

Selective Termination for Fetal Anomaly/ Genetic Disorder in Twin Pregnancy at 32+ Menstrual Weeks

Report of Four Cases

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Key Words

Selective termination · Twin · Late pregnancy · Feticide ·
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Abstract

Objectives: To conduct a pilot study of 4 cases of selective termination of a single abnormal fetus in a dichorionic, diamniotic twin pregnancy advanced to 32 or more menstrual weeks of gestation. **Study Design:** This is a case series of 4 patients in highly unusual circumstances and treatment. Four healthy patients with desired pregnancies complicated by the presence of an abnormal genetic or developmental diagnosis in 1 twin were treated by selective termination of the abnormal twin using intracardiac injection of potassium chloride. **Results:** In all 4 patients, cardiac arrest in the abnormal twin was effected without disturbance of the healthy twin or the mother. Postoperative maternal serum potassium levels remained at normal levels. Delivery of a healthy surviving twin occurred from 2 days to 4 weeks following the selective termination along with delivery of a still-born abnormal twin. **Conclusion:** Selective termination of an abnormal twin may be performed on an outpatient basis in the last weeks of pregnancy.

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Introduction

Selective termination of multiple pregnancies has commonly been performed prior to 25 menstrual weeks for the purpose of reduction of numbers of gestations, and selective termination for fetal anomaly prior to 25 weeks has been reported previously [1–3]. However, only one report of selective termination for fetal anomaly after 30 menstrual weeks has been published [4]. As the number of women who experience a desired first pregnancy in later reproductive life increases, it is critical that these women and their partners be able to carry a twin pregnancy to term in spite of the presence of severe fetal anomalies or genetic disorder in one of the twins. The alternatives have been to deliver 1 healthy and 1 severely impaired child with its attendant pain, suffering, and emotional costs, or to terminate the twin pregnancy entirely. Termination of the abnormal twin early in pregnancy may result in a significant proportion of immature delivery or spontaneous losses of the entire pregnancy including the healthy twin [1–3, 5], although Eddleman et al. [6] report an unintended pregnancy loss of 4% overall with a rate of 2.4% in twins. Selective termination of the abnormal twin in late pregnancy after 32 menstrual weeks offers the possibility of optimum fetal development in the healthy twin should

spontaneous labor occur or in case a decision must be made for any reason to perform a cesarean delivery of the healthy twin.

Methods

Four patients who were referred by private or academic centers presented for selective termination at 32–34 menstrual weeks in a private clinic specializing in late terminations of pregnancy [7]. All patients were in their late 30s and were carrying desired twin dichorionic, diamniotic, dizygotic pregnancies. For 3 of the patients, this was their first pregnancy. All 4 wished to continue the pregnancy to term or as long as possible to assure survival of the healthy twin. All patients had been evaluated extensively at experienced prenatal centers, including university teaching hospitals, prior to treatment. All 4 had knowledge of the abnormality affecting the unhealthy twin, its immediate recent location in the uterus, and the prognosis for severe impairment in the abnormal twin. In 1 patient, polyhydramnios accompanying the abnormal twin had an adverse effect on the mother and on the healthy twin.

Three of the patients were in excellent health. One patient was basically healthy but was moderately obese, and she began developing early signs of preeclampsia just before the end of the selective termination treatment. She experienced a cesarean delivery of both her stillborn and healthy twin 2 days following the selective reduction. The other 3 continued the pregnancies for several weeks following selective reduction and delivered 1 healthy twin as well as 1 stillborn infant.

In each patient, care was taken to be certain about the location of the abnormal twin by immediate recent clinical history including review of all medical records and consultation with the patient's attending perinatologist. Preoperative ultrasound evaluations were made several times on the day of the procedure and just before the procedure began. Visualization of the presence and location of the amniotic membrane between the two amniotic sacs was made each time. Because of concerns for the possibility of maternal absorption of potassium from the fetal injection, a precautionary intravenous line for infusion of 1,000 cm³ normal saline was established preoperatively in order to dilute any excess potassium levels that might be experienced and to facilitate a fluid load that could accelerate excretion of excessive potassium ions.

With the patient lying on the operating table, sometimes with a pad under a hip to prevent vena cava compression, the heart of the abnormal twin was visualized with ultrasound and the maternal skin marked at that site. A povidine/iodine preparation was applied to the skin around the injection site, and the area was covered with a sterile drape. The ultrasound probe was covered with a sterile probe cover and controlled by the surgeon. At the injection site, 12 cm³ of 1% lidocaine buffered by 8.4% sodium bicarbonate were infiltrated into the skin and subcutaneous tissues down to the level of the uterine wall. The skin surface was then punctured with a 16-gauge IV needle. At that point, a 15-cm 20-gauge echotip spinal needle was introduced percutaneously through the uterine wall and into the cardiac ventricle of the abnormal fetus. Following aspiration of cardiac blood, a solution of 15% potassium chloride (KCl; 2 mEq/ml) was injected until cardiac arrest occurred. The lack of cardiac activity was observed for several minutes before terminating the procedure.

Following the intracardiac fetal injection, the cardiac activity of the healthy twin was observed and confirmed to be normal. The patient was then returned to the recovery room and observed for periods of up to 2 h. Vital signs were monitored, and postoperative serum potassium levels were followed. All patients were discharged from the private office setting recovery room on the same day as the procedure and returned home immediately.

Cases

Case 1

Patient No. 1 was Gr 1 P 0 Ab 0 with a pregnancy duration of approximately 32 menstrual weeks at the time of the first visit. Twin A, a female, had been diagnosed with Goldenhar syndrome several weeks previously. Although the patient had arrived at Boulder, Colo., USA, 2 weeks prior to the scheduled procedure in early February 2000, she began to have periodic contractions 1 week after arriving. She was evaluated by an obstetrical colleague and treated with parenteral terbutaline, and her procedure was rescheduled for the same day.

The needle tip was placed in the cardiac ventricle of the abnormal fetus, a small amount of cardiac blood was aspirated, and 6 mEq of KCl were injected. Cardiac arrest occurred immediately, and this was observed for 5 min before the needle was withdrawn. The patient was placed in the recovery room and displayed no adverse effects. All vital signs remained within normal limits. Approximately 5 weeks following the selective termination, the patient delivered a healthy male twin by cesarean delivery. The abnormal female twin A had an appearance consistent with Goldenhar syndrome. The surviving twin has shown exuberant health and normal development since delivery in March 2000.

Case 2

Patient No. 2 was a primigravida who presented at 32 weeks with a diagnosis of 1 healthy male twin and 1 female twin afflicted with a 3-chambered heart and trisomy 21. The patient was moderately obese at 200 lb and 5' but had no other apparent health problems. Her blood pressure was slightly elevated at 142/84 at the time of the first visit. She was given a premedication of meperidine 75 mg and prochlorperazine 10 mg intramuscularly approximately half an hour prior to the anticipated selective termination procedure.

Following routine preoperative procedures, 10 mEq of KCl were injected into the cardiac ventricle of the abnormal fetus. Fetal cardiac rhythm slowed briefly but did not completely stop. After a few minutes, an apparently normal cardiac rhythm resumed. The patient was returned to the recovery room to rest, and she displayed no change in status including vital signs.

Two hours after the first injection, and 2 1/2 h after the first premedication, the patient was given another parenteral dose of meperidine 75 mg and prochlorperazine 5 mg intramuscularly. She returned to the operating room, where 10 mEq of KCl were again injected into the cardiac ventricle of the abnormal fetus. The same sequence was observed: a slowing of the fetal heart rate for several minutes followed by a return to normal rhythm.

The serum potassium sample drawn from the patient 1 1/2 h following the second fetal intracardiac injection was normal at 4.6 mEq/l. The patient and her husband were invited to return in 2 weeks for another attempt, which they did.

At the time of the second visit, the patient now had a blood pressure reading of 142/90 and showed 3+ protein in the urine. Her physicians at the university hospital back home were concerned about the development of preeclampsia. She was now pregnant for 34 weeks. A premedication of 100 mg meperidine and 10 mg prochlorperazine was again given about 45 min prior to the attempted fetal intracardiac injection. Just before the fetal injection, the patient's blood pressure was 150/102 with a pulse of 80.

Following the usual preoperative preparations, 20 mEq of KCl were injected into the cardiac ventricle of the abnormal twin. Immediate fetal cardiac arrest occurred. Following return to the recovery room 45 min later, the patient's blood pressure was 148/98 with a pulse of 76. Serum potassium concentration at that time was 4.1 mEq/l, and all other laboratory values were within normal limits. Diastolic blood pressures continued to drop, with readings of 148/80 and 148/74 observed just before discharge.

The patient was discharged in good condition in the company of her husband 3 h following the selective termination. She returned home by air the next day, and the following day, due to increasing signs of preeclampsia, she experienced a cesarean delivery of a healthy twin B and stillborn twin A. The surviving twin has shown normal health and development during the 2 1/2 years since birth.

Case 3

Patient No. 3 was Gr 3 P 2 Ab 0 with no history of cesarean delivery. She presented with a dichorionic/diamniotic/dizygotic twin pregnancy in which twin A was healthy and twin B showed genetic and ultrasonographic evidence of skeletal dysplasia. Both fetuses were male.

At the time of presentation, the patient was approximately 34 menstrual weeks from last menstrual period by ultrasound measurement. Twin B had been found to have an abnormal karyotype of 47,XY,+mar de novo [8], extramarker chromosome. Ultrasound exam had shown abnormally short tibia and femur with polyhydramnios. The patient was on maintenance terbutaline orally for contractions. The patient was in excellent physical health but requested prophylactic intravenous antibiotic treatment. Cefotetan 1 g was prepared in 500 cm³ normal saline for intravenous infusion during and after the procedure.

Following routine preparation, 20 mEq of KCl were injected into the cardiac ventricle of the abnormal twin B. Cardiac activity slowed but did not stop. An additional 10 mEq were injected, which caused a further slowing but not a cessation of cardiac rhythm. Therefore, 5 mEq more of KCl were injected, i.e. a total of 35 mEq, before the procedure was terminated. Fetal cardiac arrest had not occurred.

After observation for 30 min in the operating room, the patient was taken to the recovery room to rest. A serum potassium sample was drawn 90 min following the fetal intracardiac injection, and it was 3.6 mEq/l.

Two hours after the original procedure, the patient was returned to the operating room, where twin B, the abnormal twin, showed no cardiac activity. In twin A, the cardiac activity was normal.

The patient was discharged in good condition 1 h later to the care of her perinatologist. Four weeks later, labor was induced, and she delivered a healthy baby boy and a stillborn male infant. Since delivery 1 year prior to the preparation of this report, the surviving twin has been healthy showing normal development.

Case 4

Patient No. 4 is a primigravida who was approximately 32 weeks from last menstrual period at the beginning of February 2003. The patient presented with a diagnosis of a twin pregnancy with 1 healthy female fetus (twin A) in the lower uterine segment and an abnormal male twin B with a diagnosis of myelomeningocele and Arnold/Chiari malformation. The patient was in excellent physical health with normal vital signs and a normal physical exam.

The preoperative serum potassium concentration was 4.2 mEq/l. Following routine preparation, 20 mEq of KCl were injected into the cardiac ventricle of the abnormal twin B. It appeared that part of the injected material entered the pericardial sac. Cardiac rhythm slowed but did not stop. The procedure was terminated at that point. A serum potassium sample drawn 10 min later was 4.3 mEq/l.

One hour later, the injected heart of the abnormal fetus had changed in appearance with the cardiac walls and septum appearing thicker. Cardiac rhythm was slow. This time, the injection of approximately 6 mEq of KCl resulted in immediate cessation of cardiac activity. The remainder of the 20 mEq of KCl in the syringe were injected for a total of 40 mEq. There was no return of cardiac activity. The cardiac activity of healthy twin A remained normal.

The patient was discharged in good condition and in the company of her husband 2 h following the repeat intracardiac fetal injection to the care of her university hospital physician. She returned home by air that evening. Three days later, she reported that she felt well, was experiencing few contractions, and was anticipating a routine prenatal visit the next week. Twenty-four days after the selective termination, the patient gave birth by cesarean delivery to a healthy baby girl weighing a little over 2,600 g.

Conclusion

There are many ethical issues that can be raised concerning selective termination of an abnormal fetus in a twin pregnancy. The one group that has reported selective terminations at the early third trimester expressed objections to the application of this technique in late pregnancy [4]. Chervenak et al. [8] stated that termination of pregnancy in the third trimester is morally justified only in the case of a lethal or catastrophic abnormality such as anencephaly. Others state that, while controversial, multifetal pregnancy reduction has become an 'integral part' of infertility therapy, and that it can improve outcome for the remaining fetus in the case of twins [9, 10].

It is our view that the decision to choose third-trimester selective termination may be made by the woman and her partner in the case of a valid and documented fetal abnormality. It is up to the physician to determine whether he or she accepts the potential risks and ethical questions of this procedure and fully discusses these issues with the requesting patient and her partner.

Since the physician does not act alone, it is necessary to have the assistance of skilled ancillary personnel who support the couple's decision and the physician's actions.

While the selective termination by intracardiac KCl injection of an abnormal fetus in late pregnancy may present some risk to the normal fetus, to continuation of the pregnancy, and to the mother, it offers many advantages for a couple with a desired dichorionic, diamniotic twin pregnancy complicated by serious abnormality in one fetus. A shared placental circulation in a known monochorionic twin pregnancy contraindicates this specific procedure because of the risk to the healthy fetus or risk of total pregnancy loss [11].

It appears that the amount of KCl necessary for the selective termination of a fetus at 32+ weeks is considerably more than the amounts routinely used for selective reductions/terminations in previously reported series up to 24 menstrual weeks. In the first patient, the recommended dosage of 6 mEq of KCl was instantly effective, but other cases required as much as 20–35 mEq in one dose.

Under the adage 'primum non nocerum', no physician wants or accepts harm to his primary patient, and the

greatest fear is that the amount of material used for selective termination might harm the healthy fetus or worse, the woman carrying the pregnancy. Fortunately, it appears from our repeated serum potassium levels that this does not present a serious danger to patients requesting selective termination.

With respect to the lateness in pregnancy at which this technique can or should be applied, we note that one of our patients was experiencing an increasingly serious polyhydramnios in the abnormal twin which threatened her well-being as well as the safety of the healthy twin. While repeated removal of excessive amniotic fluid in such a case might offer one alternative, depending on the circumstances, this procedure also carries risks that might outweigh those of selective termination in late pregnancy. Such a consideration could bear heavily on the ethical question of whether it is appropriate to cause selective termination of one abnormal fetus late in the third trimester of pregnancy.

References

- Berkowitz RL, Stone JL, Eddleman KA: One hundred consecutive cases of selective termination of an abnormal fetus in a multifetal gestation. *Obstet Gynecol* 1997;90:606–610.
- Evans MI, Goldberg JD, Horenstein J, Wapner RJ, Ayoub MA, Stone J, Lipitz S, Achiron R, Holzgreve W, Brambati B, Johnson A, Johnson MP, Shalhoub A, Berkowitz RL: Selective termination for structural, chromosomal, and Mendelian anomalies: International experience. *Am J Obstet Gynecol* 1999;181:893–897.
- Evans MI, Berkowitz RL, Wapner RJ, Carpenter RJ, Goldberg JD, Ayoub MA, Horenstein J, Dommergues M, Brambati B, Nicolaidis KH, Holzgreve W, Timor-Tritsch IE: Improvement in outcomes of multifetal pregnancy reduction with increased experience. *Am J Obstet Gynecol* 2001;184:97–103.
- Shalev J, Meizner I, Rabnerson D, Mashiach R, Hod M, Bar-Chava I, Peleg D, Ben-Rafael Z: Improving pregnancy outcome in twin gestations with one malformed fetus by postponing selective fetocide in the third trimester. *Fertil Steril* 1999;72:257–260.
- Lipitz S, Shale E, Meizner I, Yagel S, Weinraub Z, Jaffa A, et al: Late selective termination of fetal abnormalities in twin pregnancies: A multicenter report. *Br J Obstet Gynaecol* 1966;103:1212–1216.
- Eddleman KA, Stone JL, Lynch L, Berkowitz RL: Selective termination of anomalous fetuses in multifetal pregnancies: Two hundred cases at a single center. *Am J Obstet Gynecol* 2002;187:1168–1172.
- Hern WM: Laminaria, induced fetal demise and misoprostol in late abortion. *Int J Gynecol Obstet* 2001;75:279–286.
- Chervenak FA, Farley MA, Walters L, Hobbins JC, Mahoney MJ: When is termination of pregnancy during the third trimester morally justifiable? *N Engl J Med* 1984;310:501–504.
- Evans MI, Krivchenia EL, Gelber SE, Wapner RJ: Selective reduction. *Clin Perinatol* 2003;30:103–111.
- Evans MI, Wapner RJ, Ayoub MA, Shalhoub AG, Feldman B, Yaron Y: Spontaneous abortions in couples declining multifetal pregnancy reduction. *Fetal Diagn Ther* 2002;17:343–346.
- De Catte L, Camus M, Foulon W: Monochorionic high-order multiple pregnancies and multifetal pregnancy reduction. *Obstet Gynecol* 2002;100:561–566.