IMR Press

Original Research

The early second-trimester multifetal pregnancy reduction improves pregnancy outcome

Jing-Jing Jiang[1], Ting Han[1], Yan-Hui Zhu[2,*]

[1] Center for Reproductive Medicine, Cheeloo College of Medicine, Shandong University, Jinan, 250021 Shandong, P. R. China

[2] Medical Informatics Center, Peking University, 100191 Beijing, P. R. China

*Correspondence: medic@bjmu.edu.cn (Yan-Hui Zhu)

DOI:10.31083/j.ceog.2021.01.5519

Submitted: February 05, 2020 Revised: August 31, 2020 Accepted: September 02, 2020 Published: February 15, 2021

Purpose: To evaluate pregnancy outcome of selective second-trimester multifetal pregnancy reduction (MFPR) compared with that of first-trimester MFPR, and control group which consists of women with ongoing primary twin pregnancies. *Materials and Methods*: This retrospective cohort study included all women with triplet pregnancies who underwent fetal reductions to twin pregnancies from January 2010 to December 2019 in Shandong Provincial Hospital. 154 MFPR were performed by intracardially injection of potassium chloride, 8 MFPR were performed by intracranially injection of potassium chloride. Reductions to monochorionic twins and reductions to one embryo were excluded. All procedures were performed at 12-24^{+6} wks gestation. The outcome of pregnancy in women with reduced triplets was compared with that of the control group. *Results*: We identified 162 women with reduced triplet pregnancies who underwent fetal reductions to twin pregnancies, and 160 women with ongoing primary twin pregnancies as the control group. There was a significant difference in the abortion rate between MFPR and control group. The abortion rate of the early second trimester MFPR group (at gestation 14-15^{+6} wks) (13.3%, 5/35) was not significantly different compared with that of the first trimester MFPR group (at gestation 12-13^{+6} wks) (8.3%, 8/96) or that of the control group (6.9%, 11/160). There were no significant differences in average gestation time at delivery, delivery rate in 28-34 wks, neonatal birth weight, gestational diabetes mellitus, or hypertensive disorder complicating pregnancy among the first trimester MFPR group , the early second trimester MFPR group, and the control group. *Conclusion*: In women with triplet pregnancy, fetal reduction in the early second trimester is an effective way to avoid delivery of abnormal fetuses, reduce complications during delivery, and improve neonatal quality.

Keywords

Multiple pregnancy; Multifetal pregnancy reduction

1. Introduction

Multiple births have steadily increased in recent years because of increased usage of assisted reproductive technologies in China and other countries [1–5]. Compared with women with singleton and twin pregnancies, those with triplets have significantly increased risks of maternal morbidity [6], which includes gestational diabetes [7], hypertensive disorders [8], Cesarean delivery [9, 10], excessive hemorrhage [11], and non-spontaneous heterotopic triplets [12]. To decrease the risks associated with triplet pregnancies, multifetal pregnancy reduction (MFPR) has been proposed [13, 14]. The most frequently used method is ultrasound-guided transabdominal injection of potassium chloride into the fetal heart in the chest cavity [15]. Our objective in the present study was to evaluate pregnancy outcomes after selective MFPR in the second trimester and to compare it with the those after first-trimester MFPR. Ongoing twin pregnancies were used as a control group.

2. Materials and methods

This retrospective study included all women with triplet pregnancies who underwent fetal reductions to twin pregnancies from January 2010 to December 2019 in Shandong Provincial Hospital, which lies in Shandong provincial peninsula in eastern China with a population of 98 million. 154 MFPR were performed transabdominally after local anesthetics by using a 20G needle to intracardially inject potassium chloride, 8 MFPR were performed to intracranially inject potassium chloride. Reductions to monochorionic twins and reductions to one embryo were excluded. All procedures were performed at 12-24^{+6} wks gestation. The reductions were carried out by highly skilled physicians with at least 5 year's experience in multifetal reduction. The outcome of pregnancy in women with reduced triplets was compared with that of the control group which consists of women with ongoing twin pregnancies. All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Reproductive Hospital, Shandong University (#202060).

3. Statistical analysis

Data are expressed as means ± standard deviation. Comparisons between groups were performed with Student's *t*-test for parametric data. Homogeneity of sample variances was performed with the homogeneity test of variances and

Table 1. Comparison of abortion rate in MFPR and control (ongoing twin pregnancy) groups.

Group	Cases	Abortion	
		Cases	Percentage (%)
MFPR	162	23	14.2
12–13^{+6} wk	96	8	8.3
14–15^{+6}wk	35	5	13.3
16–24^{+6}wk	31	9	$29.0^{a,b}$
Control	160	11	6.9

the chi-square test for proportions. Data were analyzed with SPSS for Windows statistical package version 13.0 (SPSS Inc., Chicago, IL, USA). A P value of < 0.05 was considered statistically significant.

4. Results

We identified 162 women with triplet pregnancies who underwent fetal reductions to twin pregnancies after excluding 23 women due to chorionic disease and congenital anomaly. We classified the MFPR groups into MFPR group at gestation 12-13^{+6} wks (the first trimester), 14-15^{+6} wks (the early second trimester), and 16-24^{+6} wks (the late second trimester). The abortion rate of the MFPR group (14.2%, 23/162) was significantly higher compared with that of the control twin group (6.9%, 11/160; $\chi^2 = 4.570$, $P < 0.05$). The abortion rate of the late second trimester MFPR group wks (29.0%, 9/31) was significantly higher compared with that of the first trimester MFPR group (8.3%, 8/96, $\chi^2 = 9.768$, $P < 0.01$) and that of the control group (6.9, 11/160, $\chi^2 = 15.140$, $P < 0.001$). The abortion rate of the early second trimester MFPR group (13.3%, 5/35) was not significantly different compared with that of the first semester MFPR group (8.3%, 8/96) or that of the control group (6.9%, 11/160) (Table 1).

The average gestation time at delivery of the MFPR group (36.8 $\pm$ 1.8 wks) was not significantly different compared with that of the control group (36.9 $\pm$ 1.4 wks) (t = -0.346, -0.163, -0.136; $P > 0.05$). The incidences of high and low fetal weight in the MFPR group were not significantly different compared with those of the control group. The delivery rates at 28-34 wks of gestation in the MFPR and control groups were 6.5% (9/139) and 7.4% (11/149) respectively (χ^2 = 0.010); incidences of asymmetric fetus growth were 12.2% (17/139) and 10.7% (16/149) respectively (χ^2 = 0.057); incidences of GDM were 2.9% (4/139) and 2.0% (3/149) respectively (χ^2 = 0.662); and incidences of HDCP were 11.5% (16/139) and 8.1% (12/149), respectively (χ^2 = 0.013); there were no statistically significant differences between the MFPR and control group for any of these variables ($P > 0.05$ for all) (Table 2).

5. Discussion

The hospital was the first in China to perform MFPR during the second trimester [15]. Since the first MFPR in the second trimester was performed in January 2002 [16], we have performed hundreds of MFPR by injection of potassium chloride into the fetal heart by now; the success rate is 90.04%, the abortion rate is 9.06%. The reason of abortion includes bleeding and infection after MFPR as well as natural abortion led by abnormal embryos.

We have also tried other methods, such as intracranial injection of potassium chloride and radiofrequency ablation, when frequent fetal movements, the awkward position of fetuses, poor thoracic display, and extremely small thorax because of fetal thoracic abnormality happened. We postponed MFPR to the second trimester. By contrast, most MFPR in China were performed during the first trimester [3]. During the first trimester, it was often difficult to confirm suspected fetal defects, and there were a higher fetal damage rate and a higher infection rate associated with transvaginal procedures.

In Ata *et al*'s study, it suggests that the obstetric outcomes of IVF triplets which spontaneously reduce to twins are similar to that of elective reduction to twins and pregnancies conceived as dichorionic twins. In our study, we try to find a better opportunity to reduce fetuses [17]. Our results suggest that MFPR in the early second trimester does not increase the risk of complications for pregnant women and newborn infants. The early second trimester MFPR is an effective way to reduce fetal defects associated with first trimester MFPR, as wells as to avoid the birth of abnormal fetuses, reduce complications of pregnant women, and improve neonatal quality. Of course, there are some limitations in our study, one of which is that we did not study the result of reducing the triplet pregnancies into singletons. In Haas *et al*'s study, it suggests that triplet pregnancies reduced to singletons rather than twins, result in better obstetric outcomes [18]. We will study the early second-trimester multifetal pregnancy reduction to singleton in the coming stage.

Abbreviations

ART, assisted reproductive technologies; GDM, gestational diabetes mellitus; HDCP, hypertensive disorder complicating pregnancy; MFPR, multifetal pregnancy reduction.

Author contributions

Yanhui Zhu designed the research study. Ting Han collected data. Jingjing Jiang performed statistics and wrote the method and results. Yanhui Zhu finished the left parts of writing and polished the whole paper. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Acknowledgment

I would like to express my gratitude to all those who helped me during the writing of this manuscript.

The authors thank Dr. Yan Sheng (Center for Reproductive Medicine, Cheeloo College of Medicine, Shandong University) for the critical reading of this manuscript.

Thank numerous individuals participated in this study.

Thanks to all the peer reviewers and editors for their opinions and suggestions.

Table 2. Comparison of pregnancy outcome and complications among MFPR and control groups.

Groups	Delivery after 28 wk gestation	Average gestation time before delivery (mean ± SD, wk)	Delivery at 28–34 wk		Birth weight (mean ± SD, g)		Asymmetric fetal growth		GDM		HDCP	
			Cases	Percentage (%)	A	B	Cases	percentage (%)	Cases	Percentage (%)	Cases	Percentage (%)
MFPR	139	36.8 ± 1.8	9	6.5	2729.2 ± 449.4	2411.5 ± 424.3	17	12.2	4	2.9	16	11.5
12–13^{+6} wk	88	36.4 ± 1.9	8	9.1	2692.9 ± 445.8	2368.3 ± 401.9	9	10.2	2	2.2	10	11.4
14–15^{+6} wk	30	37.7 ± 1.2	0	0	2849.0 ± 454.9	2534.1 ± 389.5	5	16.7	1	3.3	3	10
16–24^{+6} wk	22	36.1 ± 1.8	1	4.5	2731.5 ± 521.1	2414.0 ± 491.4	3	13.6	1	4.5	3	13.6
Control	149	36.9 ± 1.4	11	7.4	2741.6 ± 406.5	2420.5 ± 475.8	16	10.7	3	2	12	8.1
χ^2 value[a]	4.57	−0.338		0.01	−0.158	−0.138		0.057		0.662		0.013
P value[a]	0.033	0.813		0.865	0.868	0.885		0.874		0.425		0.916
χ^2 value[b]	8.653	1.281		2.693	1.31	1.396		1.652		0.418		0.298
P value[b]	0.011	0.294		0.281	0.288	0.276		0.447		0.832		0.883

Conflict of interest

The authors declare no competing interests.

References

[1] Multiple gestation pregnancy. The ESHRE Capri Workshop Group. Human Reproduction. 2000; 15: 1856-1864.

[2] Elster N. Less is more: the risks of multiple births. The Institute for Science, Law, and Technology Working Group on Reproductive Technology. Fertility and Sterility. 2000; 74: 617-623.

[3] Li R, Chen X, Yang S, Yang R, Ma C, Liu P, *et al.* Retain singleton or twins? Multifetal pregnancy reduction strategies in triplet pregnancies with monochorionic twins. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2013; 167: 146-148.

[4] Vaidya A, Stafinski T, Nardelli A, Motan T, Menon D. Assisted reproductive technologies in Alberta: an economic analysis to inform policy decision-making. Journal of Obstetrics and Gynaecology Canada. 2015; 37: 1122-1130.

[5] Sunderam S, Kissin DM, Crawford SB, Folger SG, Jamieson DJ, Warner L, *et al.* Assisted reproductive technology surveillance - United States, 2014. MMWR Surveillance Summaries. 2017; 66: 1-24.

[6] Witteveen T, Van Den Akker T, Zwart JJ, Bloemenkamp KW, Van Roosmalen J. Severe acute maternal morbidity in multiple pregnancies: a nationwide cohort study. American Journal of Obstetrics and Gynecology. 2016; 214: 641.e641-641.e610.

[7] Raval DB, Naglak M, Iqbal SN, Ramsey PS, Craparo F. Outcomes of Triplets reduced to Twins versus non-reduced Triplet Pregnancies. Journal of Clinical Gynecology and Obstetrics. 2015; 4: 160-163.

[8] Foo JY, Mangos G, Brown M. OS096. Characteristics of hypertensive disorders in twin versus singleton pregnancies. Pregnancy Hypertension. 2012; 2: 230-231.

[9] Monson M, Silver RM. Multifetal gestation: mode of delivery. Clinical Obstetrics and Gynecology. 2016; 58: 690-702.

[10] Albano B, Del Sette M, Roccatagliata L, Gandolfo C, Primavera A. Cortical subarachnoid hemorrhage associated with reversible cerebral vasoconstriction syndrome after elective triplet cesarean delivery. Neurological Sciences. 2012; 32: 497-501.

[11] Kalu E, Wayne C, Croucher C, Findley I, Manyonda I. Triplet pregnancy in a Jehovah's witness: recombinant human erythropoietin and iron supplementation for minimising the risks of excessive blood loss. BJOG. 2002; 109: 723-725.

[12] Korkontzelos I, Vlachioti A, Mavridou P, Rapi A, Tsanadis G, Stefos T. Heterotopic triplet pregnancy after in vitro fertilization and intracytoplasmatic sperm injection complicated with ovarian hyperstimulation syndrome single twin fetal demise and cervical incompetence: a successful obstetrical outcome. Clinical and Experimental Obstetrics & Gynecology. 2019; 46: 1007-1010.

[13] Berkowitz RL, Lynch L, Chitkara U, Wilkins IA, Mehalek KE, Alvarez E. Selective reduction of multifetal pregnancies in the first trimester. The New England Journal of Medicine. 1988; 318: 1043-1047.

[14] Wapner RJ, Davis GH, Johnson A, Weinblatt VJ, Fischer RL, Jackson LG, *et al.* Selective reduction of multifetal pregnancies. Lancet. 1990; 335: 90-93.

[15] Monni G, Illescas T, Iuculano A, Floris M, Mulas F, McCullough LB, *et al.* Single center experience in selective feticide in high-order multiple pregnancy: clinical and ethical issues. Journal of Perinatal Medicine. 2017; 44: 161-166.

[16] Wang Y. Ultrasound-guided selective pregnancy reduction: analysis of 43 cases. Journal of Medical Imaging. 2009; 19: 595-598.

[17] Ata B, Rasillo LJ, Sukhdeo S, Son WY, Tan SL, Dahan MH. Obstetric outcomes of IVF trichorionic triamniotic triplets which are spontaneously or electively reduced to twins. Journal of Assisted Reproduction and Genetics. 2012; 28: 1217-1222.

[18] Haas J, Hourvitz A, Dor J, Yinon Y, Elizur S, Mazaki-Tovi S, *et al.* Pregnancy outcome of early multifetal pregnancy reduction: triplets to twins versus triplets to singletons. Reproductive Biomedicine Online. 2015; 29: 717-721.