

Multifetal Pregnancy Reduction*

Committee on Ethics

ABSTRACT: Counseling for treatment of infertility should include a discussion of the risks of multifetal pregnancy, and multifetal pregnancy reduction should be discussed with patients before the initiation of any treatment that could increase the risk of multifetal pregnancy. In almost all cases, it is preferable to terminate an ovulation induction cycle or limit the number of embryos to be transferred to prevent a situation in which fetal reduction will have to be considered. The best interests of the patient and the future child or children should be at the center of the risk-benefit equation. Although no physicians need to perform fetal reductions if they believe that such procedures are morally unacceptable, all obstetricians and gynecologists should be aware of the medical and ethical issues in these complex situations and be prepared to respond in a professional, ethical manner.

The ethical issues surrounding the use and consequences of reproductive technologies are highly complex, and no one position reflects the variety of opinions within the membership of the American College of Obstetricians and Gynecologists. The purpose of this Committee Opinion is to review the ethical issues involved in multifetal pregnancy reduction. For the purposes of this document, multifetal pregnancy reduction is defined as a first-trimester or early second-trimester procedure for termination of one or more fetuses in a multifetal pregnancy, to increase the chances of survival of the remaining fetuses and decrease long-term morbidity for the delivered infants (1).

To many, the ethical issues involved in multifetal pregnancy reduction are somewhat different from the issues involved in abortion, as discussed in the "Analysis" section. Although no physicians need to perform multifetal pregnancy reductions if they believe that such procedures are morally unacceptable, all physicians should be aware of the medical and ethical issues in these complex situations and be prepared to respond in a professional, ethical manner to patient requests for information and procedures.

Background

Spontaneous occurrences of multifetal pregnancies always have been a medical problem. More recently, increased use of potent ovulation-induction drugs and assisted reproductive technology (ART), such as in vitro fertilization (IVF), have been effective in the treatment of infertility but subsequently also have increased the risk of multifetal pregnancy (2). Thousands of patients previously unable to have children have been assisted to achieve conception. In a small percentage of these patients, the resultant pregnancy has involved more than two fetuses, thereby creating potentially serious problems (2-6). There is widespread agreement that the risks of perinatal morbidity and mortality and maternal morbidity increase with the number of fetuses. Recent reports have shown improving outcomes with multifetal pregnancies, but the risks are still significant (6).

Prevention

The first approach to this problem is or should be prevention. It might be argued that the problem is best remedied by discontinuing technologic assistance to reproduction. On the one hand, this approach discounts the major benefits that ART offers to patients and suggests an unwarranted coercive restriction on parental choice and autonomy. On the other hand, the association of an



**The American College
of Obstetricians
and Gynecologists**

*Women's Health Care
Physicians*

*Update of "Multifetal Pregnancy Reduction" in *Ethics in Obstetrics and Gynecology*, Second Edition, 2004.

increased rate of multifetal pregnancies with infertility treatment deserves serious attention. Some multifetal pregnancies will inevitably occur despite the best of intentions, knowledge, skill, and equipment, but it is essential that those providing infertility treatment exercise a high degree of diligence to minimize the problem.

Both ovulation induction alone and IVF contribute to high-order multiple births (more than two). In 1977, 43.3% of all births of triplets or greater were the result of ART (ie, IVF) and 38.2% were the result of the use of ovulation drugs (5). In 1996, the order was reversed; 40.4% of births of triplets or greater were the result of ovulation drugs, whereas 38.7% were the result of ART (5). According to the Centers for Disease Control and Prevention, 3,390 infants were born in triplet or higher-order multiple deliveries after ART treatment in 2003, accounting for 44% of all infants born in triplet or higher-order multiple deliveries (7). Similar data are not available for ovulation induction cycles.

Ovulation induction with gonadotropin cycles in which ultrasound imaging demonstrates the presence of many mature follicles, each capable of releasing an ovum, presents a difficult decision on whether to give human chorionic gonadotropin (hCG) to induce ovulation. If an hCG injection is withheld, the patient will have spent considerable time and emotional and financial resources for a nonovulatory cycle. Yet, if hCG is given to trigger ovulation, a high-order multifetal pregnancy may result. Attempts have been made to develop criteria for withholding hCG (eg, more than six large follicles or estradiol levels greater than 1,500 pg/mL). However, a large study showed that the occurrence of high-order multifetal pregnancies after gonadotropin therapy increases with higher estradiol levels but cannot be reliably predicted by the number of mature follicles on ultrasound examination (8). The authors concluded that adherence to criteria for withholding hCG will not prevent high-order multiple births and that better criteria cannot easily be established. They suggest that the use of treatment protocols with less-intensive stimulation of the ovaries may reduce the incidence of high-order multifetal pregnancies, but only to a limited extent and at the expense of pregnancy rates. When many follicles are present, alternative approaches would be conversion of the gonadotropin cycle to an IVF cycle or selective aspiration of the supernumerary follicles (9).

In ART, there may be pressure to be successful because of both prospective parents' and programs' interests. Direct costs for IVF cycles are many times higher than those for ovulation induction alone with gonadotropins. Ovulation induction with gonadotropins may be more likely to be covered by insurance. Patients who choose to undergo IVF may be paying for treatment out of pocket, and this may add pressure to achieve pregnancy on the first attempt. In addition, IVF programs face public scrutiny not faced by programs that offer only ovulation induction. Although success rates for individual

IVF programs are public information, published by the Centers for Disease Control and Prevention, similar reporting is not done for ovulation induction alone (2). As the number of embryos transferred increases, program success rates may increase, but so does the risk of a multifetal pregnancy (2).

The physician who makes decisions about the circumstances for triggering ovulation or guidelines for embryo transfer must, as in any medical situation, place the best interests of the patient and the future child or children at the center of the risk-benefit equation. In some countries, such as England, where ART is centrally regulated, limitations are placed on the number of embryos that can be transferred, and subsequently fewer multifetal pregnancies result.

In the United States, the decision is left to individual physicians and programs. In almost all cases, it is preferable to terminate a gonadotropin cycle used for ovulation induction alone or limit the number of embryos to be transferred in IVF to prevent a situation in which patients and physicians will have to consider fetal reduction. The Practice Committee of the American Society for Reproductive Medicine (ASRM) has issued a report suggesting prognosis-dependent guidelines for limiting the number of embryos to be transferred. These guidelines limit risk while allowing individualization of patient care for optimal results (10). Multifetal pregnancy reduction should be viewed as a response to a consequence of ovulation induction that cannot always be avoided; it should not be a routinely accepted treatment for an iatrogenic problem.

The ultimate goal in prevention is to significantly reduce the likelihood that any multifetal pregnancy will occur, including twins. This will require patients, physicians, and payers to support a culture in which IVF may replace gonadotropin-only therapy in treatment algorithms. When IVF is performed, the eventual goal in the future may be to transfer only the embryo with the greatest chance for growth and implantation; currently ASRM recommends that consideration be given to transferring only a single embryo for patients with the most favorable prognosis (10). Nonetheless, data from the Centers for Disease Control and Prevention indicate that approximately 56% of embryo transfers that used fresh non-donor eggs in 2003 involved the transfer of three or more embryos (2).

Another strategy under study is transfer of blastocysts instead of cleavage-stage embryos, hoping that higher pregnancy rates would allow fewer embryos to be transferred. Yet, although some randomized trials have found higher pregnancy or live-birth rates with the transfer of a single blastocyst-stage embryo over a single cleavage-stage embryo (11, 12), the transfer of blastocyst-stage embryos has not been supported by others (13). The current position of ASRM is that either blastocyst transfer or cleavage stage-embryo transfer may be performed (10).

Counseling

As with all medical care, counseling for treatment of infertility should incorporate discussions of risks, benefits, and treatment alternatives, including the option for no treatment. Counseling should be considered an ongoing process, beginning before treatment decisions are made and continuing throughout the patient's care. The risks of certain treatments of infertility include, but are not limited to, the occurrence of multifetal pregnancy, with its associated risks of spontaneous abortion, preterm labor and delivery, and neonatal morbidity and mortality. The informed consent process must include information about the potential for multifetal pregnancy and associated maternal risks, such as prolonged hospitalization, antepartum bleeding, postpartum hemorrhage, hypertensive diseases of pregnancy, and an increased rate of cesarean delivery. Whether patients decide to maintain or to reduce high-order multiple pregnancies, they should be assured that they will receive the best available care (14).

It also is the responsibility of the physician to inform the patient that fetal reduction as a response to multifetal pregnancy has inherent medical risks to the remaining fetuses. Pregnancy loss rates of approximately 4–6% have been reported for triplet-to-twin reduction in large samples (15–17), but higher rates also have been reported (18). Reports of lower birth weights for twins reduced from triplets also are of concern (19–20), although more recent reports have suggested that reduction from triplets or quadruplets to twins is associated with an outcome as good as with an unreduced twin gestation (15, 22–26). Nonetheless, patients should not be given the impression that multifetal pregnancies are without problems because fetal reduction is available.

Patients struggle with the ethical and emotional issues of fetal reduction. In a postdelivery informational survey of couples who had undergone multifetal pregnancy reduction, few of the small sample of respondents reported that they understood the procedure or its consequences fully at the time of fetal reduction (27). In semi-structured interviews of 10 women who had undergone multifetal pregnancy reduction, one third reported still feeling guilt 1 year after the procedure (28). Many infertility patients have unrealistic ideas about the outcomes for high-order multifetal pregnancies that leave them unprepared for feelings of loss and grief at the time of a reduction procedure (29, 30). However, in studies that used standard psychologic tests to assess the emotional state of patients after multifetal pregnancy reduction, serious long-term psychologic sequelae were not identified. Among women who underwent multifetal pregnancy reduction and subsequently miscarried the entire pregnancy, depression scores were similar to scores for a control group of women who did not undergo fetal reduction and subsequently miscarried the entire pregnancy (31).

A report that 93% of patients who decided to proceed with fetal reduction would make that decision again despite their experience of stress and sadness is somewhat reassuring, but the number of patients studied was quite small ($n = 91$) (32). The ethical issues that this option involves should be discussed with patients before the initiation of any treatment that could increase the risk of multifetal pregnancy. Although patients should be encouraged to examine their feelings about these risks and options at the onset, the counseling process should encourage them to continue this assessment at appropriate points in the treatment process (33).

Options

In the presence of an already established multifetal pregnancy, the options are inevitably difficult. No choice is without potential consequences, and the potential benefits must be carefully weighed against the potential harms. There are three options in multifetal pregnancies:

1. Abort the entire pregnancy (all of the fetuses).
2. Continue the pregnancy (all of the fetuses).
3. Perform multifetal pregnancy reduction on one or more of the fetuses.

The first option involves aborting the entire multifetal pregnancy. However, for some patients, aborting the pregnancy is not an acceptable option. For other patients who may have achieved pregnancy after infertility treatment, this option may be considered the least desirable.

The second option is attempting to carry the multifetal pregnancy to term. However, the risks of perinatal and maternal morbidity and mortality increase directly with the number of fetuses (8). These risks include losing all of the fetuses or having some survive with permanent impairment as a consequence of extreme preterm birth. The assessment of what constitutes "significant risk" varies among patients and physicians and, therefore, is not amenable to uniform definition. Physicians should respect their patients' conclusions about which risks are acceptable and which are too high.

The third option in multifetal pregnancies is multifetal pregnancy reduction. The technique brings about the demise of one or more fetuses with the intent to allow continuation of the pregnancy, resulting in the delivery of fewer infants with lower risks of preterm birth, morbidity, and mortality. Although this procedure is successful in most cases, it may raise some unsettling ethical concerns. There is a complex interrelationship between the intention to reduce the morbidity of a smaller number of surviving fetuses and the intentional sacrifice of others that demands an ethical as well as medical assessment of the relative benefits and risks of multifetal pregnancy reduction. What follows is an attempt to outline such an assessment, with the understanding that each case ultimately must be examined on its own merits.

Analysis

Many would argue that there are differences between the ethical analyses involved in multifetal pregnancy reduction and elective abortion because the intent is different. A woman has an elective abortion because, for many complex and varied reasons, she does not wish or feels unable to have a child. In contrast, an infertility patient who has a multifetal pregnancy undergoes fetal reduction precisely because she does wish to bear a child. The patient and her physician may conclude that fetal reduction is the preferred way to continue her pregnancy. For some individuals, the primary intention justifying fetal reduction may be the life and well-being of the fetuses that do survive and continue to develop. For others, it is unethical to terminate an apparently healthy fetus, even for the sake of the survival or well-being of other fetuses in the pregnancy.

Some individuals who believe that abortion is generally unacceptable find multifetal pregnancy reduction to be justified ethically when the risks of carrying the pregnancy are considerable and could be reduced if the number of fetuses were fewer. Individual patients will evaluate varying degrees of risk differently. As advances in maternal–fetal and neonatal medicine continue, the risk of extreme preterm birth is expected to decrease. The issues of patient choice and physician participation and consultation need to be analyzed on a case-by-case basis.

Summary

Although physicians may choose not to participate in multifetal pregnancy reduction, they should be knowledgeable about this procedure and be prepared to react in a professional and ethical manner to patient requests for information or services or both. The first approach to the problem of multifetal pregnancies should be prevention. Although fetal reduction will be ethically acceptable to many as a response to an unforeseen and unavoidable contingency, in almost all cases, it is preferable to terminate a gonadotropin cycle or limit the number of embryos to be transferred to prevent a situation in which the patient and physician need to consider fetal reduction. Counseling for treatment of infertility should include a discussion of the risks of multifetal pregnancy, and the ethical issues surrounding fetal reduction should be discussed with patients before the initiation of any treatment that could increase the risk of multifetal pregnancy.

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Multifetal pregnancy reduction. ACOG Committee Opinion No. 369. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2007;109:1511–5.

12345/10987

ISSN 1074-861X

