Published in final edited form as:

Obstet Gynecol. 2012 May ; 119(5): 909–916. doi:10.1097/AOG.0b013e31824ea4b2.

Antenatal Steroids for Treatment of Fetal Lung Immaturity After 34 Weeks of Gestation:

An Evaluation of Neonatal Outcomes

Beena D. Kamath-Rayne, MD, MPH, Emily A. DeFranco, DO, MS, and Michael P. Marcotte, MD

Neonatology and Pulmonary Biology, Cincinnati Children's Hospital Medical Center, Maternal-Fetal Medicine, University of Cincinnati School of Medicine, and Maternal-Fetal Medicine, Tri-Health, Cincinnati, Ohio

Abstract

OBJECTIVE—To estimate whether antenatal corticosteroids given after fetal lung immaturity in pregnancies at 34 weeks of gestation or more would improve neonatal outcomes and, in particular, respiratory outcomes.

METHODS—We compared outcomes of 362 neonates born at 34 weeks of gestation or more after fetal lung maturity testing: 102 with immature fetal lung indices were treated with antenatal corticosteroids followed by planned delivery within 1 week; 76 with immature fetal lung indices were managed expectantly; and 184 were delivered after mature amniocentesis. Primary outcomes were composites of neonatal and respiratory morbidity.

RESULTS—Compared with corticosteroid-exposed neonates those born after mature amniocentesis had lower rates of adverse neonatal (26.5% compared with 14.1%, adjusted odds ratio [OR] 0.51, 95% confidence interval [CI] 0.27–0.96) and adverse respiratory outcomes (9.8% compared with 3.3%, adjusted OR 0.33, 95% CI 0.11–0.98); newborns born after expectant management had significantly less respiratory morbidity (1.3% compared with 9.8%, adjusted OR 0.11, 95% CI 0.01–0.92) compared with corticosteroid-exposed newborns.

CONCLUSION—Administration of antenatal corticosteroids after immature fetal lung indices did not reduce respiratory morbidity in neonates born at 34 weeks of gestation or more. Our study supports prolonging gestation until delivery is otherwise indicated.

Although the administration of antenatal corticosteroids for the prevention of respiratory distress syndrome (RDS) in fetuses at less than 34 weeks of gestation is widely supported and practiced since the National Institutes of Health Consensus statement in 1994,^{1,2} little information exists on the use of antenatal steroids to promote fetal lung maturation in women at risk of preterm birth beyond 34 weeks of gestation.³

The current recommendation of the American College of Obstetricians and Gynecologists is that elective delivery before 39 weeks of gestation should not be performed without documentation of fetal lung maturity.⁴ The majority of these elective deliveries occur in the

© 2012 by The American College of Obstetricians and Gynecologists.

Corresponding author: Beena D. Kamath-Rayne, MD, MPH, Assistant Professor of Pediatrics, Neonatology and Pulmonary Biology, Cincinnati Children's Hospital Medical Center, MLC 7009, 3333 Burnet Avenue, Cincinnati, OH 45229; beena.kamathrayne@cchmc.org.

Financial Disclosure

The authors did not report any potential conflicts of interest.

Presented at the Society for Maternal-Fetal Medicine 32nd Annual Meeting, February 6–11, 2012, Dallas, Texas.

late preterm (34 0/7 to 36 6/7 weeks of gestation) and early term (37 0/7 to 38 6/7 weeks of gestation) periods, times during gestation with limited data to support a potential benefit of administration of antenatal corticosteroids. Still, with some evidence that steroid treatment after 34 weeks of gestation enhances fetal lung maturity profiles,⁵ some obstetricians give antenatal corticosteroids after fetal lung testing is immature in an effort to induce overall fetal maturation and prevent neonatal morbidity with imminent delivery of the fetus.

When the obstetrician must make decisions based on immature fetal lung indices, three clinical pathways could be taken: 1) treat with antenatal corticosteroids for planned imminent delivery; 2) await mature fetal lung indices with repeat testing; or 3) expectant management. Therefore, the aim of this study was to compare the incidence of neonatal morbidity in a group of newborns born between 34 0/7 to 38 6/7 weeks of gestation whose mothers received antenatal corticosteroids after an amniocentesis with immature fetal lung indices with a reference group of neonates of similar gestational age born after a mature amniocentesis. Because fetal lung maturity testing predicts the absence of RDS, we hypothesized that corticosteroid-exposed newborns would have more respiratory morbidity but similar rates of other morbidities associated with prematurity. We also compared the corticosteroid-exposed neonates with a second reference group, whose mothers had immature fetal lung indices and were managed expectantly. We hypothesized that neonates whose mothers were managed expectantly were likely more mature and therefore would have decreased incidence of neonatal morbidity.

MATERIALS AND METHODS

We performed a retrospective cohort study using a list of all women at 34 weeks of gestation or more who had amniocentesis for fetal lung maturity between January 1, 2005, and July 15, 2011, and subsequently delivered at Good Samaritan Hospital in Cincinnati, Ohio, the hospital with the largest delivery volume in the state. We had previously screened the charts of most of these women for inclusion into a study powered to discern differences in adverse neonatal outcomes after documented fetal lung maturity⁶; this study is a secondary analysis arising from that original study, including additional eligible women screened since February 2010. For the study described here, the study group included neonates born to women between 34 0/7 and 38 6/7 weeks of gestation who received antenatal corticosteroids after an amniocentesis with immature fetal lung indices and delivered within 1 week and were called the “corticosteroid-exposed neonates.” The reference group included neonates born between 34 0/7 and 38 6/7 weeks of gestation whose mothers had an amniocentesis with mature fetal lung indices and were called the “mature amniocentesis neonates.” We also collected data on a second reference group of neonates, whose mothers were managed expectantly after an amniocentesis performed with immature fetal lung indices and were called the “neonates born after expectant management.”

Fetal lungs were considered immature when the mother’s amniotic fluid had none of the following indices indicating maturity: TDx-FLM II 55 mg or greater surfactant per gram albumin in the nondiabetic patient (70 mg or more surfactant per gram albumin in the diabetic patient), presence of phosphatidylglycerol, or lamellar body count more than 29,000 per microliter according to the standards of our laboratory. In corticosteroid-exposed neonates, once fetal lung immaturity was noted, the mothers received antenatal corticosteroids, defined as any number of doses of either dexamethasone (6 mg) or betamethasone (12 mg) given before delivery. To be included in the study group, women had to deliver within 1 week of their last steroid dose.

Study exclusions were pregnancies complicated by congenital anomalies, chromosomal abnormalities, or multifetal gestation. Women who delivered outside the study institution

also were excluded. If women in the two reference groups received antenatal steroids at any point in pregnancy, they were excluded from the study because antenatal steroids were considered a potential confounder.

After approval by the Good Samaritan Hospital institutional review board, the charts of all women and their fetuses who met inclusion criteria were reviewed for the variables of interest. One study investigator abstracted data from all charts, and a second investigator did a quality assurance review of 10% of the charts and found discrepancies in fewer than 5% of all data variables collected. The primary outcome was a composite measurement of respiratory morbidity, which included need for oxygen supplementation, continuous positive airway pressure, mechanical ventilation, or surfactant administration. A second composite measurement for adverse neonatal morbidity was also examined, including admission to neonatal intensive care, need for ongoing respiratory support (including oxygen, continuous positive airway pressure, or mechanical ventilation), surfactant administration, hypoglycemia requiring intravenous infusion, treatment with antibiotics for presumed sepsis, gavage feeding, or treatment for hyperbilirubinemia with phototherapy. These neonatal outcomes were combined for a composite adverse outcome because they are common morbidities seen in the late preterm and early-term population^{7–9} and require a higher level of monitoring or follow-up than for the healthy, uncomplicated newborns. Secondary outcomes included each of these individual morbidities in addition to hypoglycemia (documented glucose less than 45 mg/dL), sepsis evaluation (screening complete blood count, blood culture, or both), need for central venous access, and length of hospital stay. Maternal demographic characteristics analyzed as possible confounders were mother's age, history of prior premature delivery, history of prior cesarean delivery, and presence of labor before delivery. Pregnancy complications included hypertensive disease (chronic, gestational or preeclampsia), diabetes (pre-existing or gestational), premature rupture of membranes, oligohydramnios, preterm labor, or antenatal hospitalization for pregnancy complications.

The data were analyzed using SAS 9.2. Differences were tested using χ^2 or Fisher's exact test where necessary for categorical variables and Kruskal-Wallis or analysis of variance for continuous variables. Multivariable logistic regression was used to estimate the odds of composite adverse respiratory outcome for newborns born after immature fetal lung indices and maternal administration of antenatal corticosteroids adjusting for covariates with significant effects greater than 10% on the outcome of interest with inclusion and then exclusion from adjusted analyses. Backward selection yielded a final model of statistically influential and biologically plausible covariates. Adjusted analyses were not performed for individual morbidities as a result of their low frequency, less than 10 observations per category for most outcomes.¹⁰ Comparisons with associated $P < .05$ and 95% confidence intervals not inclusive of the null value of 1 were considered statistically significant differences.

RESULTS

Of the 982 charts screened of women who had amniocenteses for fetal lung maturity testing during the study period, 102 pregnant women met inclusion criteria and had been treated with antenatal corticosteroids after immature fetal lung indices (Fig. 1). One hundred women (98%) received betamethasone and two received dexamethasone. One hundred one (99%) received a complete course of antenatal steroids; only one woman received one of a planned two-dose course of betamethasone. A mean period of 3.4 ± 2.8 days lapsed between the last dose of antenatal corticosteroids and delivery. Seventy-six women had immature fetal lung indices and were managed expectantly, delivering within 10.9 ± 11.5 days of their

amniocentesis. One hundred eighty-four women had mature fetal lung indices and delivered within 1.7 ± 2.1 days of their amniocentesis.

The most frequent reasons in all three groups for amniocentesis with subsequent fetal lung maturity testing were history of prior cesarean delivery with a classical incision (15.8%), amniotic fluid disorder (oligo or hydramnios, 14.9%), prior fetal death or abruption (9.9%), or diabetes (9.7%). When the reason for amniocentesis and fetal lung maturity testing was evaluated by study group, important differences could be seen (Table 1), as a greater proportion of elective deliveries were seen in the mature amniocentesis group.

The frequency of pregnancy complications such as hypertensive disease, diabetes, preterm labor, intrauterine growth restriction, and oligohydramnios was higher in the corticosteroid-treated group but did not differ significantly among the three groups (Table 2). Fewer women managed expectantly had cesarean deliveries. More women treated with antenatal corticosteroids after immature fetal lung indices had premature rupture of membranes.

We compared the newborns of the women with immature lung indices who were treated with antenatal corticosteroids with the other two groups (Table 3). One neonate who delivered at 38 weeks of gestation in the mature amniocentesis group required mechanical ventilation and surfactant administration. The corticosteroid-exposed neonates were born at the earliest gestational age by 0.7 weeks (approximately 5 days), and they were approximately 10 ounces less in birth weight. The corticosteroid-exposed neonates had significantly higher rates of both the composite adverse neonatal outcome and the composite respiratory outcome compared with the expectantly managed group. In addition, the corticosteroid-exposed neonates had approximately twice the rate of hypoglycemia, need for intravenous fluids for hypoglycemia, sepsis evaluation, and treatment with antibiotics for presumed sepsis. A subanalysis evaluated differences in the three groups stratified by late preterm (34 to 36 6/7 weeks of gestation) and early term (37 to less than 39 weeks of gestation) and showed that late preterm deliveries accounted for the majority of these differences (Table 4).

After adjustment for significant covariates, which included hypertension, diabetes, intrauterine growth restriction, premature rupture of membranes, and presence of labor before delivery, expectantly managed neonates were 90% less likely to have the composite adverse respiratory outcome (1.3% compared with 9.8%, adjusted odds ratio [OR] 0.11, 95% confidence interval [CI] 0.01–0.92, $P=.04$) than the corticosteroid-exposed neonates. Expectantly managed neonates managed expectantly were 40% less likely to have the composite adverse neonatal outcome (adjusted OR 0.59, 95% CI 0.28–1.28, $P=.18$) than the corticosteroid-exposed neonates, although this did not reach statistical significance. After adjustment with the same covariates, neonates born after mature amniocentesis were over 60% less likely to have the composite adverse respiratory outcome (3.3% compared with 9.8%, adjusted OR 0.33, 95% CI 0.11–0.98, $P=.04$) and 50% less likely to have the composite adverse neonatal outcome (14.1% compared with 26.5%, adjusted OR 0.51, 95% CI 0.27–0.96, $P=.04$) compared to the corticosteroid-exposed neonates.

Once immature fetal lung indices are documented, expectant management to delay delivery rather than immediate delivery after antenatal corticosteroids was protective for neonatal morbidities. Compared with corticosteroid-exposed neonates, the neonates born after expectant management had decreased risk for multiple neonatal morbidities (Table 5), including the composite adverse respiratory outcome, admission to neonatal intensive care, hypoglycemia, sepsis evaluation, treatment with antibiotics for suspected sepsis, and oxygen supplementation.

DISCUSSION

Few studies have examined the benefits of giving antenatal corticosteroids to women after 34 weeks of gestation to prevent RDS.¹¹ Although administration of antenatal corticosteroids is standard of care to decrease the severe and possibly fatal consequences of respiratory distress syndrome and intraventricular hemorrhage in neonates born at less than 34 weeks of gestation,² neonates born at 34 weeks or more of gestation with less risk of these morbidities may not incur as clear a benefit and may be exposed to undue risk. Indeed, of the 29 neonates born at greater than 34 weeks of gestation in Crowley's original meta-analysis, corticosteroids did not decrease the incidence of RDS.² The Antenatal Steroids for Term Elective Cesarean Section study, by Stutchfield et al,¹⁷ examined the use of antenatal corticosteroids given to women who planned to deliver at 37 weeks of gestation or greater by elective cesarean. Although the investigators found a significant difference in the rate of RDS between the treatment and control groups (1.1 and 0.2%, respectively), they had similar numbers of admissions to neonatal intensive care for both groups (26 and 32, respectively), indicating that although antenatal corticosteroids may have decreased the incidence of respiratory morbidity, other neonatal morbidities still necessitated intensive care.¹² Another recent study randomized women to corticosteroids compared with no treatment after immature amniocentesis between 34 0/7 and 36 6/7 weeks of gestation.⁶ Steroid administration was associated with a higher mean weekly increase in TDx-FLM II than was no treatment, although the study had insufficient power to assess differences in neonatal morbidities.⁵ A more recent clinical trial from Brazil randomized women at 34 to 36 weeks of gestation at risk of imminent premature delivery to a two-dose course of betamethasone or placebo and found no significant difference in the incidence of respiratory disorders (which included RDS and transient tachypnea of the newborn) nor the need for ongoing respiratory support between the two groups.¹³

Our study evaluates differences in neonatal morbidity depending on the clinical pathway chosen after an amniocentesis documenting immature fetal lung indices. After immature amniocentesis, some physicians may consider their patient stable enough to await mature amniocentesis before delivery or to manage expectantly based on the maternal risks of prolonging pregnancy weighed against the neonatal risks of a possible premature delivery. As a secondary analysis with a small sample size, we had insufficient power to analyze individual differences between specific morbidities when comparing between groups. However, when comparing the three groups, despite no differences in major maternal morbidities such as hypertensive disease, diabetes, oligohydramnios, and preterm labor, corticosteroid-exposed neonates had higher rates of composite adverse neonatal outcome and composite adverse respiratory outcome compared with neonates born after mature amniocentesis or expectant management. Even when we attempted to account for the differences in maternal and fetal factors such as presence of labor before delivery, intrauterine growth restriction, and premature rupture of membranes through multivariable adjusted analyses, we continued to see significantly higher rates of both composite outcomes and individual neonatal morbidities in the corticosteroid-exposed group compared with the other two groups.

Not only does steroid administration appear to have no benefit when administered in the late pre-term and early term period, but our findings suggest it may actually be harmful. Specifically, our study indicates an almost twofold increased risk of hypoglycemia and a threefold increased risk of sepsis evaluation for neonates whose mothers received corticosteroids at 34 weeks of gestation or more after immature amniocentesis compared with those managed expectantly. Considering the biologic plausibility of steroids altering glycemic profiles and response to infection, these findings are certainly provocative, hypothesis-generating, and worthy of further evaluation in larger, randomized trials.

The retrospective nature of our study also may introduce bias based on inherent differences among pregnancies in which one approach was chosen over another. Performance of lung maturity amniocentesis implies that the health care provider considered the clinical scenario elective, because the health care provider had time to ponder and then act on the results. For example, a physician may desire sooner delivery in more complicated pregnancies but be willing to await mature amniocentesis or simply follow the pregnancy expectantly in those who have a more elective reason for delivery planning. Pregnancies that are allowed to continue may be inherently different, possibly at lower risk for adverse outcome, than those in which the obstetric provider chooses to administer steroids after immature lung studies and then deliver in less than 1 week. These differences in reasons for amniocentesis testing may influence the frequency of morbidities, ie, those at highest risk needing imminent delivery may be in the corticosteroid-exposed group.

Although one can never completely account for all potential confounders in a cohort study such as this, we did adjust for important factors, which are known to influence neonatal outcome such as medical comorbidities, labor onset before delivery, and pregnancy complications such as intrauterine growth restriction and prolonged rupture of membranes. After taking these factors into account, corticosteroid exposure seems to have no benefit and may possibly be harmful to neonates born at 34 weeks of gestation or more after immature amniocentesis. Our data suggest that the choice of steroid administration and then delivery if the results are immature are associated with high rates of adverse neonatal outcomes and that if the delivery is not otherwise medically indicated, either expectant management or delivery after mature fetal lung indices may be the prudent approach.

Antenatal corticosteroids have proven benefits in neonates born less than 34 weeks of gestation,^{14,15} and these incurred benefits certainly outweigh any theoretic maternal or neonatal risks at that gestational age. For neonates born at 34 weeks of gestation and greater, who still may have risk of neonatal morbidity as a result of prematurity, but much lower risk of more devastating morbidity such as intraventricular hemorrhage, the risks of corticosteroid administration may exceed the benefits. In a discussion of Crowley's original meta-analysis regarding antenatal corticosteroid administration, Sinclair¹⁶ calculated that with a baseline risk of RDS of 50% in neonates at 30 weeks of gestation or less, five neonates would need to be treated to prevent one case of RDS. However, because the baseline risk of RDS in neonates at greater than 34 weeks of gestation is 15%, the number needed to treat rises to 145. Our findings agree with recent cohort studies showing that the benefit of antenatal corticosteroids varies for neonates born at either extreme of gestation and incurs the greatest benefit for neonates born between 29 to 34 weeks of gestation.^{17–20} Further study is needed to determine if the number needed to harm after 34 weeks gestation incurs is less than the number needed to treat for benefit.

Our work continues to support the notion that gestational maturity itself has the strongest correlation with a lack of neonatal morbidity. If delivery is able to be prolonged without undue risk to the mother, our study suggests that gestational maturity will decrease risk of subsequent neonatal morbidity. As such, we recommend that if delivery is indicated based on the maternal or fetal condition before 39 weeks of gestation, after careful consideration of the risks to the mother and fetus, the mother's pregnancy should be managed as such without the introduction of possible additional morbidity by administration of antenatal corticosteroids until further evidence is available from randomized controlled trials.

Acknowledgments

Dr. Kamath-Rayne is funded by an NIH BIRCWH K12HD051953.

The authors thank Sherri Sterwerf and John Vidas from Good Samaritan Hospital Medical Records and Eric Hall, PhD, for bioinformatics support. Study data were collected and managed using REDCap (Research Electronic Data Capture), hosted at Cincinnati Children's Hospital Medical Center under the Center for Clinical and Translational Science and Training grant support (UL1-RR026314-01 National Center for Research Resources/National Institutes of Health).

References

1. Effect of corticosteroids for fetal maturation on perinatal outcomes. NIH Consensus Statement. 1994; 12:1–24.
2. Crowley P. Antenatal corticosteroid therapy: a meta-analysis of the randomized trials, 1972 to 1994. *Am J Obstet Gynecol.* 1995; 173:322–35. [PubMed: 7631713]
3. Spong C, Mercer B, D'Alton M, Kilpatrick S, Blackwell S, Saade G. Timing of indicated late-preterm and early-term birth. *Obstet Gynecol.* 2011; 118:323–33. [PubMed: 21775849]
4. Fetal lung maturity. ACOG Practice Bulletin No. 97. American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 2008; 112:717–26. [PubMed: 18757686]
5. Shanks A, Gross G, Shim T, Allsworth J, Sadovsky Y, Bildirici I. Administration of steroids after 34 weeks of gestation enhances fetal lung maturity profiles. *Am J Obstet Gynecol.* 2010; 203:47.e1–5. [PubMed: 20478551]
6. Kamath B, Marcotte M, DeFranco E. Neonatal morbidity after documented fetal lung maturity in late preterm and early term infants. *Am J Obstet Gynecol.* 2011; 204:518.e1–8. [PubMed: 21752754]
7. Wang M, Dorer D, Fleming M, Catlin E. Clinical outcomes of near term infants. *Pediatrics.* 2004; 114:372–6. [PubMed: 15286219]
8. Dani C, Corsini I, Piergentili L, Bertini G, Pratesi S, Rubaltelli F. Neonatal morbidity in late preterm and term infants in the nursery of a tertiary hospital. *Acta Paediatr.* 2009; 98:1841–3. [PubMed: 19604170]
9. Bates E, Rouse D, Mann MCV, Carlo WT, ATN. Neonatal outcomes after demonstrated fetal lung maturity before 39 weeks of gestation. *Obstet Gynecol.* 2010; 116:1288–95. [PubMed: 21099593]
10. Kleinbaum, D.; Kupper, L.; Muller, K.; Nizam, A. Applied regression analysis and other multivariable methods. Pacific Grove (CA): Brooks/Cole Publishing Company; 1998.
11. Sotiriadis A, Makrydimas G, Papatheodorou S, Ioannidis J. Corticosteroids for preventing neonatal respiratory morbidity after elective caesarean section at term. *The Cochrane Database of Systematic Reviews.* 2009; (4):Art. No.: CD006614.10.1002/14651858.CD006614.pub2
12. Stutchfield P, Whitaker R, Russell I. Antenatal Steroids for Term Elective Cesarean Section (ASTECS) Research Team. Antenatal betamethasone and incidence of neonatal respiratory distress after elective cesarean section: pragmatic randomised trial. *BMJ.* 2005; 331:662. [PubMed: 16115831]
13. Feitosa Porto A, Coutinho I, Barros Correia J, Ramos Amorim M. Effectiveness of antenatal corticosteroids in reducing respiratory disorders in late preterm infants: randomised clinical trial. *BMJ.* 2011; 342:d1696.10.1136/bmj.d1696 [PubMed: 21487057]
14. Liggins GC, Howie RN. A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. *Pediatrics.* 1972; 50:515–25. [PubMed: 4561295]
15. Hayes E, Paul D, Stahl G, Seibel-Seamon J, Dysart K, Leiby B, et al. Effect of antenatal corticosteroids on survival for neonates born at 23 weeks of gestation. *Obstet Gynecol.* 2008; 111:921–6. [PubMed: 18378752]
16. Sinclair J. Meta-analysis of randomized controlled trials of antenatal corticosteroid for the prevention of respiratory distress syndrome: discussion. *Am J Obstet Gynecol.* 1995; 173:335–44. [PubMed: 7631714]
17. Onland W, de Laat MW, Mol BW, Offringa M. Effects of antenatal corticosteroids given prior to 26 weeks' gestation: a systematic review of randomized controlled trials. *Am J Perinatol.* 2011; 28:33–44. [PubMed: 20648416]
18. Madarek E, Najati N. The effect of glucocorticoid therapy in preventing early neonatal complications in preterm delivery. *J Perinat Med.* 2003; 31:441–3. [PubMed: 14601269]

19. Manktelow B, Lal M, Field D, Sinha S. Antenatal corticosteroids and neonatal outcomes according to gestational age: a cohort study. *Arch Dis Child Fetal Neonatal Ed.* 2010; 95:F95–8. [PubMed: 19948527]
20. Smreck JM, Schwartau N, Kohl M, Berg C, Geipel A, Krapp M, et al. Antenatal corticosteroid therapy in premature infants. *Arch Gynecol Obstet.* 2005; 271:26–32. [PubMed: 15309401]

Fig. 1. Flow of study population

Kamath-Rayne. Antenatal Steroids After Fetal Lung Immaturity. *Obstet Gynecol* 2012.

Table 1

Top Five Reasons for Amniocentesis by Group

Mature Amniocentesis (34 0/7–38 6/7 wk) (n=184)	Expectant Management (34 4/7–40 0/7 wk) (n=76)	Steroids After Immature Amniocentesis (34 0/7–38 6/7 wk) (n=102)
Prior classical incision (17.0)	Amniotic fluid disorder* (22.9)	Prior classical incision (17.9)
Elective (17.0)	Prior classical incision (10.0) Isoimmunization (10.0) Diabetes (10.0)	Amniotic fluid disorder* (14.7)
Amniotic fluid disorder* (11.9)	Prior fetal death or abruption (11.4)	Prior fetal death or abruption (11.6)
Prior fetal death or abruption (10.2)	Prior cesarean delivery with poor dating (9.1)	Intrauterine growth restriction or other growth disorder (10.5)
Preeclampsia (9.0) Diabetes (9.0)	Diabetes (9.1)	Preeclampsia (8.4)

Data are %.

* Amniotic fluid disorder includes oligohydramnios and polyhydramnios.

Table 2

Comparison of Maternal Factors Between Groups

Maternal Characteristic	Mature Amniocentesis (34 0/7–38 6/7 wk) (n=184)	Expectant Management (34 4/7–40 0/7 wk) (n=76)	Steroids After Immature Amniocentesis (34 0/7–38 6/7 wk) (n=102)	P*
Maternal age (y)	30.2±6.6	27.7±6.4	29.0±6.4	.02
History of preterm delivery	80 (43.7)	22 (29.0)	42 (41.6)	.08
Prior cesarean delivery	92 (50.0)	25 (32.9)	48 (47.5)	.06
Hypertensive disease	34 (18.5)	14 (18.4)	26 (25.7)	.30
Diabetes	48 (26.1)	20 (26.1)	25 (24.8)	.96
Lapse between amniocentesis and delivery (d)	1.7±2.1	10.9±11.5	4.6±3.1	<.01
Premature rupture of membranes	2 (1.1)	3 (4.0)	9 (8.9)	<.01
Preterm labor	15 (8.2)	8 (10.5)	15 (14.9)	.21
Intrauterine growth restriction	7 (3.8)	5 (6.6)	9 (8.9)	.20
Oligohydramnios	9 (4.9)	5 (6.6)	10 (9.9)	.27
Presence of labor before delivery	77 (41.9)	48 (63.2)	43 (42.6)	<.01
Cesarean delivery	130 (70.7)	36 (48.0)	72 (71.3)	<.01

Data are n (%) or mean±standard deviation unless otherwise specified.

* P value represents χ^2 statistic of comparison among three groups for categorical and analysis of variance for continuous variables.

Table 3

Neonatal Outcomes Among the Three Groups

Neonatal Characteristic or Outcome	Mature Amniocentesis (34 0/7–38 6/7 wk) (n=184)	Expectant Management (34 4/7–40 0/7 wk) (n=76)	Steroids After Immature Amniocentesis (34 0/7–38 6/7 wk) (n=102)	P*
Gestational age (wk)	37.1±1.0	38.2±1.6	36.4±1.1	<.01
Birth weight (kg)	3.1±0.3	3.2±0.3	2.8±0.4	<.01
Composite adverse neonatal outcome (+) [†]	26 (14.1)	14 (18.4)	27 (26.5)	.04
Composite adverse respiratory outcome (+) [‡]	6 (3.3)	1 (1.3)	10 (9.8)	.01
NICU admission	16 (8.7)	8 (10.5)	23 (22.6)	<.01
Oxygen supplementation	5 (2.7)	1 (1.3)	10 (9.8)	<.01
Continuous positive airway pressure	2 (1.1)	0 (0)	5 (4.9)	.03
Time on respiratory support (h)	2.8±24.3	0.1±0.5	3.1±14.2	.50
Hypoglycemia	38 (20.7)	12 (15.8)	38 (37.3)	<.01
Intravenous fluids for hypoglycemia	5 (2.7)	2 (2.6)	8 (7.8)	.08
Gavage feeds	5 (2.7)	2 (2.6)	7 (6.9)	.18
Phototherapy	14 (7.6)	6 (7.9)	6 (5.9)	.83
Sepsis evaluation	13 (7.1)	4 (5.3)	21 (20.6)	<.01
Treatment with antibiotics	4 (2.2)	1 (1.3)	9 (8.8)	<.01

NICU, neonatal intensive care unit.

Data are n (%) or mean±standard deviation unless otherwise specified.

* P value represents χ^2 statistic of comparison among three groups for categorical and analysis of variance for continuous variables.

[†] Composite adverse neonatal outcome consists of neonatal intensive care admission, need for ongoing respiratory support, phototherapy, antibiotic treatment, intravenous fluids for hypoglycemia, or gavage feeding.

[‡] Composite adverse respiratory outcome consists of need for oxygen supplementation, continuous positive airway pressure, mechanical ventilation, or surfactant administration.

Table 4

Neonatal Outcomes of Late Preterm Newborns

Neonatal Characteristic or Outcome	Mature Amniocentesis (34 0/7–36 6/7 wk) (n=70)	Expectant Management (34 0/7–36 6/7 wk) (n=11)	Steroids After Immature Amniocentesis (34 0/7–36 6/7 wk) (n=65)	P*
Gestational age (wk)	36.1±0.6	35.9±0.7	35.8±0.8	.07
Birth weight (kg)	2.8±0.5	2.7±0.8	2.7±0.5	.25
Composite adverse neonatal outcome (+) [†]	11 (15.7)	5 (45.5)	20 (30.8)	.03
Composite adverse respiratory outcome (+) [‡]	1 (1.4)	0	9 (13.9)	.01
NICU admission	9 (12.9)	3 (27.3)	19 (29.2)	.06
Oxygen supplementation	1 (1.4)	0	9 (13.9)	.01
Continuous positive airway pressure	0	0	4 (6.2)	.08
Time on respiratory support (h)	0.5±4.7	0	4.7±17.5	.11
Hypoglycemia	17 (24.3)	1 (9.1)	30 (46.2)	<.01
Intravenous fluids for hypoglycemia	2 (2.9)	0	7 (10.8)	.11
Gavage feeds	4 (5.7)	2 (18.2)	7 (10.8)	.31
Phototherapy	4 (5.7)	2 (18.2)	3 (4.6)	.22
Sepsis evaluation	6 (8.6)	1 (9.1)	17 (26.2)	.02
Treatment with antibiotics	1 (1.4)	0	9 (13.9)	.01

NICU, neonatal intensive care unit.

Data are n (%) or mean±standard deviation unless otherwise specified.

* P value represents χ^2 statistic of comparison among three groups for categorical and analysis of variance for continuous variables.

[†] Composite adverse neonatal outcome consists of neonatal intensive care admission, need for ongoing respiratory support, phototherapy, antibiotic treatment, intravenous fluids for hypoglycemia, or gavage feeding.

[‡] Composite adverse respiratory outcome consists of need for oxygen supplementation, continuous positive airway pressure, mechanical ventilation, or surfactant administration.

Table 5

Risk of Neonatal Morbidities in Newborns Born After Immature Fetal Lung Indices and Managed Expectantly Compared With Those Born After Antenatal Corticosteroids

Neonatal Outcome	Adjusted Odds Ratio (95% Confidence Interval)*
Composite adverse neonatal outcome [†]	0.59 (0.28–1.28)
Composite adverse respiratory outcome [‡]	0.11 (0.01–0.92)
Neonatal intensive care admission	0.39 (0.16–0.99)
Hypoglycemia	0.29 (0.13–0.64)
Intravenous fluids for hypoglycemia	0.39 (0.08–1.99)
Gavage feeding	0.31 (0.06–1.66)
Phototherapy	1.20 (0.36–3.98)
Sepsis evaluation	0.22 (0.07–0.69)
Treatment with antibiotics	0.10 (0.01–0.83)
Oxygen supplementation	0.12 (0.01–0.98)

* Adjusted for hypertensive disease, diabetes, premature rupture of membranes, intrauterine growth restriction, and presence of labor before delivery.

[†] Composite adverse neonatal outcome consists of neonatal intensive care admission, need for ongoing respiratory support, phototherapy, antibiotic treatment, intravenous fluids for hypoglycemia, or gavage feeding.

[‡] Composite adverse respiratory outcome consists of need for oxygen supplementation, continuous positive airway pressure, mechanical ventilation, or surfactant administration.