

## Fetal Reduction in Multifetal Pregnancy-Ethical Dilemmas

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As a result of the increased use of drugs that enhance fertility, and the advent of *in vitro* fertilization and embryo transfer over the last 2 decades, the incidence of multifetal pregnancies has increased exponentially. In parallel with this increase methods of care for women carrying multiple fetuses have become more complex and well developed. Importantly, it has become obvious that in the case of such pregnancies the rates of mortality and morbidity of both fetuses and mothers, particularly in cases where four or more fetuses are involved, are extremely high. Improvements in the techniques of assisted fertilization should result in fewer iatrogenic multifetal pregnancies and a commensurate decrease in related risks. Fetal reduction seems to be an acceptable method of improving maternal and fetal outcome in high order multiple pregnancies despite the many unresolved medical and ethical dilemmas.

**Key Words:** Fetal reduction, multifetal pregnancy, assisted reproduction

The introduction of various methods of assisted fertilization over the past decade has enabled many infertile couples to have offspring, but they also have an increased risk of multifetal pregnancy. In particular, the number of occurrences of twins has increased. However, there has also been a marked increase in the number of women carrying three or more fetuses. The incidence of multifetal pregnancies may be as high as 8% of all pregnancies resulting from the use of ovulation stimulators, and as high as 53% after the use of gonadotropin. *In vitro* fertilization and embryo transfer also increase the incidence of multifetal

pregnancies up to 30%.<sup>1-5</sup>

Multifetal pregnancies increase risks for both mother and fetuses. These frequently include anemia, diabetes, hyperemesis, urinary infections, hydramnios, preeclampsia, eclampsia, postpartum hemorrhage, psychological changes, and the necessity of ending the delivery by surgical methods. Miscarriages, premature deliveries, intrauterine growth retardation (IUGR), intrauterine transfusion, malformations, pathologic presentations, locked twins, prolapse of the umbilical cord, respiratory distress syndrome (RDS), and intraventricular bleeding are also common. As a result, the mortality of both mothers and fetuses has increased.<sup>2,6</sup> It is also important to note that there are numerous socioeconomic problems in families, which have experienced a multifetal birth, due to financial difficulties and to increased morbidity, and the higher levels of physical and mental handicaps in the children.

These facts make it necessary that we consider the use of fetal reduction in multifetal pregnancies to reduce the complications associated with high - order multiple gestations, by actually reducing the fetal number. As long ago as 1978, Aberg et al. performed the first fetal reduction in twins suffering from Hurler syndrome, by cardiac puncture and exsanguination by aspiration.<sup>7</sup> In 1980, Beck et al. reported a hysterotomy in the 22nd week of pregnancy, the elimination of a twin with Down syndrome, and birth at term of the remaining twin.<sup>8</sup> Over the last twenty years, there has been an increase in the use of fetal reduction in the treatment of multifetal pregnancy. Authors have reported upon the use of transabdominal puncture with exsanguination, intracardiac injections of formaldehyde or potassium chloride, and upon air embolism,<sup>9-12</sup> and upon intracardiac

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puncture and aspiration without the injection of any substances.<sup>13,14</sup> Initially, the reductions were exclusively selective in order to eliminate a sick fetus.<sup>7,8</sup> However, in the past decade, nonselective reductions have been used in order to improve the perinatal course of the remaining fetuses. To date, over 3000 fetal reductions have been used for treatment in multifetal pregnancies.<sup>15,16</sup>

## CRITERIA FOR FETAL REDUCTION

In order to improve the perinatal courses of fetuses in such circumstances, fetal reduction is frequently employed. There are two types of fetal reduction: selective which involves the elimination of a fetus, which has documented structural, chromosomal, or genetic anomalies, and non-selective reduction, which involves the elimination of some of the fetuses for the benefit of the others.

It is well known that the frequency of fetal malformations in multifetal pregnancies is twice that of single pregnancies. This frequency increases with ovarian stimulation, and is greater still in association with a larger number of fetuses. Therefore, an objective and responsible approach necessitates the use of morphological and chromosomal analyses prior to fetal reduction, to ensure that the sick, rather than the healthy fetuses are reduced.<sup>17-19</sup> The three most important criteria for selection are: growth retardation, morphological malformation and chromosomal anomalies.

This sort of analysis can be rather difficult in pregnancies with multiple fetuses and as a result placental and fetal topographic maps are often used.<sup>3</sup> The most common analytical method used is chorionic villus sampling (CVS), which may be employed after the 8th week of pregnancy. Through the use of fast-growing cultures, polymerase chain reaction (PCR), and tissue sampling, this method allows diagnosis within a few days.<sup>20,21</sup>

In cases where the possibility of malformations is excluded, non-selective fetal reduction is performed. The choice of the fetus to be eliminated in this case depends on technical considerations.<sup>15</sup> In our opinion, fetal reduction should not be performed prior to thorough diagnostic testing.

## FETAL REDUCTION TECHNIQUE AND TIMING

There are two generally used methods: transabdominal or transvaginal intracardial puncture with 2-3 mEq of potassium chloride under ultrasound guidance. Both of these methods are relatively safe. The transvaginal approach is measurably more dangerous due to the occurrence of bleeding, chorioamnionitis, and subchorionic hematoma in a significant number of cases. Since the complications associated with the transvaginal method are as high as 10% of cases, the majority of gynecologists prefer to use the abdominal approach.<sup>3,5,12,22</sup>

In general, reduction is not done prior to the tenth week of pregnancy due to the possibility of a premature birth, and due to the high incidence of miscarriages up to the tenth week.<sup>2,3,5,15,23,24</sup> The optimal time for reduction is between the 10th and the 12th week of pregnancy. In cases where reduction is performed after this time, the prognosis for the remaining fetuses is poor.<sup>12,25</sup> A number of authors encourage reduction at later gestational ages, because detection of structural and chromosomal anomalies before the procedure and selective reduction of the affected fetus.<sup>3,26</sup> Moreover, those who do so regard the 20th week of gestation as a good time since at this point it is possible to diagnose many fetal malformations.<sup>25,27</sup> There are some reports of reductions being performed later, up to and including the 28th week of gestation, however, these reductions have been performed solely for eugenic reasons.<sup>11</sup>

## OPTIMAL FETAL NUMBER FOR REDUCTION

The typical duration of pregnancy in the case of twins is 36 weeks, in triplets 33 weeks, in quadruplets 29 weeks, and in quintuplets 24 weeks. In the case of reductions to a single fetus the length of gestation is prolonged to 37 weeks, reduction to two fetuses prolongs the duration to 36 weeks, and reduction to three fetuses extends the duration of pregnancy to 34 weeks, which reflects the obvious benefits resulting from the use of this procedure.

During the past ten years, our clinic has performed 883 twin deliveries with an average gestational age of 36.4 weeks and a perinatal mortality of 3.6%, 18 triplet deliveries with an average gestational age of 34.5 weeks and a perinatal mortality of 9.5 %, and a single delivery of healthy quadruplets via Cesarean section during the 35th week.

There is some debate about the number of fetuses that should be removed. In the case of five or more fetuses there should be no dilemma as the rate of survival following reduction to four fetuses is more than doubled (76% post-reduction compared to about 40% when no reduction is performed). Survival in the case of six or more fetuses is extremely rare. In the case of quadruplets opinions are split in spite of the fact that the majority of authors agree that reduction is justifiable since the survival rate increases considerably following the reduction of quadruplets to triplets.<sup>2,28,29</sup> The usefulness of reduction in the case of triplets has been the subject of controversy. According to recent reports, mortality decreases from 21% to about 8.7%, and morbidity also decreases,<sup>29,30</sup> and preterm birth and fetal growth improve.<sup>5,7,8</sup> However, the other opinion is that fetal reduction in the case of triplets is unnecessary since the outcome of these pregnancies can be improved with better antenatal care and the prevention of premature delivery. Moreover, the reduction procedure itself does not decrease maternal complications, nor does it increase gestational age or newborn weight.<sup>31,32</sup> The results obtained at our clinic are in agreement with reported data.

Survival rate after fetal reduction to twins is about 94%, which is similar to that of 'natural' twins. Reduction to a single fetus is controversial, and it has been noticed that this type of reduction is usually requested by elderly couples, whose reasons are probably of a psychological and/or financial nature.<sup>1,14</sup> Almost all authors agree that in such instances non-selective reduction is not justifiable. There are many risks associated with this procedure (PROM, miscarriage, chorioamnionitis, and bleeding), and twin pregnancies in this age of modern gynecology are far from unmanageable.<sup>31,33,34</sup> One might consider exceptions for medical reasons, for example, uterus bicornis,

monoamniotic twins in triplets, prior premature delivery before the 30th week of gestation.<sup>29</sup> These situations present relatively justifiable reasons, and in such circumstances, the possible consequences of the reduction procedure should be carefully discussed with the mother and her partner.

## RISKS OF FETAL REDUCTION

In the hands of an expert, reductions are almost 100% successful, and rare instances of induced asystole are considered a technical failure.<sup>35,36</sup> Almost all authors prefer the transabdominal approach to the transvaginal approach, and particularly to the transcervical approach, as the latter methods are riskier due to frequent chorioamnionitis and bleeding.<sup>2,15</sup> The method of choice is the intracardial injection of 2-3 mEq potassium chloride, and the less commonly used formaldehyde or air embolism.<sup>3,5,15,23</sup>

The total estimated fetal loss following the reduction procedure is about 13%. The rate of loss is almost doubled before the 24th week compared to that at a later gestational age. The most critical period for loss after fetal reduction is during the four weeks following the procedure.<sup>35-37</sup> The most common causes of loss are the preterm rupture of membranes (PROM), contractions, chorioamnionitis, and bleeding.

Data from other centers indicate that the frequency of PROM, preeclampsia, and other maternal and fetal complications is only slightly higher in reduced pregnancies than in woman not requiring reduction with the same number of fetuses.<sup>17,38</sup> The fetal reduction procedure does not increase the frequency of IUGR, except in cases where the initial number of fetuses is five or more.<sup>39</sup>

Since unsuccessful reductions are often associated with mechanical injuries and hypoxic brain damage, some authors recommend the reduction of all fetuses in cases of unsuccessful reduction.<sup>11</sup> In non-selective reduction, the smallest and most surgically accessible embryos are usually eliminated. However, some authors do not recommend the reduction of embryos closest to the cervix as this can result in infections.<sup>5,23</sup>

## ETHICAL DILEMMAS

Medically, it seems quite clear that benefits to the mother and the fetuses cannot be overstated. However, one must also take into consideration other factors when deciding whether to perform a fetal reduction. Most importantly, there are the obvious ethical issues and the possibility of psychological consequences. This risk of negative psychological outcomes is of particular concern in the event of a post-reduction miscarriage of the remaining fetuses. As has been noted, the number of multifetal pregnancies has increased as the number of women receiving fertility treatment has increased. A woman who has placed herself in a position of seeking medical assistance to become pregnant is generally already in an emotionally vulnerable state. These women often have a pessimistic view of the outcome of the entire pregnancy and the onset of depression is frequently associated with the reduction of fetuses that had been desired for so long. In addition, the antenatal care of women carrying multiple fetuses necessitates rest, medication and hospitalization, which can cause negative psychological reactions. Postpartum depression and other psychological problems in women who have delivered three, four or more children are becoming more frequent. Therefore, the acceptance of a multifetal pregnancy and the decision for fetal reduction are difficult experiences for the pregnant woman. In spite of this, the desire to have children, and the understanding that this procedure increases the chances of survival of the remaining fetuses aids the decision making process. Feelings of loss and unhappiness, when they occur, usually last for a comparatively short time, probably because of concern for the well-being of the other fetuses. The risk of psychological consequences is also greater for women with prior psychological problems, ambivalence or deep religious beliefs.<sup>40-42</sup> Some authors prefer psychological follow-up of such patients.<sup>43</sup>

Another authors hold that the procedure is justifiable only for selective reduction.<sup>44,45</sup> Non-selective reduction could be viewed as an artificial miscarriage, however, opinions are divided on the subject. Clinical doctors hold that the procedure can not be compared with a miscarriage as long

as there is a desire to retain the remaining fetuses until the end of the pregnancy.<sup>46</sup> From this ethical and psychological perspective the difference between selective and non-selective reduction, and artificial miscarriage are evident. Unlike artificial miscarriage, fetal reduction is performed with the goal of delivering healthy offspring in cases with complicating circumstances, whether these complications are fetal malformations or a high number of fetuses.<sup>25</sup> In addition, there is some discussion about considerations of fetal sex and a mother's decision in the context of fetal reduction.<sup>47</sup> Unfortunately, there is no consensus on the independent ethical status of the embryo as a patient, and theme will probably never be one.<sup>48</sup> It is our opinion that cases should be discussed individually bearing in mind all the pros and cons with the patient and her partner. The patient should be informed of all the possible risks and advantages of the procedure, and of the risks associated with the procedure not being performed. The patient should also be encouraged to express her opinion on all questions.<sup>2,49</sup>

Multifetal pregnancies often present a socioeconomic trauma to the family. Whether it is justifiable to perform reduction for these reasons is questionable. In Britain, fetal reduction to a single fetus for socioeconomic reasons caused a storm of controversy. However, the British Medical Society took the stand that in these cases no legal or ethical norms were violated.<sup>15</sup>

In our opinion, having considered the delicacies involved in this procedure, we should establish both legal and ethical standards that will allow a mother's autonomy and a doctor's freedom. We believe that the resolution of this problem lies in the application of the assisted fertility methods and in the use of fertility drugs. Only highly qualified experts should be dealing with these problems. The use of aggressive treatments should be reduced to a minimum, and multiple pregnancies should be avoided by carefully following recommended treatment procedures.

In the past, all that could be done was to oversee these women and provide them with the best available care to allow them to deal with possibly mentally and physically challenged children. The development of selective fetal reduction in such cases has enabled couples to have healthy

offspring and spared them the emotional and financial traumas associated with having a mentally and physically challenged child.<sup>25,43</sup>

## CONCLUSIONS

It is clear that the number multifetal pregnancies will continue to increase as the number of couples seeking fertility assistance increases. The techniques for fetal reduction are also likely to improve, which may eliminate many of the medical dilemmas that exist. Today one can claim that fetal reduction is an eminently acceptable way of improving of the course of multifetal pregnancies, especially those involving four or more embryos. The advantages of fetal reduction in triplets appear to be minimal, and given the quality of modern neonatal and obstetric care triplets should not be subjected to non-selective reduction. It is evident that the fetal reduction of twins is unjustifiable except in rare medical circumstances. Each fetal reduction procedure should be preceded by a detailed genetic and ultrasonic analysis, which should be considered an integral part of the diagnosis and reduction procedure. Prior to the reduction, careful consultation with the couple is essential, and all the possible benefits and risks of this procedure should be taken into consideration with special attention paid to specific medical, socio-economic and psychological circumstances. The final decision should be made by the mother and her partner in agreement with the doctor. The resolution of the many dilemmas that exist today concerning assisted fertilization will help control iatrogenic multifetal pregnancies. Though we are less likely to face the dilemmas associated with fetal reduction in the future, some of the medical and ethical problems will remain and discussions will not diminish in relevance. Finally, we assert that fetal reduction is an acceptable way of decreasing maternal and fetal mortality and morbidity.

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