Managing Preterm Labor in Multiple Gestations

Preterm labor is one of the most important and vexing challenges complicating pregnancy. Premature babies account for an estimated 6%-10% of births, yet are likely to do well for 70%-85% of neonatal morbidity and mortality.

In multiple gestations, which are increasingly common as a result of delayed childbearing and the use of assisted reproductive technologies, preterm labor is an even greater risk. The literature points to an incidence of preterm labor of 20%-75% in multiple gestations. Although these figures may be somewhat high, I think it is safe to say that at least 1 in 10 multiple gestations seen at my institution are complicated by preterm labor. Not all of these patients will be admitted or will deliver early, but the very common nature of this problem and the potentially lethal consequences of premature multiple deliveries make this issue one that a physician and institution should approach carefully.

First, it is important to consider the delivery goal of a multiple gestation pregnancy. Overall, most twins are delivered at 37-38 weeks. For triplets, the gestational age is closer to 34 weeks, and quadruplets are born at around 30 weeks. These are reasonable numbers applicable to community practice.

If a patient arrives in preterm labor, you have to decide what to do, considering her situation and the capabilities of your local hospital and medical staff. It is clear that premature babies fare best when they are cared for in the institution where they are born. If someone needs to be transferred, it should be the mother, not the baby.

Obviously, if a patient carrying twins presents in labor at 35 or 36 weeks, most obstetricians would be inclined to do very little to cut short the labor, because—in the absence of other complications—these babies are likely to do well. However, if she presents at 29 weeks, it would make sense to be more aggressive.

Can the patient be safely and aggressively managed for preterm labor in her local community? The answer hinges on the plan for delivery if the treatment fails. Each hospital and service has to pick a gestational age at which neonatal survival is acceptably high. Then, options for the mother should be discussed with her and with the neonatal intensive care unit at your hospital or the institution to which she will be transferred.

Depending on the circumstances, the treatment of preterm labor may be undertaken for several reasons:

- To delay delivery until the patient can be transferred to a tertiary medical center with a high-level neonatal intensive care unit.
- To delay delivery 24-48 hours for the administration of corticosteroid therapy.
- To reduce the strength and frequency of uterine contractions, enabling the fetus to further develop in the uterus.
- To minimize hospital stays for the mother and the neonate.
- To reduce the risk of neonatal morbidity and mortality by preventing preterm delivery, the most dangerous complication of multiple gestation pregnancies.
- When I consult with a woman in preterm labor, I go through a list of available options. Unfortunately, a careful review of the literature reveals few really good, effective treatments.

Although new ideas emerge every few years, not many interventional strategies have withstood attempts to corroborate results from single institutions. It may be tempting to “just do something,” but we owe it to our patients to stick to scientifically valid and efficacious treatments.

Bed Rest

Bed rest or activity restriction will not prevent preterm labor. Rest neither lengthens gestation nor reduces neonatal morbidity in multiple gestation pregnancies. In some studies these patients did worse.

If a patient carrying multiples has a short cervix and threatened preterm labor, there is some evidence to support getting her off her feet rather than having her continue working at a very active job.

Once a multiple pregnancy is complicated by preterm labor, hospitalization may be necessary for observation and implementation of a treatment course.

Hydration

There is no evidence that hydration is an effective treatment for preterm labor. In fact, the initial administration of bolus intravenous fluids may pose some risk to patients with multiple gestations. These patients already have an increased blood volume and could develop pulmonary edema from fluid overload if tocolytic therapy is initiated after unnecessary fluids are administered.

Prostagangerges

A study by Paul J. Meis, M.D., and colleagues (N. Engl. J. Med. 2003;348:2379-85) suggests recurrent preterm birth in singleton pregnancies can be prevented by 17-α-hydroxyprogesterone caproate. The jury is still out on whether progesterone can be useful in managing active or threatened preterm labor in a multiple gestation pregnancy.

Studies are underway that may provide us with more guidance in the use of this agent. However, no evidence exists that it is safe and efficacious in multiple gestation pregnancies, so I suggest its use be reserved for patients already shown that some multiple gestations can be prolonged for more than 7 days (Am. J. Obstet. Gynecol. 1989;161:5475; “Multifetal Pregnancy: A Handbook for Care of the Pregnant Patient” [Philadelphia: Lippincott Williams & Wilkins, 2000]).

Each tocolytic agent carries its own benefits, risks, contraindications, and adverse effect profile. Numerous sources are available for this information; for quick reference; I recently published a summary in chart form (Clin. Obstet. Gynecol. 2004;47:216-26). Keep in mind that women with multiple gestations have an elevated risk of cardiovascular complications, such as pulmonary edema resulting from anemia, lower colloid oncotic pressure, and higher blood volume.

I would take a middle-of-the-road approach in choosing an agent or agents for tocolysis. For example, oral terbutaline, oral calcium channel blockers, and oral Indocin have been well-studied and widely used, with varying levels of success.

John P. Elliott, M.D., and Tari Radin, Ph.D., studied a number of high-order multiple gestations and found similar levels of serum magnesium in triplets and quadruplets and in singleton pregnancies after the administration of magnesium...
Continued from previous page

sulfate for tocolysis (J. Reprod. Med. 1995;40:450-2). However, they concluded that higher levels of magnesium sulfate are needed in multiple gestations to inhibit labor. They suggested administration at infusion rates of 4.5 g/h in triplet and quadruplet pregnancies.

Research on combination tocolytic therapy has produced conflicting results. Most of the studies on this topic are dated, limited in scope, and not specifically focused on multiple gestations. Some concerns, however, have been raised. For example, magnesium sulfate in conjunction with nifedipine can result in significant neuromuscular blockade and a subsequent marked hypotensive effect.

My recommendation is to administer combination tocolytic therapy only with great caution, using agents such as intravenous magnesium sulfate with oral terbutaline or indomethacin. The mother and fetus also should be monitored closely by professionals well versed in side effects linked to this form of therapy.

Should the tocolytic therapy be maintained after successful cessation of labor? A careful reading of the available evidence suggests the answer is no. In well-designed studies, maintenance tocolytic therapy has reduced neither preterm deliveries nor perinatal morbidity or mortality.

Corticosteroids

Corticosteroids are among the few non-controversial agents for use during preterm labor. These agents—which clearly reduce the incidence and severity of neonatal respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, and neonatal mortality—should be administered to any patient in preterm labor at 24 weeks or more using the same regimen as in singleton gestations.

The accepted corticosteroid treatment consists of two intramuscular doses of betamethasone or four intramuscular doses of dexamethasone.

In higher-order gestations, Dr. Elliott and Dr. Radin have observed that betamethasone can increase uterine contractions and advance labor in patients with frequent contractions. They therefore recommend that corticosteroids be reserved in these pregnancies for patients having fewer than three contractions per hour (Obstet. Gynecol. 1995;85:250-54). Uterine activity in higher-order gestations should be closely monitored before following the administration of corticosteroids.

It was suggested that multiple courses of prenatal corticosteroids might be of benefit. This recommendation is no longer made, because there is no good evidence for enhanced efficacy and because repeated doses are associated with clear risks, including decreased fetal growth and reduced birth weight.

Adjuvantive Treatments

Isolated studies have suggested a role in preterm labor for such interventions as vaginal lever pessaries, blood transfusions, and cerclage. None of these have been put to rigorous scientific scrutiny. Cerclage obviously has no role in patients who do not have an incompetent cervix, or in such specific cases as the provable delivery of one dichotonic twin when a delayed-in-terval delivery of the second twin is desired.

Treating the Whole Patient

Not infrequently, preterm labor in a multiple gestation or a singleton gestation is the prolonged hospitalization of the mother, who may be a busy professional woman or the parent of other small children. Spending 5-10 weeks in a hospital is a long, frustrating time, replete with boredom and anxiety.

At my institutional neurobehavioral special unit who was concerned with the psychosocial effect of hospitalization on the women in our unit proposed what has become a highly successful multidimensional program: Mom Matters. The program offers support, diversion, and empathy in the form of wheelchair outings, Internet access, flexible visitation for family members (including children), manicures, pedicures, movies, and relaxed atmospheres.

The success of our program and the gratitude expressed by the mothers on our service have convinced me that this is a kind and therapeutic approach worth considering and implementing elsewhere.

The Future

The road to safe and effective therapy for preterm labor has been a long and frustrating one. I am hopeful that researchers are now on the right track, focusing on subtle indications of infection and other potential causes of preterm labor.

In multiple gestations, of course, preterm labor is often caused simply because there are too many embryos in the womb. Uterine overdistension will not be an easy problem to overcome, except by reducing multiple gestations. Many of our colleagues in reproductive endocrinology have gotten the message that implanting too many embryos is not a good idea.

I believe that in the coming years, we will gain a better understanding of organic causes of preterm labor, permitting us to customize therapy according to individual circumstances of each pregnancy.