Intrafetal laser for embryo reduction from dichorionic triplets to dichorionic twins

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Short title: Embryo reduction by laser in dichorionic triplets

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Abstract

Objective: To report the outcome of dichorionic (DC) triplet pregnancies reduced to DC twins by laser ablation of the pelvic vessels of one of the monochorionic twins.

Methods: Intrafetal laser embryo reduction (ER) from DC triplet to DC twins was carried out in 61 pregnancies at 11^{+0} - 14^{+3} weeks' gestation. Pregnancy outcome was examined and compared to previous studies in DC triplets managed expectantly or by ER to twins or singleton with fetal intracardiac injection of potassium chloride (KCl).

Results: Intrafetal laser was successfully carried out in all cases, but, ultrasound examination within two weeks of the procedure demonstrated that the co-twin had died in 28 (45.9%) cases and was alive in the other 33 (54.1%). In the DC group there was one miscarriage at 23 weeks, one neonatal death after delivery at 26 weeks and in the other 31 cases there were two live births at a median gestational age of 35.3 (range 30.4-38.4) weeks. In the 28 cases where both monochorionic fetuses died there was one miscarriage at 16 weeks and in the other 27 cases the separate triplet was live born at a median gestation of 38.2 (range 32.2-42.1) weeks. In DC triplets intrafetal laser was associated with lower rate of miscarriage (3%), compared to that with expectant management (9%) or ER by intracardiac injection of KCl to monochorionic twins (13%) or singleton (18%). The rate of preterm birth (PTB) at <33 weeks (9%) was also lower than with expectant management (38%) or ER by KCl to monochorionic twins (23%), but the same as with ER to singleton (9%).

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Conclusions: In the management of DC triplet pregnancies, ER to DC twins by intrafetal laser is associated with lower rates of miscarriage or early PTB, compared to expectant management or ER by KCl. However, about half of the pregnancies result in the birth of one rather than two babies.

Introduction

In triplet pregnancies diagnosed during the first trimester management options include continuing with the whole pregnancy or embryo reduction (ER) to twins or singletons. In trichorionic (TC) triplets, ER is achieved by fetal intracardiac injection of potassium chloride (KCl). The beneficial consequence of ER is decrease in the rate of early preterm birth (PTB) at <33 weeks' gestation; a large study and review of the literature of TC triplets diagnosed at 10-14 weeks reported that PTB at <33 weeks occurred in 35% of those managed expectantly and this was reduced to 13% after ER to twins and 9% after ER to singletons.[1] However, such benefit is at the expense of the rate of miscarriage at <24 weeks, which increased from 3% with expectant management to 7% after ER to twins and 12% after ER to singletons.

In dichorionic (DC) triplet pregnancies, ER by KCl involves either the DC fetus or both monochorionic twins; the injected KCl to only one of the monochorionic twins could be transferred to the co-twin through the inter-twin placental vascular anastomoses or death of one fetus could lead to hemorrhage from the co-twin into the dead fetoplacental unit with consequent death or neurodevelopmental impairment in the survivor. In DC triplet pregnancies, compared to TC triplets, there is a higher rate of miscarriage both with expectant management (9% vs 3%),[1-5] and after ER to twins (13% vs 7%),[1] which could, at least in part, be attributed to complications arising from inter-twin placental vascular communications and / or unequal sharing of the placenta in the monochorionic pair.

We have proposed a new approach for ER of DC triplet pregnancies to DC twins by ultrasound-guided laser ablation of the pelvic vessels of one of the monochorionic twins.[6] In a series of 22 DC triplet pregnancies undergoing intrafetal laser ultrasound examination within two weeks of the procedure demonstrated that the co-twin had died in 11 cases and was alive in the other 11; in the DC group there was one miscarriage at 23 weeks and in the other 10 cases there were two live births at a median gestational age of 35 weeks, whereas in the 11 cases where both monochorionic fetuses died the separate triplet was live born at a median gestation of 38 weeks. The objective of this study of 61 DC triplet pregnancies undergoing intrafetal laser is to provide an update on the outcome of such pregnancies.

Methods

Intrafetal laser for ER from DC triplets to DC twins was carried out in 61 pregnancies referred to one of two fetal medicine units between 2004 and 2016. In all cases ultrasound examination was carried out at 10-14 weeks' gestation to demonstrate three live fetuses, determine chorionicity from examination of the inter-triplet membranes[7] and calculate gestational age from the crown-rump length of the biggest fetus.[8] Parents were counseled regarding the options of expectant management or ER. Maternal demographic characteristics, ultrasound findings and in those undergoing ER details of the procedure were recorded in a database. Pregnancy outcomes were collected into the same database when they became available from the referring hospitals, general practitioners or from the patients themselves.

Intrafetal laser ER was carried out as previously described.[6] Color flow Doppler was used to visualize the internal iliac arteries and intra-abdominal umbilical vein of one of the monochorionic twins, local anesthesia was administered to the maternal abdomen, under continuous ultrasound visualization an 18 G needle was inserted into the fetal abdomen adjacent to the pelvic vessels, a 400 µm laser fiber was then inserted into the needle and advanced to a couple of millimeters beyond the tip of the needle and laser coagulation was performed using NdYag-Laser (Dornier Med Tech, Wessling, Germany) with 40 W. This resulted in hyperechogenicity of tissues in the lower abdomen and cessation of blood flow in the iliac arteries and umbilical vein. Fetal heart activity continued for several minutes. After a period of rest for about 60 minutes another ultrasound examination was carried out to confirm death of one monochorionic twin and survival of a DC pair. The patient was discharged home and a further appointment was given for an ultrasound examination within two weeks of the procedure. Pregnancy outcome was obtained from the referring doctors

Results

In the study population of 61 DC triplet pregnancies undergoing ER to twins by intrafetal laser, conception was spontaneous in 8 (13.1%) and by *in vitro* fertilization in 53 (86.8%). The median maternal age was 34 (range 19-46) years and the median gestational age at ER was 12.3 (11.0-14.3) weeks.

Ultrasound examination had demonstrated that all three fetuses in each pregnancy were alive. There were no obvious defects in any of the separate fetuses. In the monochorionic twins, one fetus had diaphragmatic hernia, one had a major cardiac defect and one had acrania; in 18 (30.0%) cases there were early signs of twin-to-twin transfusion syndrome or selective fetal growth restriction with large discordance in CRL (>10%) and / or reversed a-wave in the ductus venosus in one of the fetuses.

At the end of the ER procedure and one hour later both remaining DC twins were alive and there was no blood flow within the dead fetus. Ultrasound examination within two weeks of the procedure demonstrated that both fetuses were alive in 33 (54.1%) cases and that the monochorionic co-twin had died in 28 (45.9%) (Figure 1). In the DC group there was one miscarriage at 23 weeks due to cervical incompetence, one neonatal death after spontaneous delivery at 26 weeks and in the other 30 cases there were two live births at a median gestational age of 35.3 (range 30.4-38.4) weeks. In the 28 cases where both monochorionic fetuses died there was one miscarriage at 16 weeks and in the other 27 cases the separate triplet was live born at a median gestation of 38.2 (range 32.2-42.1) weeks. None of the neonates had any obvious defects or neurological deficit. In the total group, the rates of miscarriage and PTB at <33 weeks were 3.3% (2 of 61) and 8.5% (5/59), respectively.

Discussion

Principal findings of this study

The findings of this study demonstrate that in the management of DC triplet pregnancies, ER to DC twins by intrafetal laser is an additional option to the traditional ones of expectant management, ER by intrafetal injection of KCl to monochorionic twins or ER by KCl to singleton. In 87% of our DC triplet pregnancies conception was by *in vitro* fertilization. The risk of monozygotic twinning in assisted conception is more than five times as high as the 0.4% rate in natural conceptions.[10-13] Such increased rate of embryo splitting have been attributed to prolonged embryo culture and delayed transfer at the blastocyst rather than cleavage stage and possibly, zona pellucida manipulation, oocyte age and type of culture medium.[12,13]

The technique of ER utilizing interstitial laser is similar to that used in interrupting the blood supply of the acardiac twin in twin reversed arterial perfusion (TRAP) sequence.[9] In our cases of DC triplet pregnancies treated by intrafetal laser although all monochorionic co-twins were alive one hour after the procedure 46% of these twins died within the subsequent two weeks. The most likely explanation for the deaths was retrograde hemorrhage into the placenta of the dead fetus or the fetus itself if the occlusion of the fetal pelvic vessels was incomplete.

In the DC triplet pregnancies undergoing intrafetal laser the rate of miscarriage (3%) was considerably lower than the rate in DC triplets managed expectantly (9%),[1-5] and those having ER by KCl to monochorionic twins (13%),[1] or singleton (18%).[1-3,5] The rate of PTB at <33 weeks' gestation was considerably lower with intrafetal laser (9%) than with expectant management (38%)[1,3] or ER by KCl to monochorionic twins (23%),[1] and it was the same as with ER to singleton (9%).[1,3]

Strengths and limitations

The strengths of this study relate to the large number of pregnancies treated by intrafetal laser, the narrow gestational range at which treatment was undertaken and the complete follow up of cases.

A limitation of any study of this nature is the positive bias in terms of favorable outcome in comparison to historical controls managed expectantly or by intracardiac injection of KCl. Ultimately accurate comparisons can be provided from randomized trials comparing different management options but it is very unlikely that such studies will ever be undertaken.

Comparison with previous studies

One other study has reported on the outcome of a series of DC triplet pregnancies managed by occlusion of the blood supply to one of the monochorionic pair.[3] In this multicenter study ultrasound guided laser or radiofrequency ablation of pelvic vessels was carried out in 12 DC triplet pregnancies at 10-14 weeks' gestation. Two (17%) pregnancies miscarried and in the remaining 10 there were two survivors in seven and one survivor in three; PTB at <33 weeks occurred in 40% (4 of 10) of cases.

Implications for practice

In DC triplet pregnancies counseling of the parents concerning management options should include intrafetal laser reduction to DC twins. Intrafetal laser is associated with a substantially lower rate of miscarriage, compared to that with expectant management or ER to twins or singleton by fetal intracardiac injection of KCl. The rate of PTB at <33 weeks' gestation is also considerably lower than with expectant management or ER by KCl to monochorionic twins, but the same as with ER to singleton. However, with intrafetal laser about half of the pregnancies will result in the birth of one rather than two babies.

Figure 1. Flow chart indicating pregnancy outcome in dichorionic triplet pregnancies reduced to dichorionic twins with ultrasound-guided intrafetal laser.

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