

Controversial Issues in the Management of Multiple Pregnancies

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The management of multiple pregnancies represents a true challenge for all sub-specialties concerned with perinatal medicine. Many issues were neglected over the years merely because they were rare and therefore considered not sufficiently important to merit clinical trials. This paper discusses a personal selection of controversial issues, such as multifetal pregnancy reduction of triplets and twins, special cases in multifetal pregnancy reduction, need for invasive genetic studies, management of twin-twin transfusion, discordant fetal conditions, the definition of "term" in multiples, and the controversy about the mode of delivery.

Physicians caring for the mother and their unborn multiples often face controversial clinical dilemmas. It is not surprising, therefore, that the management of multiple pregnancies represents a true challenge for all the sub-specialties concerned with perinatal medicine. Many such aspects of treatment are not evidence-based, simply because data are insufficient or unavailable at present. In some instances, extrapolation is made from singleton pregnancies, disregarding the obvious differences between a single and a multiple gestation. Perinatal medicine includes few issues that are as dynamic and controversial as multiple gestations.

Table 1 summarizes salient points related to multiple pregnancy and multiple birth that resound in the medical literature of the last two decades. These points serve as platform for the following discussion that addresses current controversies related to the management of multiple pregnancies. The selection of the topics deemed to be controversial is personal.

Multifetal Pregnancy Reduction

Multifetal pregnancy reduction (MFPR) is widely used to reduce the numbers of high-order iatrogenic multiples. Given the numerous limitations of the uterine milieu in the human to adequately nurture multiples, outcome is not surprisingly bettered among reduced multiples compared to their non-reduced counterparts. Little controversy exists about the use of MFPR for quadruplets or more; however, controversy regarding MFPR of triplets and twins is ongoing (Blickstein, 2001; Blickstein & Keith, 2001).

As long as outcomes are measured in terms of grams, gestational weeks, mortality and morbidity, singletons do better than twins and twins do better than triplets. At the same time, however, one should consider the long-term psychological distress of the parents (Blickstein, 1999b) as well as the risk of total pregnancy loss following MFPR as a counterbal-

ance to the improved outcomes seen in recent years for twins and triplets. The nature of changing outcomes over time forces one to frequently update the risk versus benefit arguments of MFPR and not rely on old, historical data.

Genetic Evaluation of Multiple Pregnancies

Each fetus in a multiple pregnancy has the same chance for aneuploidy as does a singleton under similar background risk. However, because the mother of multiples is often quite older on average, she is at ~1.7-fold increased risk that one of her multiples will be affected. This difference is the basis of an ongoing controversy regarding invasive cytogenetic studies. The simple facts are that biochemical screening is inadequate for twins and unavailable for high-order multiples. Moreover, nuchal translucency

Table 1

Generally Accepted Views Related to Multiple Pregnancy

- Sibs of a multiple pregnancy set should receive individual attention. At the same time, multiples should not be considered as two or three fetuses that just happen to be in the same uterus.
- The placental characteristics of zygosity — chorionicity and amnionicity — have unequivocal importance. These characteristics should be determined as early as possible during pregnancy.
- The sub-set of monochorionic pregnancies is at increased risk of mortality and morbidity. Monochorionic multiples may also face unique perinatal morbidity.
- The intrauterine environment can rarely provide for fetal growth to the same extent as in singleton pregnancies. Hence, multiples are delivered at an earlier gestational age and weigh less than singletons at the same gestational age.
- Size (birth weight) and age at birth of the multiples bear a linear inverse relationship with the number of fetuses. The starting number of fetuses is equally important.
- There are no effective prophylactic measures to reduce premature birth in multiples.
- There is a definite increased maternal morbidity in a multiple pregnancy and birth.

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measurement, despite being the only non-invasive screening procedure with promising results, is not widely employed and its efficacy in high-order multiples has not been extensively studied. In face of these deficiencies, invasive cytogenetic procedures (amniocentesis or chorionic villus sampling) are used, but carry similar but definitely increased risk for miscarriage (Blickstein, 2001).

There are currently no data, except theoretical assumptions, to support use of either invasive or non-invasive studies in multiple pregnancies at risk of aneuploidy. Because such pregnancies are often considered “premium”, late (28–30 weeks) amniocentesis has been proposed to reduce the known risk of miscarriage. This procedure is only logical when the option of late fetocide, by itself an extremely controversial issue, is feasible (Blickstein & Keith, 2001).

Special Cases of Multifetal Pregnancy Reduction

Because of the higher frequency of iatrogenic multiples, complex chorionicity combinations such as dichorionic-triamniotic triplets are seen more often and represent an area of great clinical controversy (Blickstein & Keith, 2001). Several options exist. The first is to leave the triplet pregnancy without intervention. Such a chorionic set-up, however, does not eliminate the possibility of twin-twin transfusion, which may affect the monochorionic twins in the triplet set. The second option is to reduce the “singleton” member of the triplet set. In this case, a monochorionic set of twins is left, with the obvious risk of twin-twin transfusion. The third option is to reduce the monochorionic twins, leading to a singleton pregnancy. Because outcome from three-to-one is worse compared to a three-to-two reduction, the latter option may jeopardize the whole pregnancy. To date, no data to support either of the above mentioned management options exist (Blickstein & Keith, 2001).

A second example of the special controversies related to fetal reduction involves a set of monochorionic twins, discordant for a major structural anomaly. It is clear that simple fetocide may cause the so-called fetal embolization syndrome and result in death or in major handicap of the non-reduced twin. The options in this case are terminate the pregnancy by either hysterotomy or to sever the umbilical cord of the anomalous twin. To date, all such methods are controversial and at an experimental stage (Blickstein, 1999b).

A third example relates to early mid-trimester rupture of the membranes in the presenting fetus of a poly-chorionic multiple pregnancy. Controversy exists if fetal reduction — transforming the presenting gestational sac into a missed abortion — will reduce the risk of miscarriage of the entire multiple gestation.

Finally, it is debatable if MFPR is indicated for patients with a convincing history or proven cervical incompetence. Proponents argue that if there is a background risk of pre-term birth, this risk is increased if pregnancy comprises more than one fetus. Opponents argue that because the risk of prematurity is increased anyway in twins, it is speculative if reduction to a singleton pregnancy is more advantageous to appropriate management of cervical incompetence.

Management of Twin-twin Transfusion

Twin-twin transfusion is perhaps the best example of ongoing controversy within the profession of perinatal medicine. At the beginning of the last decade, the diagnostic controversy came to an end with the publication of sonographic criteria and set the stage for dispute about the appropriate treatment modality (Blickstein, 1990). Researchers argued about the wisdom of intervention, considered sophisticated methods of fetocide, examined the role of amnioreduction versus laser ablation, etc. Only recently has the possibility that treatment should be tailored to gestational age and the severity of the syndrome been put forward. The fact that twin-twin transfusion remains one of the few clinical situations in which intrauterine surgical procedures may truly be indicated ensures that the management controversy will continue.

Discordant Fetal Conditions

Discordant inter-fetal conditions set the stage for inter-fetal conflicts. The simple example of such a conflict is growth discordance in a twin pregnancy (Blickstein, 1991; Blickstein, Goldman & Mazkereth, 2000a; Blickstein et al., 1999). With lesser degrees of discordance, no controversy is present about the role of conservative management, as is the case in moderately growth-restricted singletons. However, in a remote-from-term severely growth discordant pair, when the smaller twin has sonographic feature of severe growth restriction and Doppler studies show impending demise, the option for rescue by delivering the affected fetus concomitantly puts the normally growing fetus at increased risks of severe prematurity.

A more complex example involves non-reassuring or actually ominous fetal heart pattern seen in one twin only. At or near term, there is little doubt that delivery is a good choice. However, given the wide range of false-positive heart rate patterns and the inherent difficulty of interpreting these tracings in twins, one may argue that indicated pre-term birth to save the probably distressed fetus will result in a certainly premature birth of the co-twin.

The final example involves single fetal demise in monochorionic twins. As discussed above, the risk for the survivor is very high. However, because fetal death is invariably diagnosed after the event, there is no way to be sure that damage to the survivor has not already occurred. On the other hand, there is no data on the time interval needed for fetal death to damage the survivor and hence, the argument is put forth to prompt delivery upon diagnosis of single fetal demise (Blickstein, 1999a).

When Does Term Occur in Twins?

Although preterm delivery is of the greatest concern to obstetricians carrying for twin pregnancies worldwide, about 30% are delivered at ≥ 37 –38 weeks. If term occurs earlier in twins than in singletons, it may be argued that twins delivered beyond that age are exposed to risks normally associated with post-term pregnancy.

Several lines of evidence suggest that “term” occurs in twin pregnancies at 37–38 weeks. First, statistical inference suggests that the proportion of twins delivered at ≥ 39 weeks is similar to that of singletons delivered at ≥ 41 weeks. Second, cross-sec-

tional data clearly demonstrate arrest of growth in twins at 36–37 weeks. Third, evidence exists to suggest that pulmonary and neurological maturity is achieved by 37 weeks. Finally, data from both the USA and Japan show that perinatal mortality and morbidity decrease until 36 weeks but increase again thereafter. An example of the risk of long-term morbidity is cerebral palsy (Blickstein, 1999a). It has been shown that rates are not increased over those of singletons until 36 weeks, but twins are at a 2–3-fold increased risk for cerebral palsy at gestational age ≥ 37 weeks.

Although these lines of evidence suggest a re-definition of “term” for twins and set the gestational age at 38 weeks, there is no prospective study that actually proves the advantage of delivering all twins at that gestational age. Also, when reaching “term” by twin standards, the method of labor induction as well as the cost in terms of failed inductions, present additional controversies (Manor et al., 1999).

Mode of Delivery

Several guidelines have evolved during the last decade to increase the safety of vaginal birth of twins (Blickstein, Goldman, & Kuperminc, 2000; Blickstein et al., 1993; Blickstein et al., 1991). In the current epidemic of multiple births, many are considered “premium” pregnancies. As such, clinicians often follow the cliché “no high risk pregnancy should end with a high risk delivery” and deliver twins by cesarean section. Obviously, the higher the overall cesarean rate within a given practice, the lower the contribution of twins to the overall cesarean rate. In this manner, performing cesarean delivery for all twins would increase the overall cesarean rate by 10% in a service with an overall 10% rate but would add only 3.3% to a service with an overall 30% cesarean rate (Blickstein, 2000).

Other variables complicate matters and virtually ensure that the controversy continues: There is a 1:5 to 1:10 chance that a multipara carrying twins will have a previous cesarean; there is a 30 to 40% chance that the second twin will not be vertex; about half of the twins have a low birth weight (Blickstein, Goldman & Mazkereth, 2000b); and a significant proportion of mothers have complications during pregnancy (Blickstein, 1997). The controversy therefore is obvious and is exemplified by the question: Should we allow vaginal birth of twins under such circumstances? If one looks for clear-cut, evidence-based answers, one finds that less than 50% of these pregnancies actually need a cesarean (Blickstein, 2000).

With the skyrocketing numbers of high order multiples, there is considerable risk of extreme premature birth of all fetuses. If the cervix closes and labor ceases after birth of the presenting fetus, there is a chance that the other fetus(es) might be delivered after days or weeks. For these friable and tiny fetuses such a delayed-interval delivery may mean life or death. Opponents would indicate the increased risk for chorioamnionitis whereas proponents would cite several large series with a favorable outcome.

Summary

Usually there is no debate when a clear-cut single effective management is available or if a situation is rare. Many issues about therapy relating to multiple pregnancy were neglected over the years merely because they were rare and therefore

considered not sufficiently important enough to merit clinical evaluation. Experience-based medicine prevailed. With the advent of the present worldwide epidemic of multiples, previously rare conditions became everybody’s concern. Controversy began with awareness of the lack of evidence-based decision-making possibilities for common practice.

It is hoped that defining the controversies can be the first step in clearing up misunderstandings and to replace historical management protocols with evidence-based management.

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