

# Triple pregnancy with mixed chorionicity following in vitro fertilization: is fetal reduction necessary?

## Trojčetné těhotenství se smíšenou chorionicitou po léčbě IVF: je fetoredukce vhodná?

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### ABSTRACT

**Objective:** The increasing incidence and management of monozygotic twinning in patients undergoing in vitro fertilization (IVF) has been the subject of much debate. Here, we describe the management and outcome of two triple pregnancies with mixed chorionicity with a mono-chorionic-diamniotic twin pair and a singleton following the transfer of two embryos during IVF treatment.

**Design:** Case report.

**Setting:** Department of Obstetrics and Gynaecology, Palacký University Hospital, Olomouc, Czech Republic.

**Methods:** This study involved Patient A (30 years of age; 0 para) and Patient B (32 years of age; 1 Para), both with triplets of mixed chorionicity following the transfer of two embryos during IVF treatment, and treated in The Fetal Medicine Centre, Palacký University Olomouc. Detailed counselling led to the deployment of different management strategies for each case.

**Results:** The monochorionic twin component of Patient A was terminated by fetal reduction in the 15th week of gestation, while the remaining single pregnancy was delivered at term without complication. Patient B opted for expectant management. However, the pregnancy was complicated by severe maternal morbidity and was terminated in the 28th week of gestation following the death of one fetus.

**Conclusion:** Fetal reduction should be offered as a management tool to patients carrying triplets in order to improve perinatal survival. In triplets with mixed chorionicity, the reduction of monochorionic twins is particularly advisable in preventing the additional risk posed by a shared placenta.

### KEYWORDS

embryo transfer, in vitro fertilization, triple pregnancy, embryo reduction

### SOUHRN

**Cíl studie:** Zvýšený výskyt monozygotních více etných těhotenství po léčbě asistovanou reprodukcí je tématem mnoha studií. V této práci popisujeme průběh dvou trojčetných těhotenství po transferu dvou embryí v rámci léčby metodami asistované reprodukce, u kterých byla zvolena různá strategie.

**Typ studie:** Case report.

**Název a sídlo pracoviště:** Porodnicko-gynekologická klinika FNOL, Olomouc.

**Metodika:** Pacientka A byla 30letá, 0 para, a pacientka B byla 32letá, 1 para. U obou bylo v I. trimestru diagnostikováno trojčetné těhotenství se smíšenou

chorionicitou – biamniální monochoriální dvojčata a jedno etné těhotenství. Po podrobné konzultaci se obě rozhodly pro odlišnou strategii vedení těhotenství.

**Výsledky:** U pacientky A byla monozygotní komponenta ukončena fetocidou v 15. týdnu gravidity a pacientka porodila zbylý plod v termínu bez dalších komplikací. Pacientka B se rozhodla pro observaci těhotenství bez další intervence. Těhotenství bylo komplikováno rozvojem těžké materské morbidity a ukončeno císařským řezem ve 28. týdnu gravidity po úmrtí jednoho z plodů.

**Závěr:** Párům s troj- a více etným těhotenstvím by měla být nabídnuta možnost fetoredukce. U trojčat

se smíšenou chorionicitou je vhodné zvážit redukci monochoriální komponenty, a p edejít tak riziku, které navíc p edstavuje sdílená placenta.

#### KLÍČOVÁ SLOVA

embryo transfer, in vitro fertilizace, trojčetná gravidita, fetoredukce

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## INTRODUCTION

Assisted reproduction is associated with an increased incidence of multiple pregnancies [15]. Furthermore, recent data show that the incidence of monozygotic twins in this group of patients with multiple pregnancies is higher compared to spontaneous conception [13, 17]. Monozygotic twins have an 80% chance of being monochorionic and have a 6-fold higher abortion rate before 24 weeks of gestation and a 3-fold greater risk of stillbirth and early neonatal death than dichorionic twins. These problems predominantly arise because the placenta is not always shared equally between such twins and by the presence of arterio-venous shunts [7]. In triple pregnancies, monochorionic placentation (MC) poses additional risk factors; in fact, triplets with MC placentation have the highest risk for adverse pregnancy outcome compared with trichorionic pregnancies [6] increasing the risk of fetal growth restriction (FGR), intrauterine fetal death, preterm delivery and weight discordance [2, 3, 6]. Consequently, the clinical management of such cases is complex and is frequently debated. However, it is generally accepted that selective reduction in higher-order multiple pregnancies has a positive impact upon the duration of gestation but may increase the risk of intrauterine fetal death [19]. An expectant management strategy, on the other hand, might increase the risk of preterm birth and long-term morbidity of the fetus [1]. The purpose of the present study was to compare the outcome of two triple pregnancies, each with a monochorionic twin component, and discuss how these cases were treated by differing clinical management strategies.

## MATERIALS AND METHODS

In 2016, two patients with dichorionic triamniotic (DCTA) pregnancies were referred to The Fetal Medicine Center at Palacky University during the 12th week of gestation following IVF treatment. In both cases, embryo-transfer (ET) was carried out at the blastocyst stage and two embryos were transferred to each patient. For both patients, the embryonic disk split following ET, resulting in triamniotic triplets with mixed chorionicity. Patient A (0 para) was 30 years of age

while Patient B (1 para) was 32 years of age. Both patients were examined and carefully informed about the risk and prognosis of triple pregnancies with a monochorionic component. In both cases, we offered fetal reduction.

Patient A opted for selective fetal reduction of the monochorionic twins. The procedure was, however, delayed due to the presence of a sub-placental hematoma which led to the procedure being postponed until the 15th week of gestation. The procedure was subsequently carried out without complication via the intra-cardiac injection of 1 ml of 7.5% potassium chloride (KCl) using a transabdominal needle guided by ultrasound. Afterwards, serial ultrasound scans were used to screen the patient for potential aberrations in fetal growth and disturbances in the volume of amniotic fluid.

Patient B, however, opted to continue the pregnancy without intervention. Ultrasound diagnostic screening was performed on a weekly basis. We paid particular attention to a range of Doppler parameters, including the pulsatility index and peak systolic velocity of the middle cerebral artery, the pulsatility index of the umbilical artery and ductus venosus, the cerebroplacental ratio and amniotic fluid disturbances. In addition, we analysed the biometry of all fetuses on a bi-weekly basis.

## RESULTS

Fetal reduction (FR) was performed upon Patient A in the 15th week of gestation without complications. Subsequently, serial ultrasound scans detected no pathology and the remaining fetal material was absorbed. The remaining pregnancy was terminated at 40+1 weeks of gestation via the induction of labour owing to a suspicion of placental insufficiency, as indicated by abnormal Doppler parameters. A healthy child, weighing 3220 g, with an APGAR score of 10-10-10, was born without complication and postnatal adaptation was excellent.

The pregnancy of patient B was complicated by hypertension from the 16th week of gestation and by the development of gestational diabetes mellitus from the 24th week. Growth restriction stage I and anhydramnion were detected in the fetus with its own placenta and the patient was

hospitalized in the 25th week due to signs indicative of preeclampsia. We administered two intra-muscular doses of Betamethasone (14 mg) to help the fetal lungs mature in accordance with the standard protocol. Following extensive counselling, Patient B opted for the expectant management of her pregnancy. During the 28th week, we confirmed the intrauterine death of the fetus with its own placenta, and diagnosed growth restriction stage I of the remaining monochorionic fetuses. Ophthalmological examination of Patient B revealed hypertonic retinopathy grade II. After consultation with a gynaecologist, neonatologist and psychologist, Patient B decided to terminate her pregnancy and caesarean section was performed during the 28th week. Monochorionic twins were delivered, with birth weights of 940 g and 780 g, both with an APGAR score of 8–8–10. Afterwards, Patient B was monitored for preeclampsia and diabetes; medication was adjusted repeatedly before the patient was discharged from hospital care.

## DISCUSSION

The prevalence of monochorionic twins in triplet pregnancies following spontaneous conception is approximately 40% [1] and 10% after assisted conception [11]. Dichorionic triplets have a perinatal mortality rate which is eight times higher than trichorionic pregnancies [3] and thus represent a specific subgroup for triplets which is associated with the highest complication rate.

This case report focuses upon the clinical management and outcome of two patient cases, each with triple pregnancies with a monochorionic-diamniotic twin pair and a singleton following the transfer of two embryos during IVF treatment. When couples are faced with the dilemma of dichorionic triamniotic (DCTA) pregnancy, the first option is to adopt a conservative approach. Attempting to continue a pregnancy with all fetuses is associated with a high risk of perinatal morbidity and mortality caused mainly due to premature delivery [1]. Abel et al. [1] evaluated data from 47 triplet pregnancies with monochorionic twin pairs and found that the risk of premature delivery <30 weeks was significantly higher in non-reduced pregnancies compared to pregnancies which had been reduced (25% versus 0%) and in deliveries <34 weeks (88% versus 3%). A high proportion of triplets (28%), managed in an expectant manner, were also shown to be complicated by twin to twin transfusion syndrome [1]. In contrast, FR has been associated with a rate of miscarriage approximately two times higher than that seen in pregnancies which are managed expectantly [14]. A slightly higher early miscarriage rate was found in cases involving selective fetal

reduction from three to one than in cases involving three to two reductions (22% versus 17%) [1]. There are two predominant mechanisms underlying miscarriage following FR. The first of these relates to procedure-related trauma or infection, in which miscarriage would be expected within two weeks of FR. The second relates to the consequence of the mother resorbing dead fetoplacental tissue, which is likely to result in miscarriage several weeks, or even months, after FR [10].

A variety of techniques have been proposed for the reduction of multifetal pregnancies, including the transvaginal [8] or transabdominal [4] administration of KCl or NaCl directly into the fetal heart [20], the aspiration of embryos during the early weeks of gestation [5, 11] or umbilical cord coagulation [8]. Pregnancy loss from such procedures is known to vary from 5% to 30% [8]. In dichorionic triplets the most common approach is the reduction of a monochorionic pair to prevent the negative impact of a shared placenta. Reduction of the singleton, and maintenance of the monochorionic pair, is a less common option, as this procedure is associated with the higher rate of complications. Furthermore, Rong et al. [16] investigated 35 pregnancies and showed that monochorionic twins were associated with a higher rate of late miscarriage than retained singletons (18.5% versus 0%); retained twins also suffered from a premature birth rate (11%) and lower birth weight in comparison to a retained singleton.

The first visit was planned in the 12th week to meet criteria for the first trimester screening. After the results were obtained, we planned the strategy for ongoing pregnancy. The policy in our own department is to offer fetal reduction of a monochorionic pair to patients with DCTA. In each case, however, the final decision rests with the patient. In cases of trichorionic triplets, we offer fetal reduction for twin pregnancies, which is in line with the recommendations of Wimalasundera and Van de Mheen [18, 19], who indicated that the reduction of triplets to twins resulted in a significant reduction of risk associated with preterm delivery and intrauterine fetal death.

## CONCLUSIONS

We suggest that fetal reduction should be offered to patients with triplets as a clinical management tool to improve perinatal survival. In triplets with mixed chorionicity, which are associated with the highest rate of complications, we emphasize the reduction of monochorionic twins to prevent the additional risks posed by the shared placenta. While previous studies have reported higher miscarriage rates for pregnancies

undergoing multifetal reduction compared to an expectant management plan, it is important that these concerns are balanced against the lower risk of prematurity and fetal morbidity.

## LITERATURE

1. **Abel, J., Flock, A., Gembruch, U.** Expectant management versus multifetal pregnancy reduction in higher order multiple pregnancies containing a monochorionic pair and a review of the literature. *A. Arch Gynecol Obstet*, 2016, 5, p. 1167–1173.
2. **Adegbite, L., Ward, S., Bajora, R.** Perinatal outcome of quadruplet pregnancies in relation to chorionicity. *J Perinatol*, 2007, 27, p. 15–21.
3. **Bajoria, R., Ward, S., Adegbite, L.** Comparative study of perinatal outcome of dichorionic and trichorionic iatrogenic triplets. *Am J Obstet Gynecol*, 2006, 194, p. 415–424.
4. **Berkowitz, RL., Lynch, L., Chitkara, U., et al.** Selective reduction of multiple pregnancies in the first trimester. *N Engl J Med*, 1988, 318, p. 1043–1047.
5. **Jirsová, S., Mardešić, T., Hulvert, J., Muller, P.** Zhoršuje redukce více etné gravidity perinatální výsledky u dvou etných gravidit? *es Gynek*, 2000, 65, s. 230–235.
6. **Geipel, A., Berg, C., Katalinic, A., et al.** Prenatal diagnosis and obstetric outcomes in triplet pregnancies in relation to chorionicity. *BJOG*, 2005, 112, p. 554–558.
7. **Gibson, J., Cameron, A.** Complications of monochorionic twins. *Paediat Child Health*, 2008, 18, p. 568–573.
8. **Gonen, Y., Blankier, J., Casper, RF.** Transvaginal ultrasound in selective embryo reduction for multiple pregnancy. *Obstet Gynecol*, 1990, 75, p. 720–722.
9. **Has, R., Kalelioglu, I., Corbacioglu, A., et al.** Bipolar cord coagulation in the management of complicated monochorionic twin pregnancies. *Fetal Diagn Ther*, 2014, 36, 3, p. 190–195.
10. **Chaveeva, P., Kosinski, P., Puglia, D., et al.** Trichorionic and dichorionic triplet pregnancies at 10–14 weeks: outcome after embryo reduction compared to expectant management. *Fetal Diagn Ther*, 2013, 34, p. 199–205.
11. **Chow, J., Benson, B., Racowsky, C., et al.** Frequency of a monochorionic pair in multiple gestations. Relationship to mode of conception. *J Ultrasound Med*, 2001, 20, p. 757–764.
12. **Itskovitz, J., Boldes, R., Thaler, I., et al.** First trimester selective reduction in multiple pregnancy guided by transvaginal sonography. *J Clin Ultrasound*, 1990, 18, 4, p. 323–327.
13. **Luke, B., Brown, MB., Wantman E., Stern JE.** Factors associated with monozygosity in assisted reproductive technology pregnancies and the risk of recurrence using linked cycles. *Fertil Steril*, 2014, 101, 3, p. 683–689.
14. **Morlando, M., Ferrara, L., D'Antonio, F., et al.** Dichorionic triplet pregnancies: risk of miscarriage and severe preterm delivery with fetal reduction versus expectant management. Outcomes of a cohort study and systematic review. *BJOG*, 2015, 122, 6, p. 1053–1060.
15. **Pandian, Z., Templeton, A., Serour, A., Bhattacharya, S.** Number of embryos for transfer after IVF and ICSI: a Cochrane review. *Hum Reprod*, 2005, 20, 10, p. 2681–2687.
16. **Rong, L., et al.** Retain singleton or twins? Multifetal pregnancy reduction strategies in triplet pregnancies with monochorionic twins. *EJOG*, 2013, 167, p. 146–148.
17. **Sobek, A. jr., Zbořilová, B., Procházka, M., et al.** High incidence of monozygotic twinning after assisted reproduction is related to genetic information, but not to assisted reproduction technology itself. *Fertil Steril*, 2015, 3, p. 756–760.
18. **Van de Mheen, L., Everwijn, SM., Haak, MC., et al.** 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*, 2015.
19. **Wimalasundera, R.** Selective reduction and termination of multiple pregnancies. *Semin Fetal Neonatal Med*, 2010, 15, 6, p. 327–335.
20. **Yovel, I., Yaron, Y., Amit, A., et al.** Embryo reduction in multifetal pregnancies using saline injection: comparison between the transvaginal and the transabdominal approach. *Hum Reprod*, 1992, 7, 8, p. 1173–1175.

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