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Selective termination and elective reduction in twin pregnancies: 10 years experience at a single centre

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Selective termination is employed in multifetal pregnancies, in the presence of an abnormal fetus, in order to improve the prognosis of the normal fetuses. The term elective reduction is used to describe reduction in twin pregnancies for maternal medical conditions, psychological, or socio-economic reasons. The purpose of this study was to evaluate the factors that influence outcome in such pregnancies. Eighty-two twin pregnancies underwent selective termination ($n = 59$) or elective reduction ($n = 23$) over a 10-year period. Early procedures, performed ≤14 weeks ($n = 31$), had a pregnancy loss of 9.7% and a mean procedure-to-loss interval of 4.1 ± 2.8 weeks; mean birthweight was 3299 ± 395 g in survivors, with a mean gestational age at delivery of 38.4 ± 2.3 weeks. In comparison, procedures performed > 14 weeks ($n = 51$) had a pregnancy loss of 7.8%, with a procedure-to-loss interval of 1.2 ± 0.6 weeks. Mean birthweight was 2577 ± 999 g, with a mean gestational age at delivery of 35.7 ± 5 weeks. In conclusion, outcomes were more favourable among patients who underwent a first trimester procedure. The slight increase in pregnancy loss may be attributed to a higher than expected rate of spontaneous abortions in the first trimester, as manifested by the higher procedure-to-loss interval after a first trimester procedure. These facts underscore the importance of early detection of fetal abnormalities in twin pregnancies by ultrasonography and chorionic villus sampling.

Key words: elective reduction/multifetal pregnancy reduction/selective termination

Introduction

Selective termination is defined as the termination of an anomalous fetus in a multifetal gestation. The objective in this case is to allow the pregnancy to continue with the expectation that one or more healthy fetuses will subsequently be delivered (Committee on Ethics, 1991). The first selective termination was successfully performed on a fetus affected with Hurler syndrome in a twin gestation (Aberg *et al.*, 1978). Multifetal pregnancy reduction (MFPR) refers to the termination of one or more, presumably normal, fetuses in a multifetal pregnancy. This is performed in order to improve the survival rates for the remaining fetuses, and to decrease maternal morbidity. This procedure was first reported in 1986 (Dumez *et al.*, 1986). Over the past decade, MFPR has become a widely employed technique as a consequence of the prevalent use of infertility therapy (Dumez *et al.*, 1986; Berkowitz *et al.*, 1988; Evans *et al.*, 1988, 1990, 1993, 1994; Lynch *et al.*, 1990; Tabsh, 1990; Wapner *et al.*, 1990; Timor-Tritsch *et al.*, 1993). There is evidence that MFPR reduces complications in multifetal pregnancies; however, following MFPR to twins, there is still a higher incidence of pregnancy complications (miscarriage, pregnancy-induced hypertension, preterm labour) than with spontaneous twins (Groutz *et al.* 1996, Sebire *et al.*, 1997). While the benefit of MFPR is established in improving the outcome of pregnancies with quadruplets or more fetuses, there is still some controversy concerning whether it improves outcomes in triplets (Porreco *et al.*, 1991; Lipitz *et al.*, 1994a).

There are currently no data to suggest that pregnancy reduction in twins can improve pregnancy outcome. However, there are instances where a reduction procedure is performed in twin pregnancies when both twins are apparently normal. In this case, the term elective reduction should be used. Elective reduction may be employed because of maternal medical conditions (heart disease or uterine abnormalities), maternal psychological reasons, or social and economic concerns. The role of elective reduction for maternal medical conditions is controversial. Moreover, the ethical issues surrounding this procedures are, as yet, unresolved (Berkowitz, 1996). The purpose of this study was to evaluate the factors that influence pregnancy outcome in patients who undergo selective termination or elective reduction in twin pregnancies.

Materials and methods

The study group included 82 patients with dizygotic twin pregnancies who underwent selective termination or elective reduction over a 10-year period at the Center for Fetal Diagnosis and Therapy, Hutzel Hospital, Wayne State University, Detroit, MI, USA. Of these, 45 patients conceived spontaneously, 18 pregnancies resulted from standard in-vitro fertilization (IVF), 14 patients conceived after ovulation induction, and five patients conceived after oocyte donation. The indications for performing the procedures in the first or second trimesters are described in Table I. In this study there was no reported elective reduction for sex selection purposes. Prior to the procedure, patients were counselled extensively regarding the possible risks and

Table I. The indications for selective termination in nine first trimester and 50 second trimester dizygotic twin gestations

Fetal anomalies	Gestation period	
	⩽14 weeks (n = 9)	>14 weeks (n = 50)
Neural tube defects	–	17
Trisomy 21	1	11
Trisomy 18	2	3
Trisomy 13	–	4
Hydrocephalus	–	4
Multiple anomalies	2	1
Translocations	2	1
Klinefelter syndrome	–	3
Severe oligohydramnios	–	2
Cystic hygroma	1	–
Triploidy	–	1
Severe IUGR	–	1
Marker chromosome	–	1
Tetralogy of Fallot	–	1
Encephalocele	1	–

IUGR = intrauterine growth retardation.

Table II. Pregnancy outcome in 31 first trimester, and 51 second trimester selective terminations and elective reductions in twin pregnancies

	Procedure performed at		*P*-value
	⩽14 weeks (n = 31)	>14 weeks (n = 51)	
Maternal age (years) (mean ± SD)	35.8 ± 4.8	32.6 ± 5.9	NS
Gravida (mean ± SD)	2.5 ± 1.5	2.4 ± 1.5	NS
Para (mean ± SD)	0.7 ± 0.8	0.9 ± 1.1	NS
Gestational age at procedure (weeks) (mean ± SD)	11.4 ± 1.9	18.8 ± 2.2	< 0.0001
Pregnancy loss <24 weeks n (%)	3 (9.7)	4 (7.8)	NS
Preterm delivery[a] n (%)	2 (7.1)	13 (27.6)	0.06
Procedure-to-loss interval (weeks) (mean ± SD)	4.1 ± 2.8	1.2 ± 0.6	0.08
Birthweight (mean ± SD)	3299 ± 395	2577 ± 999	0.005
Gestational age at delivery (weeks) (mean ± SD)	38.4 ± 2.3	35.7 ± 5.0	0.04

[a]Rate of total viable deliveries.
NS = not significant.

complications of the procedure. In cases with pre-existing maternal medical conditions, the possible risks of carrying a twin gestation to term were discussed with regard to the expected outcome of the procedure.

Chorionicity was established ultrasonographically, using membrane thickness and the presence or absence of a chorionic peak (twin peak sign) (Barss *et al.*, 1985, Finberg, 1992). All procedures were performed by the transabdominal approach under real-time ultrasound guidance. The fetus chosen for selective termination would obviously be the one with the known abnormality. In elective reduction, the fetus chosen for reduction would be the one with suspicious ultrasonographic findings such as increased nuchal translucency, or delayed growth in comparison with its co-twin. In the absence of any abnormal ultrasonographic findings, the fetus most readily accessible was chosen, usually the one most fundal in location. A 22-gauge needle was inserted transabdominally and manoeuvred into the fetal thorax. Potassium chloride (KCl) was injected until cardiac asystole was noted for at least one minute. The resultant pleural effusion is usually a good indicator of proper placement. The amount of KCl required was usually 1 ml; however, at higher gestational ages, a larger amount would most often be needed (as much as 10 ml at 20 weeks). Pregnancy losses were defined as those occurring <24 weeks of gestation. Results were compared with two groups of patients having non-reduced twin gestations: 605 from the Wayne State University Perinatal Database, and 207 from the Quest Diagnostics Database (formerly, Corning Clinic Laboratories, Teterboro, NJ, USA).

Data were entered prospectively into a computerized database (FileMaker Pro for Macintosh version 3.0v2, Claris Corporation, USA). Patient variables and pregnancy outcome data were obtained from patient charts and hospital records. Additional information was obtained by physician-conducted telephone interviews. Patient variables included maternal age, gravidity, parity, method of conception, the indication for performing the procedure, and gestational age at the time of procedure. Outcome variables evaluated included gestational age at delivery, birthweight, pregnancy loss, procedure-to-loss interval, and neonatal complications. Statistical analysis was performed using Fisher's exact test, Student's *t*-test, and analysis of variance as appropriate (StatView© for Macintosh, and StatXact©Turbo version 2.11). A *P*-value < 0.05 was considered statistically significant. Numbers are presented as mean ± SD.

Results

Of the 82 procedures performed, 59 were due to fetal chromosomal or structural abnormalities. These included nine selective terminations performed in the first trimester and 50 selective terminations performed in the second trimester. The indications for selective terminations in the first and second trimesters are listed in Table I. A total of 23 elective reductions were performed, all but one were in the first trimester. The indications for elective reduction included six for maternal medical conditions (history of previous Caesarean sections, preterm labour in previous pregnancies, or history of severe pre-eclampsia), and 16 procedures were performed because of maternal psychological or socio-economic reasons.

Pregnancy outcome is described in Table II. The overall pregnancy loss was 8.5% (seven pregnancies). Of the remaining 75 patients, preterm deliveries were noted in 15 cases, a preterm delivery rate of 20%. Thirty-one patients underwent an early procedure (⩽14 weeks). These early procedures resulted in three pregnancy losses (9.7%). The procedure-to-loss interval was 4.1 ± 2.8 weeks. Mean birthweight was 3299 ± 395 g, and mean gestational age at delivery was 38.4 ± 2.3 weeks. In comparison, 51 other patients underwent a pregnancy reduction procedure after >14 weeks gestation, the upper range being 23.5 weeks. All but one were performed due to fetal anomalies (See Table I). Procedures performed >14 weeks were associated with four pregnancy losses (7.8%). Notably, the procedure-to-loss interval was only 1.2 ± 0.6 weeks. Mean birthweight was 2577 ± 999 g, and mean gestational age at delivery of 35.7 ± 5.0 weeks.

No significant effects on the various outcome variables were noted for maternal age, gravidity, parity, and method of conception. Table II compares pregnancy outcomes between early (⩽14 weeks) and late (>14 weeks) procedures. No differences were noted in the mean maternal age, gravidity, parity, or the overall pregnancy loss rate <24 weeks. However, early procedures were associated with a significantly lower rate of preterm deliveries, a significantly higher birthweight and a higher gestational age at delivery. There was also a trend,

Table III. A comparison of pregnancy outcome in 23 elective reductions (normal fetuses) and two groups of twin pregnancies: from the Wayne State University (WSU) Perinatal Database, and from the Quest Diagnostics Database

Group	Number of pregnancies	Miscarriage rate (%)[a]	Duration of gestation (weeks)[b]	Birthweight (g)[c]
Elective reduction	23	1 (4.3)	38.3 ± 2.4	3194 ± 478
Twins (Quest)	207	12 (5.8)	35.8 ± 3.9	2254 ± 653
Twins (WSU)	605	40 (6.3)	34.4 ± 3.6	2123 ± 634

[a]Not significant.
[b]$P < 0.0001$ (analysis of variance).
[c]$P < 0.0001$ (analysis of variance).

bordering on statistical significance, for a longer procedure-to-loss interval. Analysis of pregnancy loss over time during this 10-year interval did not reveal any significant trend.

Table III compares outcomes of patients undergoing elective reduction (normal fetuses) with results of two groups of patients with twin pregnancies: 605 from the Wayne State University Perinatal Database, and 207 from the Quest Diagnostics Database. Miscarriage rates were not significantly different when comparing all three groups. However, mean length of gestation and mean birthweights were both significantly higher in patients who underwent elective reduction than those of non-reduced twins.

Discussion

The presence of a twin pregnancy with one abnormal fetus poses a complicated medical and ethical issue. In the past, couples have been left with the unenviable choice of either keeping both fetuses, one of whom is abnormal, or terminating the entire pregnancy, including the normal fetus. This issue is compounded by the fact that the incidence of major birth defects in twins is more than just twice the rate of birth defects in singletons. For monozygotic twins, the risk of a significant birth defect approaches 10%, and is mostly a function of the timing of the embryonic split. The later the split of the embryo into two halves, the greater the chance of birth defects due to laterality (Luke, 1990). For the more common dizygotic twins, the incidence of various birth defects is also increased. For chromosome abnormalities, a woman with monozygotic twins has the same risk as one with a singleton pregnancy since monozygotic twins originate from a single embryo. However, a woman with dizygotic twins has twice the risk of having a chromosomally abnormal fetus as the age-related incidence.

In 1978, Aberg was the first to perform selective termination for an abnormal twin (Aberg *et al.*, 1978) and, in 1981, Kerenyi *et al.* (1981) reported on selective termination of a fetus with Down's syndrome. Many of the initial attempts at performing selective termination failed. This was most likely due to the fact that they were performed on monozygotic twins with a shared placenta. In such cases, the death of one fetus results in disseminated intravascular coagulation and sequelae of thromboemboli in the remaining fetus, causing devastating results such as porencephalic cysts. It has been suggested that the risk is ~80% for fetal demise when one monozygotic twin dies either naturally or iatrogenically (Golbus *et al.*, 1988). Currently, selective termination in monozygotic twins can be achieved by umbilical cord ligation under ultrasound guidance or by fibre-optic fetoscopy (Quintero *et al.*, 1994). Obviously, selective termination for dizygotic twins has a better chance of succeeding, and has been shown to be technically successful in virtually 100% of cases, and to result in a live-born singleton in approximately 85% of cases (Evans *et al.*, 1994).

There is, however, some degree of pregnancy loss, which may be attributed to either technical issues or patient variables. It has been suggested that technical dexterity is related to overall success, and is the result of accumulating experience (Lipitz *et al.*, 1994b). Other patient variables that may influence success rates include patient age, parity, and gestational age at the time of procedure. The purpose of this study was to assess the influence of such variables on pregnancy outcome after selective termination or elective reduction in a single centre with an accumulated experience of over 500 pregnancy reduction procedures.

Our data suggest that an important variable that affects pregnancy outcome is the timing of the procedure. Early procedures (≤14 weeks) were associated with a lower rate of preterm deliveries (bordering on statistical significance), a significantly longer gestation, and a significantly higher birthweight, compared with procedures performed after 14 weeks. Although pregnancy loss was not statistically different in both groups, the procedure-to-loss interval was higher among patients who had an early procedure (4.1 ± 2.8) than in those who had a late one (1.2 ± 0.6). This finding suggests that the underlying cause for pregnancy loss is different in each group. The shorter interval observed with the late procedures most likely reflects procedure-associated pregnancy loss. Conversely, the average 4-week interval associated with early procedures cannot all be explained by procedure complications. At least in part, it is probably due to the higher expected background miscarriage rate earlier in pregnancy. This underscores the importance of early diagnosis of chromosomal or ultrasonographic abnormalities in twin pregnancy. Indeed our data suggest that procedures performed early have a better outcome. However, to achieve such early diagnosis of abnormalities in twins, one would need early transvaginal ultrasonography and chorionic villus sampling.

When comparing the outcomes of patients undergoing elective reduction with those of non-reduced twin pregnancies, no significant difference was noted in miscarriage rates. However, mean length of gestation and mean birthweights were both

significantly higher in patients who underwent elective reduction than those of non-reduced twins. This suggests that elective reduction does not have an adverse effect on overall pregnancy outcome. Most importantly, there does not seem to be an increased risk of losing both fetuses as a result of the procedure. This is stated with caution because of the relatively small number of cases ($n = 23$).

Regarding the maternal medical indications for elective reduction, recent studies show that, in women with twins, a trial of labour after a previous Caesarean section is a safe and effective alternative to routine repeat Caesarean delivery (Miller *et al.*, 1996). However, even in this series, delivery by elective Caesarean section without a trial of labour was performed in 56% of patients. Moreover, haemodynamic changes in twin gestation place a greater demand on the cardiovascular system than in singleton pregnancies. This would have greater adverse effects on patients with a pre-existing cardiac disease. Finally, twin pregnancies have a statistically higher rate of pregnancy-induced hypertensive disorder than singleton pregnancies, particularly in nulliparous women (Santema *et al.*, 1995). Taken together, these data suggest that elective reduction may be considered for maternal medical conditions in some cases, although the benefit may still be controversial.

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