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Oxytocin Regimen for Labor Augmentation, Labor Progression, Perinatal Outcomes

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Abstract

Objective—To examine the effects and safety of high-dose (compared with low-dose) oxytocin regimen for labor augmentation on perinatal outcomes.

Methods—Data from the Consortium on Safe Labor were used. A total of 15,054 women from six hospitals were eligible for the analysis. Women were grouped based on their oxytocin starting dose and incremental dosing: 1, 2, and 4 mU/min. Duration of labor and a number of maternal and neonatal outcomes were compared among these three groups stratified by parity. Multivariable logistic regression and generalized linear mixed model were used to adjust for potential confounders.

Results—Oxytocin regimen did not affect the rate of cesarean delivery or other perinatal outcomes. Compared to 1 mU/min, the regimens starting with 2 mU/min and 4 mU/min reduced the duration of 1st stage by 0.8 hours (95% confidence interval 0.5 – 1.1) and 1.3 hours (1.0 – 1.7), respectively, in nulliparas. No effect was observed on the second stage of labor. Similar patterns were observed in multiparas. High-dose regimen was associated with a reduced risk of meconium stain, chorioamnionitis, and newborn fever in multiparas.

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For a list of institutions that participated in this study, see the Appendix online at <http://links.lww.com/xxx>.

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Conclusion—High-dose oxytocin regimen (starting dose at 4 mU/min and increment of 4 mU/min) is associated with a shorter duration of first stage of labor in all parities without increasing the cesarean delivery rate or adversely affecting perinatal outcomes.

Introduction

Oxytocin for the purposes of augmentation and induction of labor is one of the most frequently used medications in obstetrics. Recent studies show that oxytocin is used in over 50% of laboring women in some hospitals.¹ Yet, there is tremendous variability in the dose and dosing interval in clinical practice. The Institute for Safe Medication Practices designated oxytocin as a high-alert medication.² Concerns have been raised whether such frequent use, particularly with high dose regimens, has potential unwanted consequences.³ A recent meta-analysis of 10 randomized controlled trials concluded that high-dose oxytocin for labor augmentation was associated with a decrease in cesarean section and shortened labor with no increase in adverse maternal or perinatal outcomes.⁴ However, these 10 trials were conducted in 5 continents and published from 1987 to 2004. Further confounding the issue, the dose regimen varied among the studies. Given the frequent use of oxytocin in obstetric management and rising cesarean section rate, we reexamined the dose regimens that are commonly used in the U.S. in a contemporary population.

Materials and Methods

The Consortium on Safe Labor is a retrospective observational study conducted by the *Eunice Shriver Kennedy* National Institute of Child Health and Human Development, National Institutes of Health, in collaboration with 12 institutions across the U.S. A detailed description of the study is provided elsewhere.⁵ The goal of the study was to collect comprehensive information on contemporary labor and delivery practice in multiple institutions. Participating institutions extracted detailed information from their electronic medical records on maternal demographic characteristics, medical history, reproductive and prenatal history, labor and delivery summary, postpartum and newborn information. Information from the neonatal intensive care unit (NICU) was linked to the newborn records. Data on oxytocin use were extracted from a medication database. A validation study on several key variables indicated that the electronic medical records are an accurate representation of the medical charts.⁵ This project was approved by the Institutional Review Boards of all participating institutions.

Not all participating hospitals had detailed information on oxytocin regimen, dose and increments. We chose 6 hospitals that had such data (N = 73,628). (We compared women in these hospitals with those in the excluded hospitals on model of delivery and neonatal outcomes. No substantial differences were found (data not shown)). The following subjects were selected in a descending order: singleton gestation (remaining N=72,041), spontaneous onset of labor (46,523), livebirth (46,374), no previous uterine scar (37,002), no congenital anomalies (34,477), use of oxytocin augmentation (17,351), vertex presentation (17,043), and gestational age between 37 and 41 completed weeks (15,054). Only oxytocin for labor augmentation prior to delivery was studied.

Women were grouped based on their oxytocin starting dose and incremental dosing: 1, 2, and 4 mU/min. Maternal characteristics were compared according to starting dose of oxytocin. We then compared maternal and perinatal outcomes by starting dose. Since severe maternal and neonatal morbidity is rare, we created two composite indices in addition to relatively more common outcomes. The maternal complication composite index includes any of the following conditions: intrapartum placental abruption, postpartum hemorrhage, intrapartum and postpartum blood transfusion and hysterectomy. The neonatal complication

composite index includes asphyxia, hypoxia-ischemic encephalopathy, neonatal seizure, neonatal death, respiratory distress syndrome, continuous positive airway pressure, ventilation use and transient tachypnea.

All data analyses were stratified by parity (nulliparas vs. multiparas). Chi-square test was used for categorical variables; analysis of variance was used for continuous variables with a normal distribution; and Kruskal-Wallis test was used for continuous variables with a non-normal distribution. We then estimated adjusted odds ratios for binary outcomes and adjusted differences for continuous outcomes. For the adjusted odds ratio, a multivariable logistic regression model was used to adjust for maternal age (continuous), race/ethnicity (white, black, Hispanic and other), insurance type (private vs. public), use of fetal scalp electrode (yes/no), epidural analgesia (yes/no), birthweight (continuous), gestational age (continuous), body mass index at admission (continuous), cervical dilation (continuous), effacement (continuous), fetal station (continuous), frequency of uterine contraction at admission (continuous), cervical dilation at oxytocin administration (continuous) and hospital site (6 categories). For the adjusted difference, a generalized linear mixed model was used to adjust for the above factors. Hospital was used as a random effects variable. All analyses were conducted in SAS Version 9.2 (PROC LOGISTIC and PROC GLIMMIX).

Results

The oxytocin regimen for augmentation in the selected hospitals is summarized in Table 1. We compared the institutional oxytocin protocol with detailed oxytocin data. It should be noted that none of these hospitals had a specific active management of labor protocol. In total, the starting doses of 1, 2 and 4 mU/min. were used in 2,691, 4,994 and 7,369 women, respectively. Women in the high dose group received substantially higher maximal dose than low dose groups:

A number of baseline characteristics of nulliparous women differed by starting dose of oxytocin (Table 2). However, no statistical significance was found in maternal BMI at admission, prevalence of hypertensive disorders or diabetes. There were no clinically important differences in gestational age or birth weights. At the start of oxytocin, cervical dilation was at 3 – 4 cm. The median maximal doses for the three groups were 7, 9.5 and 12 mU/min. ($p < 0.0001$).

The unadjusted and adjusted labor outcomes among these three different oxytocin regimens in nulliparous women are presented in tables 3 and 4. Cesarean delivery was lower in the starting dose of 4 mU/min group (14% versus 17% in the other two regimens) but after we adjusted for potential confounders and hospitals, the risk of cesarean delivery was the same with all three oxytocin regimens. No other maternal and neonatal outcomes (except one) significantly differed among the regimens, including intrapartum fetal distress, shoulder dystocia or 3rd/4th degree perineal laceration. However, higher oxytocin doses were associated with a 60% reduced risk of Apgar score < 7 at 5 minutes but the confidence interval ranged from 0.1 and approached 1.0. The duration of 1st stage of labor from admission to complete cervical dilation was decreased in a dose-response pattern. Compared to 1 mU/min., the regimens starting at 2 mU/min. and 4 mU/min. reduced the duration of 1st stage by 0.8 hours (95% confidence interval [CI] 0.5 – 1.1) and 1.3 hours (1.0 – 1.7), respectively, in nulliparas. No effect was observed on the duration of the 2nd stage of labor.

The results in multiparas differed from those of nulliparas (Tables 5 to 7). After adjusting for a number of potential confounders, the high dose oxytocin was associated with a reduced risk of meconium staining, chorioamnionitis and newborn fever (Table 7). Compared to 1 mU/min., the regimens starting at 2 mU/min. and 4 mU/min. reduced the duration of 1st

stage by 0.7 hours (95% CI 0.4 – 0.9) and 1.1 hours (0.9 – 1.4), respectively. Oxytocin dose had no effect on the 2nd stage of labor.

Our database does not have information on the incidence of hyperstimulation. Thus, we used the need for intrapartum tocolytics as a surrogate. The use of tocolytics was infrequent, 1.0 – 1.8% (Tables 3 and 6) and the differences were not clinically significant.

We further examined the effects of oxytocin regimen by cervical dilation at the start of oxytocin augmentation (< 6 cm versus ≥ 6 cm) since we have previously shown this to be the cervical dilation associated with onset of active labor.⁶ The overall patterns of dose effects were similar regardless of early versus late initiation (Results not shown).

Discussion

Our large, observational study demonstrates that in parturients who received oxytocin for labor augmentation, the duration of 1st stage of labor is significantly reduced with increasing oxytocin dose in a dose-response pattern. No effect was found on 2nd stage of labor. These patterns are consistent in nulliparas and multiparas. A shorter duration of labor may also decrease the risk of meconium staining, chorioamnionitis and newborn fever in multiparas. However, we found no reduction in cesarean delivery rate amongst the high dose group.

Our findings are largely consistent with those in a recent meta-analysis of 10 randomized controlled trials.⁴ The latter showed that the duration of labor was reduced by 1.54 hours (95% CI 0.64 – 2.44) in the high versus low dose groups. It also found a decreased risk of chorioamnionitis (RR = 0.75, 95% CI 0.50 – 1.14) and intrapartum meconium (RR= 0.82, 95% CI 0.62 – 1.09), though neither of them were statistically significant.

Compared to the meta-analysis, our study has several advantages. The oxytocin regimens are more homogenous among our study hospitals than those in the meta-analysis of various studies. Our regimens also more closely reflect contemporary obstetric practice. Nonetheless, our retrospective observational study did not have a common labor management protocol, although one may argue that the differences in labor management style may even be greater among previous trials conducted in 5 continents than among our study hospitals in the U.S. Hyperstimulation was also not assessed in our study. However, the similar cesarean delivery rates and lack of difference in neonatal outcomes support the safety of the higher dose regimen. Finally, although we don't have information on patient satisfaction, the shorter duration of labor with the high dose regimen may be considered an advantage.

The significant reduction in the risk of poor Apgar score at 5 minutes by 60% in nulliparas is difficult to explain. The event was rare and the confidence intervals were wide. In addition, none of other neonatal outcomes were associated with oxytocin regimen. Given the large number of outcomes and comparisons were made, we speculate that this finding may be due to chance.

In summary, our study found that high dose oxytocin regimen (starting dose at 4 mU/min. and increment of 4 mU/min.) is associated with a shorter duration of 1st stage of labor in both nulliparas and multiparas without increasing the cesarean rate or adversely affecting perinatal outcomes. It may, in turn, reduce the risk of meconium staining, chorioamnionitis and newborn fever in multiparas.

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References

1. Walsh J, Foley M, O'herlihy C. Dystocia correlates with body mass index in both spontaneous and induced nulliparous labors. *J Matern Fetal Neonatal Med.* 2010 Dec 15. Epub ahead of print.
2. Institute for Safe Medical Practices. [Accessed February 20, 2011] High alert medications. Available at: www.ismp.com
3. Clark SL, Simpson KR, Knox GE, Garite TJ. Oxytocin: new perspectives on an old drug. *Am J Obstet Gynecol.* 2009; 200:35.e1–6. [PubMed: 18667171]
4. Wei SQ, Luo ZC, Qi HP, Xu H, Fraser WD. High-dose vs low-dose oxytocin for labor augmentation: a systematic review. *Am J Obstet Gynecol.* 2010; 203:296–304. [PubMed: 20451894]
5. Zhang J, Troendle J, Reddy U, Laughon SK, Branch DW, Burkman R, et al. Contemporary cesarean delivery practice in the United States. *Am J Obstet Gynecol.* 2010; 203:326.e1–326.e10. [PubMed: 20708166]
6. Zhang J, Landy HJ, Branch DW, Burkman R, Haberman S, Gregory K, et al. Contemporary patterns of spontaneous labor with normal neonatal outcomes. *Obstet Gynecol.* 2010; 116:1281–7. [PubMed: 21099592]

Table 1

Oxytocin regimen for labor augmentation in selected institutions

Hospital	Institutional oxytocin protocol			Oxytocin database			
	Starting dose (mU/min.)	Increments (mU/min.)	Time interval between increments (minutes)	Maximum dose (mU/min.)	Starting dose (N)	Median increment dose (mU/min.)	Highest dose used (median, 10 th and 90 th percentile)
A					1= 659 2= 415 4= 174	2 2 3	7 (3, 17) 8 (4, 18) 12 (6, 20)
B					1= 441 2= 687 4= 1010	2 2 4	7 (3, 19) 6 (4, 18) 12 (6, 20)
C	Low=1 or 2 High= 4	Low = 1-2 High = 4	Low = 30 High = 30	Low = 20 High = 20	1= 1149 2= 391 4= 804	2 2 4	7 (3, 19) 6 (4, 18) 12 (5, 20)
D					1= 56 2= 245 4= 2683	2 3 4	8 (3, 19) 8 (4, 20) 12 (6, 20)
E					1= 171 2= 443 4= 1914	2 2 4	6 (3, 16) 6 (4, 16) 12 (4, 20)
F		Low=2 High=4	Low=15 High=15	Primiparas=36 Multiparas=24	1= 215 2= 2813 4= 784	2 3 3	8 (2, 15) 11 (8, 26) 16 (8, 34)

Table 2
Maternal characteristics by the starting dose of oxytocin for labor augmentation in nulliparas

	Starting dose			P*
	1 mU/min. N=1319	2 mU/min. N=2383	4 mU/min N=4073	
Maternal race White (%)	73	48	67	<.0001
Black (%)	2	23	7	
Hispanic (%)	13	19	16	
Other or unknown (%)	12	10	10	
Insurance Private (%)	79	57	67	<.0001
Public (%)	21	43	33	
Maternal age (mean ± SD, year)	25.0 (4.9)	24.0 (5.3)	23.9 (4.7)	<.0001
Epidural analgesia (%)	95	84	94	<.0001
Intrauterine pressure catheter use (%)	46	31	38	<.0001
Fetal scalp electrode use (%)	44	41	39	0.0015
Cervical dilation at admission (mean ± SD, cm)	2.5 (1.5)	2.9 (1.5)	2.6 (1.4)	<.0001
No. of contractions/10 minutes at admission (mean ± SD)	3.5 (1.2)	3.1 (1.5)	3.7 (1.4)	<.0001
Effacement at admission (mean ± SD, %)	81 (13)	79 (17)	80 (14)	<.0001
Station at admission (median, 10 th , 90 th centiles)	-1 (-2, 0)	-2 (-3, -1)	-2 (-3, 0)	<.0001
Cervical dilation at start of oxytocin	3 (1, 7)	4 (1, 8)	3 (1, 7)	<.0001
Highest dose of oxytocin (mU/min) (median, 10 th , 90 th centiles)	7 (2, 19)	9.5 (2, 24)	12 (4, 20)	<.0001

* Chi-square test for categorical variables; analysis of variance for continuous variables with a normal distribution; Kruskal-Wallis test for continuous variables with a non-normal distribution.

Table 3
Perinatal outcomes by the starting dose of oxytocin for labor augmentation in nulliparas

	Starting dose			P*
	1 mU/min. N=1319	2 mU/min. N=2383	4 mU/min N=4073	
1 st stage (L&D admission to full dilation) (h) (median, 10 th , 90 th centiles)	10.2 (6, 18)	8.9 (5, 15)	8.5 (5, 15)	<0.0001
Duration from time starting oxytocin to delivery (h) (median, 10 th , 90 th centiles)	6.9 (3, 14)	5.3 (2, 11)	6.3 (2, 13)	<0.0001
2 nd stage (min.) (median, 10 th , 90 th centiles)	79 (28, 181)	56 (16, 159)	68 (23, 166)	<0.0001
Intrapartum tocolytics (%)	1.8	1.9	1.0	<.0001
Meconium staining (%)	14	17	14	0.009
Chorioamnionitis (%)	12	8.0	8.7	0.0001
Intrapartum fetal distress (%)	6.8	7.6	5.2	0.0001
Shoulder dystocia (%)	1.2	0.8	1.5	0.084
Mode of delivery vaginal (%)	68	69	67	<.0001
Vaginal assisted (%)	15	14	18	
Cesarean (%)	17	17	14	
Estimated blood loss (cc) (median, 10 th , 90 th centiles)	300 (200, 700)	350 (250, 700)	350 (200, 700)	<.0001
Maternal complication composite index [#] (%)	14	6.5	11	<.0001
3 rd /4 th degree perineal laceration (%)	6.8	5.2	6.1	0.13
Newborn resuscitation [¶] (%)	0.83	0.97	1.80	0.003
Newborn fever (%)	8.2	2.9	5.4	<.0001
NICU admission (%)	7.1	6.6	7.0	0.78
Birth injury (%)	2.1	1.8	2.0	0.74
Apgar score at 5 min. <7 (%)	1.0	0.7	1.1	0.34
Neonatal complication composite index [†] (%)	3.4	3.2	2.9	0.60
NICU length of stay (day) (median, 10 th , 90 th centiles)	3.6 (1, 9.5)	3 (0, 8)	3.7 (1, 7.7)	0.32

* Chi-square test for categorical variables; analysis of variance for continuous variables with a normal distribution; Kruskal-Wallis test for continuous variables with a non-normal distribution.

[#] Maternal complication composite index includes: intrapartum placental abruption, postpartum hemorrhage, intrapartum and postpartum blood transfusion and hysterectomy.

[¶] Newborn resuscitation includes: intubation, chest compression, epinephrine or other related medicine and continuous positive airway pressure.

[†] Neonatal complication composite index includes: asphyxia, hypoxia-ischemic encephalopathy, neonatal seizure, neonatal death, respiratory distress syndrome, continuous positive airway pressure, ventilation use and transient tachypnea.

Table 4
Adjusted odds ratios of and differences in adverse perinatal outcomes by starting dose of oxytocin augmentation in nulliparas

	Starting dose		
	1 mU/min. N=1319	2 mU/min. N=2383	4 mU/min N=4073
	OR	aOR* (95% CI)	aOR* (95% CI)
Cesarean delivery	1.0	1.0 (0.8 – 1.3)	0.9 (0.7 – 1.1)
Meconium stain	1.0	1.1 (0.9 – 1.4)	0.9 (0.7 – 1.1)
Chorioamnionitis	1.0	1.2 (0.9 – 1.6)	1.0 (0.8 – 1.2)
Intrapartum fetal distress	1.0	1.1 (0.8 – 1.5)	0.8 (0.6 – 1.2)
Shoulder dystocia	1.0	0.7 (0.3 – 1.6)	1.0 (0.5 – 2.0)
3 rd /4 th degree perineal laceration	1.0	1.0 (0.7 – 1.4)	1.1 (0.8 – 1.5)
Maternal complication composite index [#]	1.0	0.9 (0.7 – 1.2)	1.1 (0.9 – 1.4)
Newborn resuscitation [¶]	1.0	1.1 (0.5 – 2.7)	1.0 (0.5 – 2.3)
Newborn fever	1.0	1.1 (0.8 – 1.6)	1.1 (0.8 – 1.5)
NICU admission	1.0	1.1 (0.8 – 1.5)	1.0 (0.7 – 1.3)
Birth injury	1.0	0.8 (0.4 – 1.6)	1.3 (0.7 – 2.3)
5 min. Apgar score < 7	1.0	0.4 (0.1 – 0.97)	0.4 (0.1 – 0.9)
Neonatal complication composite index [‡]	1.0	1.0 (0.7 – 1.6)	0.9 (0.6 – 1.4)
	<i>Difference</i>	<i>Difference* (95% CI)</i>	<i>Difference* (95% CI)</i>
Estimated blood loss (ml)	Ref.	-2.8 (-28.1, 22.6)	-11.6 (-35.7, 12.5)
NICU length of stay (day)	Ref.	0.35 (-1.31, 2.0)	1.18 (-0.4, 2.8)
1 st stage (admission to full dilation) (h)	Ref.	-0.8 (-1.1, -0.5)	-1.3 (-1.7, -1.0)
2 nd stage of labor (min.)	Ref.	1.2 (-15.6, 18.1)	-8.8 (-24.7, 7.2)

[#] Maternal complication composite index includes: intrapartum placental abruption, postpartum hemorrhage, intrapartum and postpartum blood transfusion and hysterectomy.

[¶] Newborn resuscitation includes: intubation, chest compression, epinephrine or other related medicine and continuous positive airway pressure.

[‡] Neonatal complication composite index includes: asphyxia, hypoxia-ischemic encephalopathy, neonatal seizure, neonatal death, respiratory distress syndrome, continuous positive airway pressure, ventilation use and transient tachypnea.

* For adjusted odds ratios, a multivariable logistic regression model was used to adjust for maternal age, race/ethnicity, insurance type, use of fetal scalp electrode, epidural analgesia, birthweight, gestational age, body mass index at admission, cervical dilation, effacement, fetal station, frequency of uterine contraction at admission, cervical dilation at oxytocin administration, and hospital site. For adjusted difference, a generalized linear mixed model was used to adjust for the above factors. Hospital was used as a random effects variable.

Table 5
Maternal characteristics by the starting dose of oxytocin for labor augmentation in multiparas

	Starting dose			p
	1 mU/min. N=1372	2 mU/min. N=2612	4 mU/min N=3296	
Maternal race White (%)	66	40	71	<.0001
Black (%)	8.5	29	4.6	
Hispanic (%)	18	24	18	
Other or unknown (%)	8.1	6.1	6.7	
Insurance Private (%)	70	48	66	<.0001
Public (%)	30	52	34	
Maternal age (mean \pm SD, year)	29.0 (5.0)	27.1 (5.4)	28.2 (4.8)	<.0001
Epidural analgesia use (%)	87	79	93	<.0001
Intrauterine pressure catheter use (%)	23	13	19	<.0001
Fetal scalp electrode use (%)	32	25	25	<.0001
Cervical dilation at admission (mean \pm SD, cm)	3.3 (1.4)	3.8 (1.5)	3.4 (1.5)	<.0001
No. of contractions/10 minutes at admission (mean \pm SD)	3.1 (1.3)	2.7 (1.5)	3.6 (1.3)	<.0001
Effacement at admission (mean \pm SD, %)	74 (15)	69 (19)	75 (13)	<.0001
Station at admission (median, 10 th , 90 th centiles)	-2 (-3, -1)	-2 (-3, -1)	-2 (-3, -1)	<.0001
Cervical dilation at start of oxytocin	4 (2, 7)	4.5 (2.5, 8)	4 (2, 7)	<.0001
Max dose of oxytocin (mU/min) (median, 10 th , 90 th centiles)	7 (1, 16)	8 (2, 20)	10.5 (4, 20)	<.0001

* Chi-square test for categorical variables; analysis of variance for continuous variables with a normal distribution; Kruskal-Wallis test for continuous variables with a non-normal distribution.

Table 6
Perinatal outcomes by the starting dose of oxytocin for labor augmentation in Multiparas

	Starting dose			p
	1 mU/min. N=1372	2 mU/min. N=2612	4 mU/min N=3296	
1 st stage (L&D admission to full dilation) (h) (median, 10 th , 90 th centiles)	7.2 (4, 13)	6.6 (4, 12)	6.1 (3, 11)	<.0001
Duration from time starting oxytocin to delivery (h) (median, 10 th , 90 th centiles)	3.8 (1, 8.5)	3.1 (1, 6.9)	3.4 (1, 7.6)	<.0001
2 nd stage (min.) (median, 10 th , 90 th centiles)	19 (5, 55)	15 (4, 45)	20 (7, 51)	<.0001
Intrapartum tocolytics (%)	0.4	0.9	0.1	<.0001
Meconium staining (%)	10	11	7.6	0.0001
Chorioamnionitis (%)	2.5	1.6	2.2	0.11
Intrapartum fetal distress (%)	3.6	2.5	1.9	0.002
Shoulder dystocia (%)	1.6	1.5	2.0	0.26
Mode of delivery vaginal (%)	92	92	92	0.006
Vaginal assisted (%)	4.5	4.5	5.5	
Cesarean (%)	3.7	3.5	2.2	
Maternal complication composite index [#] (%)	11	5.7	10	<.0001
3 rd /4 th degree perineal laceration (%)	0.4	0.6	0.6	0.55
Newborn resuscitation [¶] (%)	0.66	0.34	1.20	<.001
Newborn Fever (%)	8.2	2.9	5.4	<.0001
NICU admission (%)	4.9	4.0	5.9	0.003
Birth injury (%)	0.7	1.0	0.5	0.09
Apgar score at 5 min. <7 (%)	0.3	0.4	0.5	0.65
Neonatal complication composite index [†] (%)	2.5	1.6	2.8	0.02
Estimated blood loss (cc) (median, 10 th , 90 th centiles)	300 (150, 400)	300 (250, 400)	300 (200, 400)	<.0001
NICU length of stay (day) (median, 10 th , 90 th centiles)	4 (1, 17.4)	2 (0, 10.9)	4 (1.3, 10.4)	<.0001

* Chi-square test for categorical variables; analysis of variance for continuous variables with a normal distribution; Kruskal-Wallis test for continuous variables with a non-normal distribution.

[#] Maternal complication composite index includes: intrapartum placental abruption, postpartum hemorrhage, intrapartum and postpartum blood transfusion and hysterectomy.

[¶] Newborn resuscitation includes: intubation, chest compression, epinephrine or other related medicine and continuous positive airway pressure.

[†] Neonatal complication composite index includes: asphyxia, hypoxia-ischemic encephalopathy, neonatal seizure, neonatal death, respiratory distress syndrome, continuous positive airway pressure, ventilation use and transient tachypnea.

Table 7
Adjusted odds ratios of and differences in adverse perinatal outcomes by starting dose of oxytocin augmentation in multiparas

	Starting dose		
	1 mU/min. N=1372	2 mU/min. N=2612	4 mU/min N=3296
	OR	aOR* (95% CI)	aOR* (95% CI)
Cesarean delivery	1.0	0.9 (0.6 – 1.4)	0.7 (0.4 – 1.2)
Meconium stain	1.0	0.9 (0.7 – 1.2)	0.6 (0.5 – 0.8)
Chorioamnionitis	1.0	0.8 (0.4 – 1.3)	0.5 (0.3 – 0.8)
Intrapartum fetal distress	1.0	0.8 (0.5 – 1.3)	0.7 (0.4 – 1.2)
Shoulder dystocia	1.0	1.4 (0.7 – 2.8)	1.4 (0.7 – 2.7)
3 rd /4 th degree perineal laceration	1.0	2.2 (0.7 – 6.7)	2.8 (0.9 – 8.5)
Maternal complication composite index [#]	1.0	1.1 (0.9 – 1.5)	0.9 (0.7 – 1.2)
Newborn resuscitation [¶]	1.0	0.9 (0.3 – 2.9)	1.0 (0.3 – 2.7)
Newborn fever	1.0	0.8 (0.4 – 1.5)	0.5 (0.3 – 0.96)
NICU admission	1.0	0.7 (0.5 – 1.02)	0.9 (0.6 – 1.3)
Birth injury	1.0	0.7 (0.3 – 1.8)	0.5 (0.2 – 1.5)
5 min. Apgar score < 7	1.0	4.7 (0.5 – 42.8)	3.2 (0.4 – 28.1)
Neonatal complication composite index [‡]	1.0	0.6 (0.3 – 1.1)	1.0 (0.6 – 1.6)
	<i>Difference</i>	<i>Difference* (95% CI)</i>	<i>Difference* (95% CI)</i>
Estimated blood loss (ml)	Ref.	16.2 (-0.6, 33.1)	-5.1 (-22.7, 12.6)
NICU length of stay (day)	Ref.	-1.8 (-4.5, 0.8)	-0.9 (-3.3, 1.4)
1 st stage (admission to full dilation) (h)	Ref.	-0.7 (-0.9, -0.4)	-1.1 (-1.4, -0.9)
2 nd stage of labor (min.)	Ref.	-0.3 (-3.2, 2.6)	-0.6 (-3.4, 2.3)

[#] Maternal complication composite index includes: intrapartum placental abruption, postpartum hemorrhage, intrapartum and postpartum blood transfusion and hysterectomy.

[¶] Newborn resuscitation includes: intubation, chest compression, epinephrine or other related medicine and continuous positive airway pressure.

[‡] Neonatal complication composite index includes: asphyxia, hypoxia-ischemic encephalopathy, neonatal seizure, neonatal death, respiratory distress syndrome, continuous positive airway pressure, ventilation use and transient tachypnea.

* For adjusted odds ratios, a multivariable logistic regression model was used to adjust for maternal age, race/ethnicity, insurance type, use of fetal scalp electrode, epidural analgesia, birthweight, gestational age, body mass index at admission, cervical dilation, effacement, fetal station, frequency of uterine contraction at admission, cervical dilation at oxytocin administration, and hospital site. For adjusted difference, a generalized linear mixed model was used to adjust for the above factors. Hospital was used as a random effects variable.