

Early transvaginal embryo aspiration: a safer method for selective reduction in high order multiple gestations

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Assisted reproduction technologies and ovulation induction for treatment of infertility continue to cause high order multiple gestations. Increased perinatal morbidity and mortality, as well as maternal morbidity, may complicate these pregnancies. Selective fetal reduction, an acceptable therapeutic approach in these cases, is usually performed at or after the ninth week of gestation, with KCl injected in the vicinity of the fetal heart, and is associated with a total pregnancy loss rate of 11.7%. We report our experience with 90 women who underwent early (mean 7.5 weeks gestation, range 7.0–8.0 weeks) transvaginal selective embryo aspiration. The mean number of viable embryos before and after reduction was 3.5 and 2.1 respectively. Six (6.7%) pregnancies were lost before 24 gestational weeks. One miscarriage occurred at the tenth gestational week. The other five pregnancies were aborted at 17.3–21.6 weeks gestation. Additional interventions were performed in three of these pregnancies: genetic amniocentesis in two cases and cervical suture in one case. In the subset of 39 patients with ≥ 4 embryos, only one (2.6%) pregnancy loss was recorded. This loss rate is significantly lower ($P < 0.05$) than the 15.3% loss rate in patients with ≥ 4 fetuses calculated from other work. Four (4.4%) other pregnancies were complicated by premature delivery (25–28 weeks gestation). Mean gestational age of delivered pregnancies in our series was 35.7 weeks. In conclusion, early transvaginal embryo aspiration is a simple and relatively safe method for multiple pregnancy reduction. The overall pregnancy loss rate associated with early embryo aspiration is similar to that of procedures performed at later gestational age, but is significantly lower when the initial number of embryos is four or greater.

Key words: embryo aspiration/multiple pregnancy/selective fetal reduction/ultrasound-guided procedures

Introduction

Selective fetal reduction has been advocated as an effective modality to reduce fetal and maternal risks associated with high-order multifetal pregnancies (Berkowitz *et al.*, 1988; Hobbins, 1988; Evans *et al.*, 1988). The procedure is usually

performed at or after the ninth gestational week and several techniques have been suggested (Berkowitz *et al.*, 1988; Wapner *et al.*, 1990; Lynch *et al.*, 1990; Tabsh, 1990; Timor-Tritsch *et al.*, 1993; Evans *et al.*, 1994), usually employing KCl injected into the fetal heart or in its vicinity.

A recent collaborative report (Evans *et al.*, 1996) estimated that following multifetal pregnancy reduction the overall pregnancy loss rate (before 24 gestational weeks) is 11.7%, and the early premature delivery rate (between 25–28 gestational weeks) is 4.5%. This study also documented a direct relationship between the starting or the final number of embryos and the rate of complications—the higher the initial number of gestational sacs, the worse the prognosis. The reported pregnancy loss rate was 7.6% when the initial number of embryos was three and increased to 15.3% with quadruplets and higher order multiple gestations.

Previously (Itskovitz *et al.*, 1989; Itskovitz-Eldor *et al.*, 1992), we suggested that early selective fetal reduction be performed by transvaginal embryo aspiration. Our preliminary results (5.3% pregnancy loss rate) showed that this procedure is at least as safe as the transabdominal or transcervical route (Itskovitz-Eldor *et al.*, 1992). Other advantages of transvaginal embryo aspiration include the possibility of performing it 2–4 weeks earlier than other methods for selective fetal reduction, thus making the procedure potentially more acceptable from religious and ethical points of view, and obviating the need to use KCl or other toxic substances.

The aim of this communication, based on experience accumulated over 10 years, is to re-evaluate the outcome of pregnancies after early transvaginal embryo aspiration for selective fetal reduction.

Materials and methods

Transvaginal embryo aspiration was performed in 90 patients with multifetal gestations, defined as three or more fetuses. Nineteen patients who had been included in a previous report (Itskovitz-Eldor *et al.*, 1992) were also included in this report. Pregnancies were the result of in-vitro fertilization (IVF) ($n = 61$) or of induction of ovulation with gonadotrophins ($n = 27$) or clomiphene citrate ($n = 2$). The initial number of embryos in the 90 pregnancies included in this study is detailed in Table I. The mean gestational age at reduction was 7.5 weeks (range 7.0–8.0 weeks). Appropriate informed consent was obtained from all patients.

The procedure used has been described previously in detail (Itskovitz *et al.*, 1992). Briefly, following vaginal cleansing with a povidone-iodine solution, the patient was mildly sedated and i.v. antibiotic prophylaxis was employed. The ultrasound machinery used was the Elscint ESI 1000[®] sector scanner (Elscint Ltd, Haifa, Israel) equipped with a 6.5 MHz transvaginal transducer and puncture guide.

Table I. The number of pregnancies reduced to singleton, twins and triplets versus the number of embryos at presentation

Order of pregnancy after reduction	Initial number of embryos ($n = 90$)				
	8 ($n = 1$)	7 ($n = 1$)	5 ($n = 7$)	4 ($n = 30$)	3 ($n = 51$)
Singleton	0	0	0	0	1
Twins	1	1	6	26	50
Triplets	0	0	1	4	0

The uterus was scanned, and the configuration and position of each gestational sac relative to the uterine cavity and to each other was recorded. A 30 cm long, 1.6 mm outer diameter needle was inserted through the puncture guide and was advanced with a brisk movement through the vaginal fornix and the uterine wall into the most easily accessible sac. Alternatively, the embryo with the inappropriate smaller crown-rump length (CRL) or gestational sac was chosen for reduction. The needle tip was positioned close to the embryo and suction was applied abruptly with a 20 ml syringe. This resulted in complete or partial aspiration of the embryo. A new needle was used each time the needle had to pass through the vaginal wall. However, when the location of the sacs permitted, we penetrated additional sacs with the same needle without reinserting it through the vaginal mucosa. All the procedures were performed by the same operator (J.I.E.). Our policy is to advise for reduction to twins unless the couple prefers otherwise.

Results

Most pregnancies ($n = 84$) were reduced to twins. One triplet was reduced to singleton, that being indicated by the reproductive history (repeated premature deliveries) of the patient. This woman delivered a healthy daughter at 39 weeks gestation.

Five pregnancies were reduced to triplets, four of them because of patient request. Among those four, three delivered triplets at 31, 34 and 35 gestational weeks. All neonates were well and healthy. The fourth delivered twins on her 36th week of gestation, following an additional late reduction of the third fetus, indicated for hydrops fetalis. In the fifth case (a quadruplet) reduction to triplets was accomplished because the location of three of the sacs did not allow reduction to twins without significant danger of losing the whole pregnancy. Intrauterine death of a second fetus occurred at 24 weeks gestation. Twins were born by Caesarean section at 29 weeks gestation.

In seven pregnancies with quadruplets or higher number of fetuses, selective fetal reduction was completed in two sessions, because of technical difficulties or clinical impression that spontaneous fetal demise would follow. The outcome of these cases is detailed in Table II. In the first session, the number of fetuses was reduced to triplets, followed by reduction to twins some days or weeks after the first procedure. All patients delivered twins at 34–38 weeks gestation.

Six pregnancies (6.7%) were lost before 24 gestational weeks (Table III). One quadruplet gestation which had been reduced to twins miscarried at 10 weeks of gestation. Five losses occurred in triplet gestations, three of them in pregnancies complicated by additional surgical or diagnostic

Table II. Outcome of selective fetal reduction performed in two sessions

Starting no. of fetuses	Interval (weeks)	Method (second session)	Genital age at delivery (weeks)
5	<1	Aspiration	35
4	<1	Aspiration	35
4	<1	Aspiration	34
4	<1	Aspiration	38
8	2	KCl	37
5	2	KCl	35
4	2	KCl	34

interventions (one cervical suture and two amniocenteses). These miscarriages occurred at 18.5, 18.5 and 21.6 weeks gestation respectively. Two other losses occurred at 17.3 and 21.6 weeks gestation.

Another four pregnancies (4.4%) were complicated by early (24–28 weeks) premature delivery. In three of these pregnancies, all six newborns were lost. The fourth delivered twins, who thrived, in the 28th gestational week. Eight women (9.6%) delivered between 29 and 32 gestational weeks, 36 (43.4%) delivered between weeks 33 and 36 and the rest 36 (43.4%) delivered after 37 completed weeks. The Caesarean section rate in our series was 55.8%. This rate was similar to that observed over a similar period in other patients with multiple gestation at our centre.

Discussion

Pregnancies with three or more fetuses are associated with increased maternal and perinatal morbidity as well as perinatal mortality. Selective fetal reduction has been suggested as a therapeutic option for these pregnancies, in order to increase the chance of survival of the remaining fetuses (Berkowitz *et al.*, 1988; Hobbins, 1988; Evans *et al.*, 1988). Recently, the experience with 1789 multifetal pregnancy reductions was summarized in a collaborative study (Evans *et al.*, 1996), which convincingly reaffirmed that gestational age at delivery is inversely related to either the initial number of fetuses or the final number of fetuses remaining after selective termination. It seems that the inherent tendency for early delivery of a high order pregnancy is not completely eliminated by reducing the total number of fetuses in that pregnancy. The mean gestational age at delivery in our series was 35.7 weeks, similar to 35.6 weeks reported in the collaborative study (Evans *et al.*, 1996).

Our results indicate that early transvaginal embryo aspiration is a safe procedure, with a 6.7% total loss rate before 24 gestational weeks. This compares favourably with the 11.7%

Table III. Pregnancy outcome following selective fetal reduction

Starting no. of fetuses at selective termination	Loss at <24 weeks	Gestational age at delivery (weeks)				Total no.	Mean gestational age at delivery (weeks)
		25–28	29–32	33–36	>37		
≥5			2 (22.2)	4 (44.4)	3 (33.3)	9	35.2
4	1 (3.3)	1 (3.3)	3 (10)	13 (43.3)	12 (40)	30	35.8
	5 (9.8)	3 (5.9)	3 (5.9)	19 (37.3)	21 (41.2)	51	35.7
Total no.	6 (6.7)	4 (4.4)	8 (9.6)	36 (43.4)	36 (43.4)	90	35.7

Values in parentheses are percentages.

in the collaborative study (Evans *et al.*, 1996). Comparing these results with those reported in by Evans *et al.* (1996), we could not document a statistically significant difference between the two studies in the complication rate for triplets that were reduced to twins. However, our procedure appeared to be significantly ($P < 0.05$) safer when the initial number of fetuses was four or greater (one loss out of 39 procedures versus 141 losses out of 919 procedures in the collaborative study). In our series there was no difference between the timing of reduction among triplets (mean 7.5 gestational weeks) and quadruplets or higher order pregnancies (7.5 weeks on average). Therefore, this would not explain the better results we obtained with those pregnancies. Moreover, performing selective termination in two sessions did not increase the risk of pregnancy loss. Compared to later performed procedures, transvaginal embryo aspiration is easier to accomplish. It is also possible that avoiding the burden of aborted fetuses that is left after the ‘late’ procedures is beneficial and confers the observed advantage of our procedure. Early selective fetal reduction is more acceptable to some of our patients, both from moral and from religious points of view. In Judaism, a medically indicated abortion might be performed up to 40 days from conception (7 + 5/7 weeks menstrual age, Grazi and Wolowelsky, 1991). In addition, our method obviates the use of KCl or other toxic substances, and the potential fetal complications that might be associated with their use. The use of intracardiac KCl in multifetal pregnancy reduction was reported as a possible risk factor for periventricular leukomalacia in premature newborns (Geva *et al.*, 1998).

A potential disadvantage of transvaginal aspiration at 7–8 weeks gestation would be selective fetal reduction performed too early, i.e. before the ‘natural’ phenomenon of ‘vanishing twins’ could occur (Landy *et al.*, 1982; Dickey *et al.*, 1990; Landy and Keith, 1998). The whole pregnancy may be endangered if additional embryos were to be lost spontaneously after selective reduction to the desired number of fetuses had been completed. In our study the total number of retained living embryos following selective reduction was 183. The total number of lost fetuses (both because of early pregnancy loss and premature delivery) amounted to 18. This represents 9.8% of the total and sharply contrasts with the 30–60% rate of ‘vanishing twins’ reported by others (Landy *et al.*, 1982; Dickey *et al.*, 1990). Moreover, if whole pregnancy losses are excluded, spontaneous fetal demise after heart activity had been documented on ultrasound was very low (one out of 183 embryos in this series), confirming our previous observation (Kol *et al.*, 1993). Kol *et al.* (1993) also showed that the fetus

with the smaller CRL has a greater chance of spontaneous demise. In the present series, if an embryo smaller than the rest was identified, it was chosen for aspiration.

A considerable disadvantage of early transvaginal aspiration is the inability to identify the fetus with a structural anomaly that might be detected on ultrasound when the reduction is performed early in the second trimester. In triplet gestations, an alternative option (after appropriate counselling) is to defer selective reduction to the early second trimester, when ultrasound screening for fetal structural anomalies should be attempted. The rate of non-chromosomal structural malformations is indeed increased in multifetal pregnancies, but mainly in monozygotic gestations. Most multiple gestations occurring as a result of ovulation induction are derived from different zygotes. Ultrasonographic detection of congenital anomalies in multiple gestations may be hampered by fetal positioning and crowding, oligohydramnios and increased distance between the ultrasound transducer and the target organ. In twins, ultrasound screening for fetal anomalies is apparently as effective as in singleton gestations (Allen *et al.*, 1991), but data are not available regarding the efficacy of ultrasound diagnosis of fetal structural anomalies in multiple gestations of higher order.

In summary, early transvaginal embryo aspiration is a simple and relatively safe procedure. In quadruplets or higher order gestations, this procedure is apparently safer than other methods of selective fetal reduction. Moreover, it might be more acceptable to patients from emotional and religious points of view. We suggest that early transvaginal embryo aspiration should be offered to all patients with four or more fetuses. In these cases, early reduction to twins should be attempted. Either an abnormal ultrasound or the relative position (most accessible and highest in the uterus) should target the fetus for selective reduction. Most important, further studies are needed for development of safer methods of selective fetal reduction and, more pressing, for the initial avoidance of iatrogenic high order multiple pregnancies *per se*.

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Received on October 29, 1998; accepted on March 24, 1999