

Multiple Pregnancies and Fetal Reduction After ART : How Frequent are the Vanishing Embryos ?

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Summary

The advent of ART (assisted reproductive technology) has increased the number of multiple pregnancies. Due to the fear of the negative outcome with expensive procedures like in vitro fertilization and intracytoplasmic sperm injection, centers world wide adopted the procedure of transferring three to four embryos leading to pregnancies of multiple order. As the perinatal outcome is severely compromised with high order pregnancies resort was taken to embryo reduction to minimize the number of living fetuses to one or two. Different procedures like aspiration of embryos through vaginal route, injection of Potassium chloride (KCl) into the fetal heart either by transvaginal or trans-abdominal route were adapted. These procedures themselves lead to a number of complications viz. abortion, premature delivery and intrauterine growth retardation. It was observed that all these complications were increased in magnitude when embryo reduction was done late in pregnancy, as the remnants of the dead fetus led to liberation of toxic materials and thromboplastins into the circulation, jeopardizing the outcome. Recent publications as discussed in detail below have shown decreased incidence of complications if the extra embryos were aspirated at about six weeks of gestation. This technique has considerably reduced the incidence of complications noted with late embryo reduction. The details of the procedure and outcome are discussed in detail in the paper. Emphasis in the paper is laid on easy technique, less anesthesia time and better outcome in early fetal reduction as compared to late fetal reduction.

Introduction

The last two decades have seen a dramatic increase in the use of ovulation induction drugs for various assisted reproductive techniques and this in turn has increased the multiple pregnancy rate. The incidence of multiple gestations can be reduced by limiting the number of embryos per transfer. However, this is not always feasible and so multiple pregnancies continues to be an unavoidable situation with IVF, posing a difficult situation both for the patient and the clinician.

Multifetal pregnancy reduction was first introduced to avoid the increased incidence of abortion and premature labor that are usually associated with multiple pregnancies (Kanhai et al; 1986). In general, it has not been recognized that many twin or multiple

gestations are lost in utero early in pregnancy (Landy et al 1982). Until the advent of ultrasound, the ability to document early human fetal loss in multiple gestation was difficult. However, since 1980's serial ultrasound examinations of pregnant women have documented the 'disappearance' of at least one or two gestational rings. Furthermore, the number of twins observed at delivery was significantly less than the number of twin conceptions originally identified by ultrasound during the first trimester. These observations led to the concept of the 'the vanishing twin' (Landy et al, 1982).

Our Centre has done 200 cycles of IVF since 1999 June and among these we encountered 30 multiple pregnancies which included 21 twins, 6 triplet and 3 quadruplet pregnancies. In cases of higher order pregnancies (3 or more gestational sacs) multifetal

reduction was offered to the patients following adequate counseling. We report our experience in multifetal reduction and also the vanishing twin syndrome.

Material and Methods

We counselled 9 patients with high order multiple gestations for embryo reduction of which 6 patients gave consent and underwent the procedure. Of these 6 patients, 4 were carrying triplets and 2 quadruplets. All patients were counselled to reduce the number of sacs to two. One patient requested the reduction to a single sac but we convinced her to leave two viable fetuses.

Embryo reduction was done as an outpatient procedure under short general anaesthesia. The vagina was prepared with betadine and then thoroughly rinsed with sterile normal saline. Transvaginal ultrasound was used (ATL color Doppler Model Apogee 800).

The number of gestational sacs with pulsating echoes was confirmed.

The most accessible gestational sac was chosen, and the fetal heart visualized and aligned with the biopsy needle guideline on the screen. An oocyte retrieval needle (CCD Catalog # 1301001) was advanced sharply towards the fetal heart.

We injected 0.5 - 2.0 ml of KCI (15% w/v) according to previously described technique (Evans et al; 1993) in 3 patients (1 triplet, 2 quadruplets) with gestation of 10 weeks +. In the remaining 3 patients, we eliminated the use of KCI completely. In case : 1 after introduction of needle into the fetal echoes, we aspirated out all the amniotic fluid and made repeated punctures on the fetus. The fetus was of 9 weeks gestation. Fetal movement stopped and the sac was deformed but a faint heart beat was recorded. In case : 2 & 3 with gestation 7.5 and 7.0 weeks respectively, after introduction of needle into the fetal echoes, we applied suction using a 20 gauge syringe repeatedly until all or most of the embryonic parts were aspirated. We did not aspirate any amniotic fluid. The fetal echo disappeared completely and the sac remained of the same size or slightly smaller but empty of fetal parts. After complete aspiration of the fetus, needle was withdrawn.

Patients were discharged 3 hours after the procedure. Follow up ultrasound examination was done 1 week after the procedure. All patients received routine antenatal care and regular check up of the pregnancy.

Results

The gestational age at reduction was between 7-10 weeks. In case 1 wherein we emptied amniotic fluid and made multiple punctures, repeat scan after 1 week showed that fetus was still alive with fetal pulsations visibly apparent on ultrasound. So a repeat procedure was done on the patient and this time KCL was injected directly into the heart and needle was withdrawn when no more pulsations were seen. Follow up scan after 1 week showed just two sacs with fetal heart beat. In case 2 and 3, repeat scan after a week showed empty sac devoid of all embryonic contents slightly smaller in size. In the 3 cases where KCL was injected, in one or two sacs, follow up scan after one week showed that remaining sacs were normal and the injected sac was amorphous and shrunk without any pulsations. Color Doppler scan showed total absence of blood flow in the heart.

No immediate complications of the procedure (eg. vaginal bleeding) occurred, and all cases were technically successful. However case 1 aborted at 28 weeks. Currently all other 5 pregnancies are ongoing smoothly and have reached 30-32 weeks without any complication and the obstetric outcome is awaited.

Of the total multiple pregnancies, the vanishing twin syndrome was observed in 6 cases (Table I) which had twin gestational sacs in 4 cases and 3 gestational sacs in 1 case and 4 gestational sacs in 1 case. All 6 cases reported vaginal bleeding and a repeat scan showed that 1 sac had vanished in each of these cases.

Discussion

In this study, we adopted different techniques of multifetal reduction viz. aspiration of amniotic fluid and multiple punctures, aspiration of embryonic parts and injection of KCL into the fetal heart.

Several reports have been published with regard to reduction in multifetal pregnancies. Antsaklis et al

Table I: Showing the incidence of multiple pregnancies and vanishing twins.

Total No. of Cycles	Total No. of pregnancies	Total No. of multiple Pregnancies	Quadruplets	Triplet	Twins	Vanishing Twins
200	50	30	3	6	21	6 out of 21

(1999) reported that multifetal pregnancy reduction to twins does not appear to increase obstetric or perinatal risks. Early transvaginal embryo aspiration in high order multiple gestations was reported by Ragaa et al (1999) as a simpler and relatively safer method for embryo reduction. The overall pregnancy loss rate associated with early embryo aspiration was found to be similar to that of procedures performed at later gestational age. Injection of KCl in one of the 3 cases we performed went on to abort at 28 week gestation. Injection of KCl is not restricted to the fetal heart. During injection, the fetus is sometimes pushed away from the needle and KCl diffuses into the amniotic sac; consequently it may diffuse to the adjacent gestational sacs. Toxic effects of KCl on the remaining fetuses have been reported by Tabsh (1990) and Wapner et al (1990).

We recommend performing the procedure as early as possible by complete aspiration of embryonic tissue as opposed to injection of KCl. Aspiration leaves a minimum amount of necrotic tissue, which may have detrimental effects on the remaining gestational sacs. The embryo at 6-8 weeks is composed of 3 primary germ layers (ectoderm, endoderm and mesoderm) folding to form the head, tail and lateral body folds and these soft tissues and membranes are easily removed with repeated suction.

It was demonstrated that multifetal pregnancy reduction gave better outcomes than expectant managements of triplets (Bollen et al, 1993, Smith - Levitin et al; 1996). In a large British study (Botting et al, 1987), the perinatal mortality rate was 41.6% in sextuplets, 21.9% in quintuplets, 20% in quadruplets and 16.4% in triplets.

On the other hand, a very high rate of vanishing embryos was observed. This is in agreement with previous observations made in twin gestations (Landy et al, 1986). The chances of experiencing a miscarriage of all 3 sacs is reported to be varied by different authors viz. 2.6% to 8.3-10% (Botchan et al 1993, Dickey et al, 1990). We observed the vanishing twin syndrome in twin, triplet and quadruplet gestation. It is well established that detection of a fetal heart confers a great probability of ongoing pregnancy for that particular embryo. This issue has been well demonstrated in singleton gestations (Rosen et al, 1990), with an approximately 5% chance of fetal demise after visualizing a fetal heart beat. In multiple pregnancies, these figures vary between 5% and 30% (Dickey et al, 1990, Kol et al, 1993). Our study did not make a correlation between age and the vanishing twin syndrome as most of the patients were >30 years of age.

No apparent risk factor could be detected for predicting the occurrence of a vanishing embryo in a specific patient, as patients experiencing 1 or 2 embryo resorption had comparable mean age, number of oocytes - embryos transferred and obstetric history. This phenomenon leaves us in a dilemma in opting for multifetal reduction. Fetal reduction is possible as early as 6 weeks and from our experience, its best done earlier but the vanishing twin syndrome occurs at about the same time. Therefore certain clinicians prefer to wait upto 9 weeks before performing multifoetal reduction. However, we recommend performing the procedure as early as possible without excessive concern of the phenomenon of vanishing twins because two gestational sacs will remain. Even if one sac vanishes, a singleton pregnancy will result.

The question that arises now is whether limiting the number of embryos transferred will reduce the incidence of multiple gestations or not? It is evident that any women treated with ovulation induction drugs has a higher risk of conceiving a multiple pregnancy, particularly if undergoing ART, if her age is <49 or if donor oocyte from a younger women are used. On the other hand, it has been demonstrated that it is the quality of embryos transferred rather than the number itself that correlates better with clinical pregnancy rates in IVF (Stassen et al, 1992). Higher order multiple pregnancies are no longer rare among modern infertility practice, accounting for 4% to 6% of ART conceived gestations. Spontaneously, almost 50% of these with more than 3 sacs will experience at least 1 embryo resorption (Alejandro et al, 1995).

Multifetal pregnancy reduction is a difficult situation for both the patient and the physician. Adequate counselling is very important in these cases and we have to emphasise the risks of the procedure, long term effects of the procedure, incidence of early pregnancy loss and the perinatal complications of prematurity and also the fact that the procedure could result in total loss of the pregnancy.

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