

Original Article

Outcome and risk of abortion in pregnant women with triplets who underwent fetal reduction

Guirong Qin¹, Yan Huang², Xun Lan³

¹Family Planning Ward, Department of Gynecology, The First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi Zhuang Autonomous Region, China; ²Department of Obstetrics, The Second Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi Zhuang Autonomous Region, China; ³School of Clinical Medicine, Weifang Medical University, Weifang, Shandong Province, China

Received January 17, 2019; Accepted March 3, 2020; Epub May 15, 2020; Published May 30, 2020

Abstract: Objective: To explore the outcome and risk of abortion after fetal reduction in women with triplet pregnancy. Methods: The clinical data of 184 women with triplet pregnancy who underwent selective fetal reduction were retrospectively analyzed. The women were divided into two groups, one with twins (n=141) and the other with a single fetus (n=43) after fetal reduction. The intracardiac injection of potassium chloride in the fetus was adopted for selective fetal reduction. Pregnancy outcome and neonatal condition after fetal reduction between the two groups were compared. Results: The pregnancy success rate of 184 women originally with triplet pregnancy was 91.30%. Compared with the twins group, women in single fetus group had a significantly higher pregnancy success rate, lower abortion rate and cesarean section rate, heavier newborns at birth, and longer gestational period (all $P < 0.05$). Conclusion: Selective fetal reduction in women with triplet pregnancy can improve the safety of mother and infants, achieves significantly better pregnancy outcome with fetal reduction to a single fetus than that of twins. Therefore, in order to improve the pregnancy outcome of women with triplet pregnancy and reduce the abortion rate, the number of fetal reductions can be determined according to the actual condition of the pregnant women.

Keywords: Pregnancy, fetal reduction, pregnancy outcome, abortion

Introduction

With the development and improvement of assisted reproductive technology in clinics, multiple pregnancy rates have increased significantly. Studies show that triplet pregnancy causes a threefold higher risk of disability in newborns than in single pregnancies; with the incidence of functional growth retardation at about 12%-34%, the incidence of eclampsia up to 40%, and the incidence of preterm births at 87.8%, multiple pregnancy greatly increases the incidence of maternal complications and poor perinatal outcomes, such as anemia, preterm birth and abortion, and it also can bring an economic and mental burden to the family [1, 2]. Current prenatal screening and prenatal diagnosis techniques allow multiple pregnancies to be easily to detect before delivery, and corresponding interventions can be carried out. Selective multi-fetal pregnancy reduction is a multi-fetal reduction technique commonly

used in the second trimester of pregnancy, and is a technique that selectively terminates the development of dysplastic, malformed or excessive fetuses to reduce maternal and neonatal complications and ensure the normal survival and healthy development of fetuses [3].

Potassium chloride fetal reduction has been recognized in clinical technology since the 1980s [4, 5]. The pregnancy success rate increases with the fetal reduction technique, which effectively decreases the occurrence of maternal complications [6, 7]. Potassium chloride fetal reduction has been widely used as a relatively safe, simple, convenient, and effective measure for dichorionic multiple pregnancies. Especially for pregnant women with more than 3 fetuses, selective fetal reduction can be beneficial for pregnancies with high complications [8, 9]. However, there is a great controversy about the advantages and disadvantages of fetal reduction in triplet pregnancy, and the

Fetal reduction improves pregnancy outcomes

risk of maternal and neonatal complications caused by triplet pregnancy should not be ignored [4, 10]. In fetal reduction, potassium chloride is injected into the heart of the fetus that is planned to be terminated during the second trimester of pregnancy, without any adverse effects on the mother and other fetuses [11, 12]. In this study, selective fetal reductions from triplets to a single fetus and from triplets to twins were carried out in women with triplet pregnancy, to analyze their effects on pregnancy outcome.

Materials and methods

Study subjects

A total of 184 women with triplet pregnancy who underwent fetal reduction in the Second Affiliated Hospital of Guangxi Medical University from April 2016 to April 2019 participated in this study. Pregnancy outcomes and risks with twins or single fetus after fetal reduction were retrospectively analyzed. Of the 184 women, 163 became pregnant by using assisted reproductive technology, and 21 women became pregnant naturally. The 184 women were divided into two groups according to the number of the remaining fetuses: twins group (reduction to twins, n=141) and single fetus group (reduction to a singleton, n=43). The pregnant women and their families signed the informed consent before the study. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Guangxi Medical University.

Inclusion criteria

Pregnant women that were diagnosed with triplet pregnancy by B-mode ultrasound initiatively requested fetal reduction or had abnormal fetuses; the gestation period was 12-25 weeks; women with triplet pregnancy had monochorionic twins; women did not have liver dysfunction nor coagulation disorders; both the husband and wife gave informed consent to the fetal reduction.

Exclusion criteria

Women had contraindications of continued pregnancy; vaginal bleeding and other threatening abortion manifestations appeared within one week before fetal reduction; women had liver dysfunction or coagulation disorders.

Indications of fetal reduction

In this study, 141 women who received fetal reduction to twins had tri-chorionic tri-amniotic sac triplet pregnancy, of which 19 women requested the fetal reduction due to abnormal fetal development during the gestation period and the rest of the women initiatively reduced the number of fetuses. In the single fetus group, 14 of 43 women initiatively reduced the number of fetuses; 29 women had dichorionic tri-amniotic sac triplet pregnancy, in whom the fetal reduction of one fetus would cause the other fetus to be lost to fetal heart failure within 24 h, thus only one fetus could be retained, equivalent to reduction to a single fetus [13].

Methods

Preoperative preparation: Routine preoperative inspection was performed for all pregnant women before selective fetal reduction, and women with surgical contraindications mainly including vaginal bleeding and reproductive system inflammation were excluded. The pregnant women and their families were informed in detail about the purpose, methods, outcomes, possible complications and matters needing attention in fetal reduction before the surgery. The fetal reduction was carried out after the pregnant women signed the informed consent. *Selection of the fetus to be reduced:* The size, morphology and nuchal translucency thickness of fetuses were detected by ultrasound before the surgery; if abnormality was found during ultrasonic examination, the abnormal fetus was reduced; if no abnormality was found, the fetus with lighter body weight, less amniotic fluid or one located at the bottom of the uterus was selected for the surgery. Before the surgery, the pregnant women were guided to empty the bladder. Then the pregnant women were placed in a supine position to perform ultrasonic examination to determine the number and position of the fetuses, and the chorionic properties; the fetus to be reduced was positioned to avoid incorrect termination.

Surgical method: The surgery used in this study was a traditional fetal reduction by injecting potassium chloride (Specification: 10 mL:1 g, Guangdong Leiyunshang Pharmaceutical Co. Ltd., China) into the heart of the target fetus [14, 15]. After routine disinfection and draping,

Fetal reduction improves pregnancy outcomes

Table 1. Analysis of general data of pregnant women in two groups

	Twins group (n=141)	Singleton group (n=43)	t	P
Age (years)	29.6±2.8	29.8±3.1	1.063	0.853
Maternal weight (kg)	62.3±10.9	61.1±10.6	0.703	0.483
Gestational weeks in fetal reduction (weeks)	15.2±3.5	15.1±3.1	0.314	0.754
Total number of delivery (times)	1.2±1.4	1.1±1.3	-0.361	0.677
Fertilization way				
In vitro fertilization-embryo transfer	51	13	2.592	0.386
Natural way	16	5		
Ovulation induction	65	21		
Other assisted reproductive technologies	9	4		

Note: Other assisted reproductive technologies mainly included intracytoplasmic sperm injection and preimplantation genetic diagnosis.

abdominal ultrasonography was performed in the pregnant woman and the fetus was located. The operator quickly and accurately inserted a 23 G puncture needle into the heart of the fetus to be reduced and immediately pulled back the needle. After the blood appeared, 2-5 mL 10% potassium chloride was injected into the heart of the fetus to be reduced. Under ultrasound monitoring, the heartbeat of the injected fetus was observed until it stopped. The puncture needle was then pulled out, and ultrasound monitoring continued for more than 15 min to determine fetal asystole. Pregnant women were ordered to stay in bed for 24 h after surgery. Antibiotics were used prophylactically to prevent infection in the pregnant women, and tocolytic therapy was performed. Ultrasonic examination was performed again 24 h after the surgery to determine the effect of the surgery.

Outcome measurements

All pregnant women were admitted to the hospital for coagulation function and routine blood tests at 20-24 weeks of pregnancy after the surgery. Meanwhile, obstetric ultrasound was used to measure the length of the cervical canal of the pregnant women, and cervical vaginal secretions were obtained to detect fetal fibronectin. The pregnancy outcome and abortion rate of the 184 pregnant women were acquired by telephone follow-up and by consulting the delivery records of the pregnant women that enrolled in this study. Pregnancy outcome indicators included delivery mode, pregnancy complications (gestational diabetes mellitus and gestational hypertension), gestational weeks at the end of pregnancy, and newborn birth weight. The survival of at least one newborn was used as the criterion for a suc-

cessful pregnancy, and the pregnancy success rate of the pregnant women in the two groups was calculated.

Statistical analysis

All data were analyzed by using SPSS 22.0 statistical software (IBM, USA). The measurement data were tested for normality; the data that followed a normal distribution were shown as mean ± standard deviation ($\bar{x} \pm s$), and t test was used for comparison between groups. The enumeration data were expressed as the number of pregnant women/percentage (n%), and the chi-square test was used. $P < 0.05$ indicated that the difference was statistically significant.

Results

General data

There were no differences in average age, average gestational weeks at fetal reduction and fertilization method between the twins group and the single fetus group (all $P > 0.05$, **Table 1**).

Pregnancy success rate and newborn survival rate

Of the 184 women with triplet pregnancy in this study, 168 women successfully completed their pregnancies, with a pregnancy success rate of 91.30%. Of the 141 pregnant women in the twins group, 6 pregnant women had only 1 newborn that survived, of which 3 pregnant women had newborns that died with a body weight of less than 1500 g, and the other 3 pregnant women had 1 fetus that died in utero. Of the 16 women with pregnancy failures, 13 pregnant women aborted before the 28th ges-

Fetal reduction improves pregnancy outcomes

Table 2. Analysis of pregnancy success rate in two groups

	Live birth	Stillbirth
Twins group (n=141)	126 (89.36%)	15 (10.64%)
Singleton group (n=43)	42 (97.67%)	1 (2.33%)
t	7.371	
P	0.021	

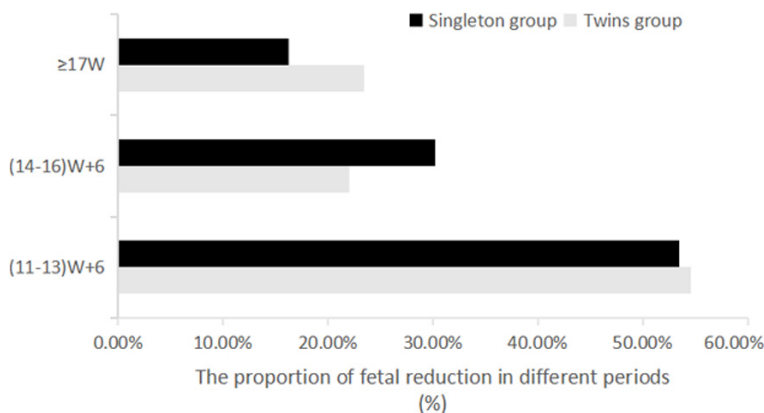


Figure 1. Analysis of the average gestational week ratio of the two groups during the reduction.

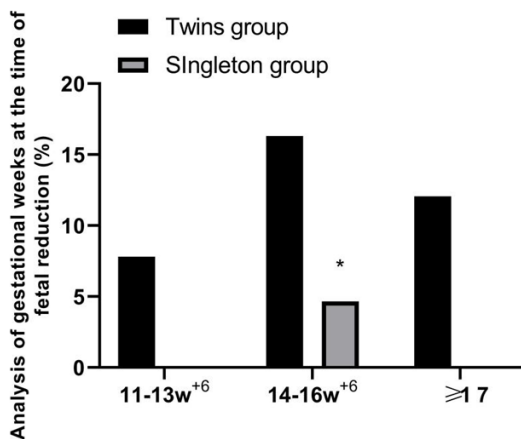


Figure 2. Analysis of abortion rate of pregnant women at different gestational period in two groups. Compared with the twins group, *P<0.05.

tational week, and 3 pregnant women experienced neonatal death after delivery after 29 gestational weeks. The pregnancy success rate of pregnant women with fetal reduction to a single fetus was significantly higher than that of pregnant women with fetal reduction to twins (P=0.021, **Table 2**).

In this study, 141 pregnant women with fetal reduction to twins successfully delivered 252

newborns; 3 newborns died after birth, and 249 newborns survived. In the single fetus group, a total of 42 newborns were delivered, and one fetus was aborted in the second trimester of pregnancy. There was a difference in the newborn survival rate between the two groups (P=0.033).

Comparison of gestational weeks in fetal reduction

The average gestational week at selective fetal reduction was 15.2±3.5 weeks in the twins group and 15.1±3.1 weeks in the single fetus group (P=0.754). The gestational weeks for selective fetal reduction were divided into three periods: 11-13 weeks+6, 14-16 weeks+6 and ≥17 weeks. There were no significant differences in the

proportion of pregnant women at the three periods between the two groups (P=0.731, 0.324, and 0.442, **Figure 1**).

Gestational weeks in fetal reduction and the abortion rate

At 11-13 weeks+6, 14-16 weeks+6 and ≥17 weeks of the pregnancy, the abortion rate was 11 (7.80%), 23 (16.31%) and 17 (12.06%) in the twins group and 0 (0%), 2 (4.65%) and 0 (0%) in the single fetus group. The abortion rate at different gestational weeks in the twins group was significantly higher than that in the single fetus group (P=0.038, 0.024, and 0.021, **Figure 2**).

Analysis of complications

There were significantly more pregnant women with gestational hypertension and diabetes mellitus in the twins group than in the single fetus group. There was no significant difference in the incidence of pregnancy complications between the two groups (P=0.556, **Table 3**).

Delivery gestation time and cesarean delivery rate

The average delivery gestational period was 36.4±1.7 weeks in the twins group and

Fetal reduction improves pregnancy outcomes

Table 3. Analysis of pregnancy complications in two groups

	Gestational hypertension	Gestational diabetes mellitus	Incidence of complications
Twins group (n=141)	15 (10.64%)	4 (2.84%)	13.48%
Singleton group (n=43)	4 (9.30%)	2 (4.65%)	13.95%
X ²	0.801	0.558	0.936
P	0.530	0.428	0.556

Table 4. Analysis of gestational weeks and delivery mode of pregnant women in two groups

	Delivery gestational weeks	Cesarean delivery rate
Twins group (n=141)	36.4±1.7	124 (87.94%)
Singleton group (n=43)	38.7±1.9	23 (53.49%)
X ²	7.693	13.380
P	0.036	0.001

Table 5. Analysis of body weight at birth in two groups

	Twins group (n=141)	Singleton group (n=43)	X ²	P
<1500g	5 (3.55%)	0 (0.00%)	1.487	0.116
1500-1999 g	11 (7.80%)	2 (4.65%)	0.948	0.174
2000-2499 g	50 (35.46%)	5 (11.63%)	7.281	0.035
≥2500 g	75 (53.19%)	36 (83.72%)	8.845	0.019
Average bodyweight (g)	2415.38±235.19	3051.48±218.56	8.420	0.023

Table 6. Analysis of intrauterine infection

	Infected	Uninfected	X ²	P
Twins group	2	139	0.594	0.741
Singleton group	1	42		

38.7±1.9 weeks in the singleton group (P=0.036). Cesarean section was the main method of delivery in the singleton group and the twins group, but the cesarean delivery rate in the twins group was significantly higher than that in the singleton group (P=0.001, **Table 4**).

Neonatal condition

The body weight of newborns at birth in the singleton group was significantly higher than that in the twins group (P=0.023, **Table 5**).

Analysis of intrauterine infection

Two pregnant women suffered from intrauterine infection after the surgery in the twins group, and 1 pregnant woman suffered from intrauterine infection after surgery in the singleton group. There was no difference in the

rate of intrauterine infection between the two groups (P=0.741, **Table 6**).

Discussion

Relevant statistics show that triplet pregnancy has 4 times higher probability of delivery before 29 gestational weeks, 3 times higher mortality rate of ≥1 newborn, and about 1.4 times and 1.8 times higher incidences of gestational hypertension and gestational diabetes mellitus than in twin pregnancy [16]. Therefore, selective fetal reduction in the second trimester of triplet pregnancy can effectively improve the pregnancy success rate and reduce the perinatal mortality rate and probability of maternal complications [17].

Effect of gestational weeks in fetal reduction on pregnancy outcomes

There were significant differences in delivery gestational times and newborn birth weights between fetal reduction to twins and a single fetus. Compared with fetal reduction to twins, the average delivery gestational period in fetal reduction to a single fetus lengthened for about 2.3 weeks, and the average newborn birth weight increased about 636 g. Moreover, fetal reduction to a single fetus did not increase the risk of abortion during pregnancy. Therefore, it could be preliminarily concluded that fetal reduction from triplets to a single fetus had more advantages in delivery gestational time and newborn birth weight, which were conducive to increasing the proportion of full-term delivery. In a relevant study that followed 180 pregnant and lying-in women (44 women with fetal reduction to a single fetus and 136 women with fetal reduction to twins), there was no significant difference in the proportion of abortion rate between the two groups, while the gestational period in

Fetal reduction improves pregnancy outcomes

the singleton group lengthened significantly [18]. Another relevant study also showed that the risk of preterm birth before 34 gestational weeks in the singleton group was significantly lower than that in twins group, after fetal reduction in the second trimester of pregnancy [19-21].

Effect of number of remaining fetuses on pregnancy outcomes after fetal reduction

In a previous study by Obican et al., it showed that the rate of preterm births in fetal reduction from triplets to a singleton decreased significantly as compared to fetal reduction to twins, but there were more fetuses that stopped developing in the uterus after fetal reduction to a singleton; revealing the incidences of pregnancy complications in fetal reduction to a singleton and twins were 0.5% and 1.6%, respectively [8]. In this study, the gestational weeks in fetal reduction were divided into three periods: 11-13 weeks⁺⁶, 14-16 weeks⁺⁶ and ≥ 17 weeks. The results showed that the proportion of pregnant women at different periods was basically similar, but the abortion rate at different periods between the two groups was significantly different. Thus, fetal reduction from multiple fetuses to a singleton resulted in better pregnancy outcomes.

In this study, selective fetal reduction in women with triplet pregnancy was beneficial to improve maternal and infant safety. Fetal reduction to a singleton had significantly better pregnancy outcomes than fetal reduction to twins, and it did not increase the postoperative abortion risk. Therefore, in order to improve the pregnancy outcome of women with triplet pregnancy and reduce the abortion rate, it suggests pregnant women can reduce the fetuses to a singleton according to their actual situations. However, as this is a small sample size single-center study, it is necessary to cooperate with multiple centers and further expand the sample size.

In summary, fetal reduction can improve obstetric outcomes by reducing the number of fetuses, and the rate of abortion significantly reduced as the technology matures.

Disclosure of conflict of interest

None.

Address correspondence to: Yan Huang, Department of Obstetrics, The Second Affiliated Hospital of Guangxi Medical University, No. 166 Daxue East Road, Xixiangtang District, Nanning 530-007, Guangxi Zhuang Autonomous Region, China. Tel: +86-0771-3279332; Fax: +86-0771-3279332; E-mail: huangyangx2h@163.com

References

- [1] Anthoulakis C, Dagklis T, Mamopoulos A and Athanasiadis A. Risks of miscarriage or preterm delivery in trichorionic and dichorionic triplet pregnancies with embryo reduction versus expectant management: a systematic review and meta-analysis. *Hum Reprod* 2017; 32: 1351-1359.
- [2] Dodd JM, Dowswell T and Crowther CA. Reduction of the number of fetuses for women with a multiple pregnancy. *Cochrane Database Syst Rev* 2015; Cd003932.
- [3] Zhuo Y, Feng S, Huang S, Chen X, Kang Y, Si C, Li Z, Zhou Y, Zhou L, Zhang T, Ji W, Niu Y and Chen Y. Transabdominal ultrasound-guided multifetal pregnancy reduction in 10 cases of monkeys. *Biol Reprod* 2017; 97: 758-761.
- [4] Bebbington M. Selective reduction in multiple gestations. *Best Pract Res Clin Obstet Gynaecol* 2014; 28: 239-47.
- [5] Bajoria R, Ward SB and Adegbite AL. Comparative study of perinatal outcome of dichorionic and trichorionic iatrogenic triplets. *Am J Obstet Gynecol* 2006; 194: 415-24.
- [6] Ehsanipoor RM, Haydon ML, Lyons Gaffaney C, Jolley JA, Petersen R, Lagrew DC and Wing DA. Gestational age at cervical length measurement and preterm birth in twins. *Ultrasound Obstet Gynecol* 2012; 40: 81-6.
- [7] Peress DA, Peaceman AM and Yee LM. Evaluation of trichorionic versus dichorionic triplet gestations from 2005 to 2016 in a large, referral maternity center. *Am J Perinatol* 2017; 34: 599-605.
- [8] Obican S, Brock C, Berkowitz R and Wapner RJ. Multifetal pregnancy reduction. *Clin Obstet Gynecol* 2015; 58: 574-84.
- [9] ESHRE Capri Workshop Group. Birth defects and congenital health risks in children conceived through assisted reproduction technology (ART): a meeting report. *J Assist Reprod Genet* 2014; 31: 947-58.
- [10] Monni G, Illescas T, Iuculano A, Floris M, Mulas F, McCullough LB, Chervenak FA and Gelber SE. Single center experience in selective fetocide in high-order multiple pregnancy: clinical and ethical issues. *J Perinat Med* 2016; 44: 161-6.
- [11] Spittle A, Orton J, Anderson PJ, Boyd R and Doyle LW. Early developmental intervention

Fetal reduction improves pregnancy outcomes

- programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants. *Cochrane Database Syst Rev* 2015; Cd005495.
- [12] Morikawa M, Cho K, Yamada T, Yamada T, Sato S and Minakami H. Clinical features and short-term outcomes of triplet pregnancies in Japan. *Int J Gynaecol Obstet* 2013; 121: 86-90.
- [13] Elhenicky M, Distelmaier K, Mailath-Pokorny M, Worda C, Langer M and Worda K. Abnormal maternal echocardiographic findings in triplet pregnancies presenting with dyspnoea. *Wien Klin Wochenschr* 2016; 128: 204-9.
- [14] Luu TM, Katz SL, Leeson P, Thebaud B and Nuyt AM. Preterm birth: risk factor for early-onset chronic diseases. *CMAJ* 2016; 188: 736-746.
- [15] van de Mheen L, Everwijn SM, Haak MC, Manten GT, Zondervan HA, Knapen MF, Engels MA, Erwich JJ, Coumans AB, van Vugt JM, Bilardo CM, van Pampus MG, de Groot CJ, Mol BW and Pajkrt E. Outcome of multifetal pregnancy reduction in women with a dichorionic triamniotic triplet pregnancy to a singleton pregnancy: a retrospective nationwide cohort study. *Fetal Diagn Ther* 2016; 40: 94-9.
- [16] Chaveeva P, Kosinski P, Birdir C, Orosz L and Nicolaides KH. Embryo reduction in dichorionic triplets to dichorionic twins by intrafetal laser. *Fetal Diagn Ther* 2014; 35: 83-6.
- [17] Peng R, Xie HN, Lin MF, Yang JB, Zhou Y, Chen HQ and Zhu YX. Clinical outcomes after selective fetal reduction of complicated monochorionic twins with radiofrequency ablation and bipolar cord coagulation. *Gynecol Obstet Invest* 2016; 81: 552-558.
- [18] Savelli L, Fabbri F, Di Donato N and De Meis L. Heterotopic interstitial pregnancy successfully treated with ultrasound-guided potassium chloride injection in the ectopic embryo. *J Obstet Gynaecol* 2014; 34: 276-7.
- [19] Prefumo F, Cabassa P, Fichera A and Frusca T. Preliminary experience with microwave ablation for selective feticide in monochorionic twin pregnancies. *Ultrasound Obstet Gynecol* 2013; 41: 470-1.
- [20] Lanna MM, Rustico MA, Dell'Avanzo M, Schena V, Faiola S, Consonni D, Righini A, Scelsa B and Ferrazzi EM. Bipolar cord coagulation for selective feticide in complicated monochorionic twin pregnancies: 118 consecutive cases at a single center. *Ultrasound Obstet Gynecol* 2012; 39: 407-13.
- [21] Cabassa P, Fichera A, Prefumo F, Taddei F, Gandolfi S, Maroldi R and Frusca T. The use of radiofrequency in the treatment of twin reversed arterial perfusion sequence: a case series and review of the literature. *Eur J Obstet Gynecol Reprod Biol* 2013; 166: 127-32.