



The Value of Fetal Reduction in IVF Dichorionic Triplets: A Retrospective Controlled Study

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Abstract

Aim: To evaluate the feasibility of one fetal reduction in IVF patients with dichorionic triplets.

Methods: The clinical data of thirty-one patients (Group A) in dichorionic triplet pregnancy undergoing monochorionic twin reduction *via* transvaginal ultrasound and another forty-eight patients (Group B) in monochorionic twin pregnancy were compared and analyzed retrospectively.

Results: No statistically significant differences were found in maternal age and BMI and basal hormone levels between two groups. The abortion rate and spontaneous reduction rate were comparable in two groups. The gestational days in group A (261.0 ± 16.8 vs. 251.5 ± 11.2 ; $P < 0.05$) were significantly longer than in group B. The preterm birth rate (33.33% vs. 76.92% ; $P < 0.05$) and caesarean delivery rate (83.33% vs. 100.00% ; $P < 0.05$) in group A was significantly lower. The birth weight was heavier (2609.2 ± 502.6 vs. 2376.5 ± 400.2 ; $P < 0.05$) and low birth weight infant rate (38.89% vs. 64.18% ; $P < 0.05$) were lower in group A, with significant differences. One pregnancy complication occurred in group A and four occurred in group B. One newborn in group A and three in group B were born with deformity, with no significant differences.

Conclusion: One fetal reduction in patients with IVF dichorionic triplets is a relatively safe and effective operation which does not increase the abortion rate after the operation, thus helping improve pregnancy outcomes.

Keywords: Fetal reduction; Multiple gestation; Assisted reproductive technology; Clinical

Introduction

In recent years, the proportion of infertile couples among married ones has risen to 10% to 15% worldwide and the rapid development of Assisted Reproductive Technology (ART) enables a lot of families in despair to retrieve hope and love. However, the incidence of multiple pregnancy also shows a clear rising trend, which leads to increased pregnancy complications and prenatal mortality year by year. Since it was first published in 1988, fetal reduction has witnessed considerably changes over the past decades [1]. On the premise of keeping 1 to 2 embryos, the termination of development in other embryos under ultrasound guidance could effectively reduce the complications of mothers and infants caused by multifetal pregnancy and decrease the prevalence of maternal and neonatal disease significantly [2]. In cases of dichorionic triplets, reducing one monochorionic twin to avoid the complication such as Twin to Twin Transfusion Syndrome (TTTS) is usually recommended. There are few reports on the outcome of such untypical fetal reduction. The purpose of this study was to compare the outcome of reducing one monochorionic twin in dichorionic triplet pregnancies with monochorionic twin pregnancies so as to ascertain whether the reduction in one monochorionic twin would exert a negative impact on pregnancy and fetal growth.

Materials and Methods

Study patients

A retrospective study was conducted at the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University (Wenzhou, People's Republic of China) from Feb 2014 to Nov 2017. This study was approved by the Research Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University (Ethical Reference No: L-2018-12). All patients completed informed written consent in accordance with the ethics committee protocol. About 31 patients in dichorionic triplet pregnancy undergoing monochorionic twin reduction *via* transvaginal

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ultrasound were recruited in group A. Another 48 patients in monochorionic twin pregnancy were enrolled as a control group in group B at the same period of time. The following data were retrieved from medical records: maternal age, body mass index, basal hormone level (LH, FSH, E2, P), fasting blood glucose level, TSH level, birth weights, newborn sex, delivery pattern, gestational age (in days) at the day of abortion or delivery, pregnancy complications, number of live-born infant and any deformity of the infants. Chorionicity was determined according to Sepuvela et al., [3].

Methods

Multifetal pregnancy reduction was performed at 7 to 10 weeks of gestation in group A. Patients undergoing fetal reduction procedure were fully informed of the possible risks and informed consent was obtained. Preoperative sedation was properly used. The patients were placed in the dorsal lithotomy position after voiding the bladder. A transvaginal ultrasound scan was undertaken to determine the position of gestational sacs and the size of embryos. Monochorionic twin was chosen as the target fetus to be reduced. Fetal reduction was achieved by puncturing a 16-gauge needle (Smiths Medical International. Ltd) and aspirating the fetal parts, with no drug injection. Patients were advised to undergo bed rest for a few hours after the operation. Transvaginal ultrasound examinations were carried out after 1 day and 7 days after fetal reduction. Once the death of the reduced fetus was confirmed and the remained fetus was viable, subsequent prenatal routine follow-up would be continued. Obstetric and neonatal outcomes including gestational age at delivery, neonatal birth weight and sex were followed up by telephone calls. The definitions of certain outcomes were listed in Table 1.

Statistical methods

SPSS20.0 software was used for all statistical analysis in the study. Results were presented as mean \pm standard deviation or percentage (%). Measured data were compared with analysis of variance. Enumeration data were performed with chi-square test. $P < 0.05$ was considered statistically significant.

Results

General information

The general information of the patients in the study is shown in Table 2. Maternal age ranged from 24y to 39y in two groups. Body Mass Index (BMI), fasting glucose level, Thyroid Stimulating Hormone (TSH) level, basal levels of LH, E2, P and FSH were comparable between the two groups.

Fetal reduction and pregnancy outcomes

In group A, spontaneous reduction to another monochorionic twin after transvaginal fetal reduction occurred in twelve cases. Spontaneous abortion occurred in seven cases, early abortion in five cases and late abortion in two cases. In group B, spontaneous reduction to one monochorionic twin occurred in eleven cases and spontaneous abortion occurred in nine cases, early abortion in four cases and late abortion in five cases. The spontaneous abortion rates in two groups were comparable. Significant difference in mean gestational days of delivery were observed between groups A and B (261.0 ± 16.8 vs. 251.5 ± 11.2 ; $P < 0.05$). Women in group A also had a lower caesarean delivery rate (82.33% vs. 100% ; $P < 0.05$) and higher birth weight (2609.2 ± 502.6 vs. 2376.5 ± 400.2 ; $P < 0.05$), with significant differences. The newborn sex in two groups was comparable in two groups. No TTTS occurred in group A while two TTTS occurred in group B, which resulted in intrauterine fetal death

Table 1: Certain definition.

| | Definition |
|-------------------------|--|
| Early abortion | Occurred before 12 gestational weeks |
| Late abortion | Occurred between 12 to 27 ⁺⁶ gestational weeks |
| Preterm labour | Delivery between 28 to 36 ⁺⁶ gestational weeks |
| Full-term labour | Delivery between 37 to 41 ⁺⁶ gestational weeks |
| Spontaneous reduction | A missed abortion of one fetus in the twin pregnancy after fetal reduction |
| Low birth weight infant | Newborns weighing less than 2,500 grams |

Table 2: The comparison of general information.

| | Group A | Group B | F | P |
|-----------------------------------|-------------------|-------------------|-------|-------|
| Maternal Age (years) | 30.71 \pm 3.89 | 30.88 \pm 3.87 | 0.149 | 0.7 |
| Maternal BMI (kg/m ²) | 21.74 \pm 3.64 | 21.05 \pm 2.94 | 0.184 | 0.357 |
| Basal hormone level | | | | |
| LH (IU/L) | 5.16 \pm 3.95 | 5.25 \pm 4.02 | 1.244 | 0.92 |
| E2 (pg/mL) | 49.48 \pm 46.32 | 46.32 \pm 13.41 | 2.528 | 0.385 |
| P (ng/ml) | 0.45 \pm 0.24 | 0.49 \pm 0.20 | 0.138 | 0.406 |
| FSH (IU/L) | 77.13 \pm 2.12 | 7.44 \pm 2.56 | 0.532 | 0.572 |
| FBG (mmol/L) | 4.81 \pm 0.45 | 4.90 \pm 0.42 | 0.338 | 0.397 |
| TSH (μ IU/ml) | 2.32 \pm 0.83 | 2.11 \pm 1.01 | 1.199 | 0.325 |

*: Compared with group A, $P < 0.05$

Table 3: The comparison of fetal reduction and pregnancy outcomes.

| | Group A | Group B | P |
|----------------------------------|--------------------|---------------------|-------|
| Early abortion rate (%) | 16.13 (5/31) | 8.33 (4/48) | 0.287 |
| Late abortion rate (%) | 6.45 (2/31) | 10.42 (5/48) | 0.545 |
| Spontaneous reduction rate (%) | 38.71(12/31) | 22.92 (11/48) | 0.131 |
| gestational days (day) | 261.0 \pm 16.8 | 251.5 \pm 11.2* | 0.009 |
| Preterm birth rate (%) | 33.33 (8/24) | 76.92 (30/39)* | 0.001 |
| Caesarean delivery rate (%) | 83.33 (20/24) | 100.00 (39/39)* | 0.008 |
| Birth weight | 2609.2 \pm 502.6 | 2376.5 \pm 400.2* | 0.012 |
| Male newborn rate (%) | 69.44 (25/36) | 55.22 (37/67) | 0.16 |
| Pregnancy complication rate (%) | 3.22 (1/31) | 8.33 (4/48) | 0.239 |
| Infant deformity rate (%) | 2.78 (1/36) | 4.48 (3/67) | 0.67 |
| Low birth weight infant rate (%) | 38.89 (14/36) | 64.18 (43/67)* | 0.014 |

*: Compared with group A, $P < 0.05$

during third trimester. As for pregnancy complications, one severe preeclampsia occurred in group A while two severe preeclampsia and four gestational diabetes mellitus occurred in group B. One newborn in group A was born with gastroschisis. In group B, two newborns were born with finger swan-neck deformity and one with congenital malformation of liver and there were no significant differences between two groups. The details were shown in Table 3.

Discussion

Multiple pregnancy in ART is often caused by multi embryo transfer which mostly results in fraternal multiple pregnancies. Monochorionic multiple pregnancy is not a common condition, which accounts for about 20% to 30% of all multiple pregnancy [4]. It occurs when a single embryo splits before the eighth day after fertilization. Ovulation induction, zona pellucida micromanipulation, prolonged cultivation time of embryo could be associated to monozygotic multiple pregnancy [5-7]. By performing an obstetric ultrasound at a gestational age of 10 to 14 weeks, the presence of a "T-sign" at the inter-

twin membrane-placental junction is indicative of monochorionic-diamniotic twins, whereas dichorionic twins present with a "lambda (λ) sign [8]. Since monochorionic placenta usually contains various anastomoses between two fetal circulations, the injection of a cardiotoxic agent into one fetus is not applicable as it may affect the other twin. Fetal reduction in monochorionic pregnancies has a comparatively higher risk than that in multichorionic pregnancies and it requires superb skills that ablate or interrupt blood flow in the umbilical cord of the affected fetus. In high-order multiple fetal reduction procedure, monochorionic twin is often chosen as the targeted fetus to be reduced in order to decrease the incidence of some specific complications in monochorionic twins such as TTTS, Selective Intrauterine Growth Restriction (sIUGR), Twin Anemia Polycythaemia Sequence (TAPS), birth weight discordance and twin reversed arterial perfusion sequence [9-11]. In addition, the risk of complication in monoamniotic twins is substantially higher because of the potential umbilical cord entanglement and compression. If a woman had a triplet pregnancy with monoamniotic twins, it is usually recommended to reduce both of the twins. Although women in China are no longer restricted to family planning policy which allowed them to have only one child in their lifetime, there are still a number of women who prefer to give birth to twins as they consider it a suffering once for all.

In this study, although only one monochorionic twin was reduced in dichorionic triplets, there were still twelve (38.71%) fetuses got reduced spontaneously in the same monochorionic sac after the operation. which could be ascribed to nonspecific inflammation caused by mechanical operation? Also, the necrotic tissue of dead fetus may exert a negative effect on the other fetus *via* shared blood vessels or placenta. The overall pregnancy loss rate of fetal reduction reported was 4.7%, which indicated that the fetal reduction in dichorionic triplets has a higher pregnancy loss rate [12]. Thus, adept operative technique was an important foundation of decreasing the operative complication. Li R et al., [13] reported that at a gestational age of 6 to 8 weeks, when the distance of two monochorionic embryos was over 1 cm, aspirating one monochorionic twin without drug injection was feasible to retain the other twin. Since the ultrasonic vaginal probe is closer to the uterus and thus has a shorter puncture distance, the operation accuracy, success rate and the resolution of vaginal probe is relatively higher in comparison with abdominal probe, which can be applied in early fetal reduction. It is reported that the abortion rate in twin pregnancies was seven times higher than singleton pregnancies [14]. Among the twin pregnancies, the monochorionic twin pregnancies have doubled abortion rate than dizygotic twin pregnancies. Although spontaneous reduction might occur sometimes after fetal reduction in one monochorionic twin, certain complications such as TTTS could be effectively avoided, which consequently decreased late abortion rate.

Based on the success rate of IVF at present, it is still controversial to have only one embryo transferred as a routine method in clinical practice. However, triplet pregnancy cannot be avoided if two embryos were transferred. As for such patients, although more than half of them still stand the chance of retaining healthy twins after reducing one monochorionic twin, since it increases the rate of complications and gives heavier load to family, retaining one singleton is always the best choice when deciding about using MFPR to improve pregnancy outcomes. Recently, it has become a tendency to have only one embryo transferred in our center and the pregnancy rate was quite satisfactory.

Conclusion

In conclusion, MFPR in early pregnancy was a relatively safe and effective operation to improve the outcome of pregnancy. However, fetal reduction could only be deemed as a remedial measure. Further discussion is still needed to ensure the pregnancy success rate as well as reducing the incidence rates of multifetal pregnancy.

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