re-estimating date of delivery in multifetal pregnancies". *JAMA*, 1996, *275*, 1432.

[4] Samueloff A., Reubinoff B.E., Ben-Hayim M. *et al.*: "Outcome of twin pregnancies following in vitro fertilization". *Am. J. Obstet. Gynecol.*, 1995, *172*, 327.

[5] Tunon K., Eik-Nes S.H., Grottum O. *et al.*: "Gestational age in pregnancies conceived after in vitro fertilization; a comparison between age assessed from oocyte retrieval, crown-rump length and biparietal diameter". *Ultrasound Obstet. Gynecol.*, 2000, *15*, 41.

Address reprint requests to:
M. GOINIC, M.D., P.h.D., Assoc. of Asst.
Medical Faculty of Belgrade
Institute of Gynecology and Obstetrics
38 Milesevska Street
11000 Belgrade (Serbia and Montenegro)