Perinatal outcomes related to induction of labor: a call for randomized trials

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All obstetric clinicians know that induction of labor causes more cesarean deliveries. If you spend time on the labor floor, you can see that women who are induced end up with more cesareans than those who experience spontaneous labor. However, we have been confused and wrong regarding this issue for decades. This is because at any gestational age, the options for a clinician and patient are not induction of labor vs spontaneous labor but induction of labor vs expectant management.1

Expectant management encompasses having the patient progress into the future in which a wide variety of things could occur. She may go into spontaneous labor, but she may also develop a complication of pregnancy such as pre-eclampsia, fetal growth restriction, or oligohydramnios. If she progresses to 41 or 42 weeks’ gestation, most clinicians will induce at that point, even without another complication, but now the patient has an increased risk of fetal macrosomia as well. Similarly, it appears that with greater gestational age at term, the risk of uteroplacental insufficiency rises, leading to more cesareans for fetal intolerance of labor. Thus, expectant management at term has a number of associated complications that all may contribute to an increased risk of cesarean.

In a randomized trial, one compares induction of labor to expectant management. There are a number of these trials conducted at 41 or 42 weeks’ gestation, and in metaanalyses, induction of labor has been shown to decrease the risk of cesarean delivery compared with expectant management.2 3 There are far fewer studies conducted prior to 41 weeks’ gestation, but these, too, have demonstrated a reduction in the risk of cesarean delivery.4 One randomized trial of a preventive induction of labor was not statistically powered to show a reduction in the cesarean delivery rate but did show a reduction in fetal morbidity as measured by the adverse outcome index.5

More recently, retrospective cohort studies have attempted to mimic these randomized trials by comparing women induced at a particular gestational age and comparing them with women managed expectantly to greater gestational ages.1 6-9 Overall, these studies generally have found either a lower risk of cesarean delivery with induction of labor or no difference. However, few of these studies have investigated maternal morbidity.

The current study by Liu et al10 examines maternal outcomes such as postpartum hemorrhage, maternal sepsis, and venous thromboembolism, comparing these outcomes between women induced at a given gestational age with those expectantly managed beyond that gestational age. The authors found an increase in postpartum hemorrhage in those women induced at 38 and 39 weeks’ gestation as well as an increase in venous thromboembolism at 38 weeks’ gestation. Methodologically, I commend the authors for using the proper comparison of induction of labor to expectant management.

The finding of increased postpartum hemorrhage is in contrast to 2 prior studies. Stock et al8 demonstrated that induction of labor was consistently associated with a reduced risk of postpartum hemorrhage as compared with expectant management. Osmundson et al7 found no difference between women electively induced compared with those managed expectantly. One potential methodological issue in the current study that may have contributed to this difference in findings is how the population was defined. To create a low-risk population, the authors excluded all women with chorioamnionitis, preeclampsia, oligohydramnios, growth restriction, and macrosomia. However, although this is a reasonable thing to do in the induction of labor group, these complications can arise in an expectantly managed group and can be steps on the causal pathway from expectant management to perinatal morbidity.

One previous study found that macrosomia is consistently increased in the expectant management group.8 This is going to be true for preeclampsia and oligohydramnios as well. Furthermore, the majority of chorioamnionitis occurs intrapartum and should probably not be excluded from either group. The same can generally be said about placental abruption and fetal heart rate abnormalities.

So what do we do in response to these findings? Given the recent push to limit elective induction of labor prior to 39 weeks, I would suggest that these findings further support that, in the absence of an indication in the early term period, there may be risks to both the neonate and the mother from elective induction of labor. Furthermore, there is not adequate evidence to support a routine recommendation of nonindicated induction of labor prior to 41 weeks’ gestation.
These data give some support to the notion that without an indication, induction of labor may lead to greater risk. However, given the contrast between this work and previous work, further research certainly needs to be conducted. Although I am supportive of further, well-designed cohort studies, what is sorely needed are large, prospective trials of induction of labor vs expectant management prior to 41 weeks’ gestation.

Recently the well-designed Hypertension and Preeclampsia Intervention Trial at Term (HYPITAT) trial compared induction of labor vs expectant management of women with gestational hypertension or preeclampsia at 36 weeks’ gestation or beyond.11 These authors found that overall, maternal outcomes in this setting were improved by immediate induction of labor. Additionally, despite many deliveries in the late preterm or term periods, the neonatal outcomes were no worse overall, and there was a decrease in neonatal acidemia in the immediate induction group. This study was accomplished in The Netherlands, which has an obstetrical volume similar to or less than many states in the United States.

Given our immense resources, we have an obligation to the 4 million women for whom we care each year to answer one of the most basic obstetric questions: what are the outcomes from induction of labor as compared with expectant management? Furthermore, these outcome differences may vary by parity, maternal age, race/ethnicity, and cervical status and with such maternal and fetal conditions as gestational diabetes, fetal growth restriction, fetal macrosomia, and oligohydramnios. Thus, not one, but many such trials need to be conducted to ascertain how best to manage women with late preterm and term pregnancies.

Such trials will be expensive. Most large, well-designed studies will require ROI funding, which is generally capped at $500,000 per year over 5 years. If 4 such studies were conducted in the near future, the cost might be $10 million. Furthermore, with the current Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) payline hovering at the ninth percentile, it is unclear how many such studies can be funded in the current research environment. So please write your congressional representatives. We need more funding for research. Only with National Institutes of Health support will the trials of induction of labor vs expectant management be conducted. And without such trials, we can only make educated guesses regarding the effect of this commonly used obstetric intervention.

Meanwhile, until such trials are conducted (I hear that one such trial is being planned within the NICHD-funded Maternal-Fetal Medicine Units Network), I would strongly encourage clinicians to keep an open mind about induction of labor and its association with cesarean delivery. We should heed the advice from the recent NICHD prevention of the first cesarean conference, which suggests that an induction of labor should not be considered failed until at least 24 hours of oxytocin (this is after cervical ripening agents have been properly used), preferably in the setting of ruptured membranes.12 With a more patient response to induction of labor, evidence does not support that its use increases the risk of cesarean delivery.

REFERENCES


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