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Original Article

Effect of selective second-trimester multifetal pregnancy reduction and its timing on pregnancy outcome

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Abstract: Objective: To investigate the impact of multifetal pregnancy reduction (MFPR) on the progress and outcome of pregnancy, we compared the outcomes of this procedure performed at different stages of gestation. Methods: 302 consecutive patients admitted to the Department of Obstetrics and Gynecology of Provincial Hospital Affiliated to Shandong University from January, 2002, to February 2012 with multifetal pregnancies were included. All pregnancies were induced by assisted reproductive technology. 152 multifetal pregnancies (triplets or quadruplets) were reduced to twin pregnancies (RT) and 150 non-reduced twin pregnancies (NRT) received no intervention. MFPR was performed at 12-13^{+6} weeks of gestation (MFPR12) in 91 RT cases, 14-15^{+6} weeks in 32 cases (MFPR14), while at 16–24^{+6} weeks of gestation in 29 cases (MFPR16). The procedure was performed by transabdominal ultrasound-guided intracardiac injection of 10% KCl solution. Results: Pregnancy loss rates in the RT and NRT groups were 14.5% and 6.7%, respectively. The difference between the two groups was statistically significant (χ^2 = 4.857, P = 0.028). Pregnancy loss rate for the MFPR16 group (31.0%) was significantly higher than for MFPR12 (8.8%, P = 0.007) and NRT group (6.7%, P = 0.000). The differences between pregnancy loss rates of the MFPR12 and MFPR 14 groups and the rate of NRT group were not statistically significant (P > 0.05). Conclusion: There was an increased risk of pregnancy loss in the RT pregnancy group in comparison with NRT group. However, performing MFPR before gestational age of 16 weeks could reduce the risk of pregnancy loss significantly.

Keywords: Pregnancy, twins, multifetal pregnancy reduction, pregnancy outcome

Introduction

In recent years, MFPR has become both clinically and ethically accepted as a therapeutic option in multifetal pregnancy [1, 2] and its safety and availability has increased. However, the optimal timing for this operation remains controversial. Some studies report that the timing of this procedure does not affect pregnancy outcome [3, 4] during early stages of gestation, the operation is very difficult to perform because of the small size of the fetal thorax. To examine the effect of the timing of MFPR on the success of pregnancy, we compared the pregnancy outcomes after MFPR performed at different gestational ages.

Materials and methods

Patients

302 multifetal pregnancy patients admitted in Department of Obstetrics and Gynecology, Provincial Hospital Affiliated to Shandong University, from January, 2002, to February, 2012 were included. All pregnancies were induced by ART.

Among the 152 multifetal pregnancies (triplets or quadruplets) reduced to twin pregnancies(RT), MFPR was performed at 12-13^{+6} weeks of gestation (MFPR12) in 91 cases, at 14-15^{+6} weeks of gestation (MFPR14) in 32 cases, and in 29 cases, at 16-24^{+6} weeks (MFPR16) in 29 cases.

Table 1. Comparison between reduced to twin pregnancies (RT) and non-reduced twin pregnancies (NRT)

	RT	NRT
Pregnancy loss rate*	22 (152) 14.5%	10 (150) 6.7%
Delivery at 28-34 weeks	8 (130) 6.2%	9 (140) 6.4%
delivery after 28 weeks	36.90 ± 1.80	36.97 ± 1.82
mean high birth weight	2720.42 ± 455.04	2729.06 ± 413.79
Mean low birth-weight	2409.15 ± 412.63	2416.21 ± 436.79
Birth-weight discordance	16 (130) 12.3%	6 (140) 11.4%
GDM	4 (130) 3.1%	3 (140) 2.1%
Pregnancy-induced hypertension	15 (130) 11.5%	12 (140) 8.6%

*Reduced twins vs. non-reduced twins; (χ^2 = 44.857; *P* = 0.028).

The control group consisted of 150 cases of matched NRT (non-reduced twin pregnancies) pregnancies. Mean maternal ages in the RT group and NRT group were 29.5 ± 4.4 and 29.8 ± 4.5 (the difference was not statistically significant; t = -0.727, *P* = 0.4685).

The study has been approved by the ethics committee of Shandong University, and written consents were obtained from all patients.

Fetal reduction

Intracardiac injection of KCl was performed transabdominally guided by ultrasound by the same surgeon, the techniques as well as the treatment following the operation were as described elsewhere [5].

In all cases, the reduction procedure was undertaken 24-72 h after a detailed combined transvaginal and transabdominal examination of fetal size; anomalies and NT (nuchal translucency) had been evaluated by an expert sonographer (a consultant in fetal medicine). If a fetal anomaly or an increased risk of chromosomal or structural malformation was suspected, the fetal reduction would be performed selectively on that fetus. If no fetal anomaly was suspected, the smaller sac/sacs or the sac/sacs proximal to the uterine fundus would be selected.

Outcome measures

The period of gestation was established on the basis of the patient records. The following types of pregnancy loss after the procedure were taken into account: abortions (up to 4 weeks after fetal reduction and before 28 weeks of gestation) and intrauterine fetal death (up to 28 weeks of gestation). We calculated mean gestational ages at delivery, delivery rate at 28-34 weeks, mean birthweight, and the rate of bir-th-weight discordance. Discordance was defined using the weight of the larger twin as standard and calculated using the following equation: (the larger estimated or actual weight - the smaller estimated or actual weight)/the larger estimated or actual weight. While there is no consensus on the precise threshold of discordance that might be associated with complications, ACOG considers a 15-25% difference in weight between twins to be discordant [6]. The incidence of gestational diabetes and pregnancy-induced hypertension in RT and NRT groups were also recorded.

Statistical analysis

Statistical analysis was performed using SPSS program (version 17.0; SPSS, Chicago, IL). Probability of 0.05 was considered statistically significant. Statistical analysis was performed using analysis of variance (ANOVA) in three groups and the independent *t*-test in two groups to compare mean patients' ages, birth weights, and mean gestational ages at delivery after 28 weeks. Chi-square and Fisher's exact tests were used to compare pregnancy loss rate, delivery rate at 28-34 weeks, the rates of birth-weight discordance, the incidence of gestational diabetes and pregnancy-induced hypertension.

Results

Pregnancy loss rate

By comparing the pregnancy outcome of cases reduced to twin pregnancies (RT) with non-reduced twin pregnancies (NRT), we observed an increased risk of pregnancy loss in the RT group (**Table 1**).

Pregnancy loss rates in RT group and NRT group was 14.5% and 6.7%, respectively (the difference was statistically significant; *P* = 0.028). Pregnancy loss rates for the three MFPR groups, MFPR12, MFPR14, and MFPR16

Table 2. Comparison between the four groups (MFPR12, MFPR14, MFPR16 and NRT)

	MFPR12	MFPR14	MFPR16	NRT
Pregnancy loss rate☆	8 (91) 8.8%	5 (32) 15.6%	9 (29) 31.0%	10 (150) 6.7%
Delivery at 28-34 weeks	7 (83) 8.4%	0 (27) 0	1 (20) 5.0%	9 (140) 6.4%
Delivery after 28 weeks	36.74 ± 1.95	37.37 ± 1.12	36.91 ± 1.88	36.97 ± 1.82
Mean high birth-weight	2682.61 ± 445.98	2843.70 ± 434.19	2711.75 ± 511.31	2729.06 ± 413.79
Mean low birth-weight	2373.13 ± 395.29	2524.81 ± 400.25	2402.50 ± 487.54	2416.21 ± 436.79
Birth-weight discordance	8 (83) 9.6%	5 (27) 18.5	3 (20) 15%	16 (140) 11.4%
GDM	2 (83) 2.4%	1 (27) 3.7%	1 (20) 5.0%	3 (140) 2.1%
Pregnancy-induced hypertension	9 (8.3) 10.8%	3 (27) 11.1%	3 (20) 15%	12 (140) 8.6%

☆: 16-24^{+6} weeks vs. 12-13^{+6} weeks (χ^2 = 7.212, P = 0.007); 16-24^{+6} weeks vs. non-reduced twins (χ^2 = 12.749, P = 0.000); 12-13^{+6} weeks vs. non-reduced twins; 14-15^{+6} weeks vs. non-reduced twins or 16-24^{+6} weeks and 12-13^{+6} weeks vs. 14-15^{+6} weeks (P > 0.05).

was 8.8%, 15.6%, and 31.0%, respectively Pregnancy loss rate of the MFPR16 group (31.0%) was significantly higher than that of MFPR12 (8.8%, P = 0.007) and NRT group (6.7%, P = 0.000). The differences between pregnancy loss rate of the MFPR12 and MFPR 14 groups and that of NRT group were not statistically significant (P > 0.05) (**Table 2**).

Mean gestational ages at delivery and the delivery rate at 28-34 weeks

Comparisons of the mean gestational ages at delivery and delivery rates at 28-34 weeks for RT and NRT groups and comparisons between the three groups with MFPR performed at different gestational ages (MFPR12, MFPR14, MFPR16) revealed no statistically differences. The mean gestational ages at delivery and the delivery rates at 28-34 weeks for MFPR12 and MFPR14 groups were also compared with those of the NRT group, no significant difference was found (P > 0.05).

Birth-weight

Comparisons of mean birth-weights among RT, NRT, and MFPR groups showed no statistically significant differences. For RT and NRT groups, the mean high birth-weights were 2720.42 ± 455.04 g and 2729.06 ± 413.79 g, respectively; the mean low birth-weights were 2409.15 ± 412.63 g and 2416.21 ± 436.79 g. The rates of birth-weight discordance for those groups were not significantly different, either. Mean birth-weights for MFPR12 and MFPR14 groups were also compared with mean birth-weights of NRT group and the rates of birth-weight discordance did not differ significantly (P > 0.05).

Incidence of gestational diabetes and pregnancy-induced hypertension

No statistical difference was found in the incidences of gestational diabetes and pregnancy-induced hypertension between RT and NRT groups and among the three MFPR groups. The differences between incidence of gestational diabetes and pregnancy-induced hypertension discordance of the MFPR12 and MFPR 14 groups and that of NRT group were not statistically significant (P > 0.05) (**Table 2**).

Discussion

With the wide use of ovulation induction agents and assisted reproductive techniques, the incidence of multifetal pregnancy has been increasing continuously during the last three decades .Triplet and the higher order pregnancies are associated with a higher risk of maternal, perinatal, and long-term complications in comparison with singleton or twin pregnancies. MFPR could decrease this risk by reducing the number of fetuses [5]. The timing of this reduction is very important for the pregnancy outcome.

We found that pregnancy loss rates in the RT and NRT groups were 14.5% and 6.7%, respectively. The difference between the two groups was statistically significant (χ^2 = 4.857, P < 0.05); the pregnancy loss rate in the RT group is substantially higher than in NRT group. This may be a result of an inflammatory response to the non-viable fetal and placental tissue remains, triggering the release of cytokines, stimulation of prostaglandin synthesis, and decrease in the levels of HCG, progesterone, and estriol [7].

Nevo and co-workers [8] have compared the neonatal course and outcome as well as gestational and labor characteristics of twin pregnancies after MFPR (64 cases) and NRT pregnancies (64 cases). The study didn't show any significant differences between mean gestational ages at delivery or mean birth-weight of twin I and twin II in RT and NRT groups. In our study, here was no significant difference in the mean gestational age at delivery, mean high birth-weight and low birth-weight, the rate of delivery at 28-34 weeks, and the rate of birth-weight discordance in RT and NRT groups. The outcomes we observed were similar to those reported in the study of Nevo.

Immediately after birth, infant survival depends on a prompt and orderly conversion to air breathing. Respiratory distress syndrome (RDS) of the newborn caused by the fetal lung immaturity continues to be a clinical problem. Because the increase in the levels of pulmonary surfactant occurs late in gestation, RDS is inversely related to the gestational age at the time of birth; the risk of RDS for infants born at 29 weeks of gestation is > 60%, while only 20% at 34 weeks [9, 10]. Therefore, we believe that the rate of preterm delivery at 28-34 week might be one of the indicators of pregnancy outcome.

Multiple pregnancies are associated with an increased rate of pregnancy complication, which is likely to be the consequence of an exaggerated physiological response to the increased placental and fetal mass [11]. In a retrospective case control study, Nevo and co-workers [8] showed that the incidence of pre-eclampsia in RT and NRT groups was 14.1% and 14.1%, and the incidence of gestational diabetes in those groups was 1.5% and 7.8%, respectively; however, these differences were not statistically significant. In our study, the differences of incidence of gestational diabetes and pregnancy-induced hypertension in RT and NRT groups were not significantly different either. In our previous study analyzing 25 cases of triplet or quadruplet pregnancies, the rate of pregnancy-induced hypertension was 48% (12/25) [12]. However, in this study, the rate of pregnancy-induced hypertension in RT group was 11.5% (15/130). We concluded that reducing the fetal mass could decrease the incidence of pregnancy-induced hypertension in multiple pregnancies

Evans and co-workers [13] reported that the pregnancy loss rates for MFPR performed at different gestation stages are as follows: at 9-12 weeks of gestation, 5.4%; at 13-18 weeks, 8.7%; at 19-24 weeks, 6.8%; and at 25 weeks, 9.1% (no statistically significant differences). Geva and co-workers [3] compared 38 cases of fetal reduction at 11-12 weeks with 70 cases of fetal reduction at 14-27 weeks; the pregnancy outcomes were not statistically different. Lipitiz [4] compared the outcomes of MFPR from triplets to twins performed at 11-12 weeks of gestation (46 cases) with the outcomes performed and at 13-14 weeks of gestation (49 cases) and found no statistically significant differences. Some researchers believe that fetal reduction should be preferably performed between 11 and 14 weeks; at this gestation stage, the risk of spontaneous miscarriage is relatively low (7%) and selection of a fetus can be performed on the basis of anomaly scan (which can detect major abnormalities) and nuchal translucency assessment (NT) to screen for aneuploidy [14].

In this study, MFPR procedures (from triplets or quadruplets to twins) were performed at $12\text{-}13^{+6}$ weeks (91cases, MFPR12), at $14\text{-}15^{+6}$ weeks (32 cases, MFPR14), and at $16\text{-}24^{+6}$ weeks (29 cases, MFPR16) respectively. Pregnancy loss rate in the MFPR16 group (31.0%) was higher than in that of MFPR12 group (8.8%) and the NRT group (6.7%), and the differences were statistically significant. The differences between pregnancy loss rate of the MFPR12 and MFPR 14 groups and that of NRT group were not statistically significant. These results showed that MFPR performed at early gestational stages can decrease the pregnancy loss rate apparently. There were no significant difference in the rates of 28-34 week delivery, the rates of birth-weight discordance, gestational diabetes, and pregnancy-induced hypertension among the three MFPR groups.

In conclusion, we observed an increased risk of pregnancy loss in the RT group in comparison with NRT group. However, MFPR performed before 16 weeks of gestation can decrease this risk.

Disclosure of conflict of interest

None.

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