6 High-dose versus standard-dose oxytocin regimens to augment labor in nulliparas: a double-blind randomized clinical trial

Moeun Son[1], Archana Roy[2], Bethany T. Stetson[3], Nancy Tunney Grady[4], Mary Clare Vanecko[4], Nicole Bond[4], Kate Swanson[5], Emily S. Miller[2], Alan M. Peaceman[6]
[1]Yale University School of Medicine, New Haven, CT, [2]Northwestern University, Chicago, IL, [3]Northwestern Memorial, Chicago, IL, [4]Northwestern Memorial Hospital, Chicago, IL, [5]University of California, San Francisco, San Francisco, CA, [6]Northwestern University Feinberg School of Medicine, Chicago, IL

OBJECTIVE: To determine whether, compared to standard-dose oxytocin (SDO), high-dose oxytocin (HDO) for labor augmentation reduces the risk of cesarean in nulliparas.

STUDY DESIGN: This double-blind, single center randomized trial (NCT02487797) included nulliparas with singleton gestations≥36 weeks in spontaneous labor who required oxytocin for augmentation. Those being induced or non-English speaking were excluded. Women were randomized 1:1 to SDO (initial and incremental rate of 2 mU/min) or HDO (initial and incremental rate of 6 mU/min) dosing. Oxytocin solutions were prepared by pharmacists using different concentrations but infused at the same initial and incremental volume rates (2 mL/h) so investigators, patients, and clinicians could remain masked to allocation. The primary outcome was cesarean delivery. Secondary maternal outcomes were labor duration, chorioamnionitis, endometritis, and postpartum hemorrhage. Secondary perinatal outcomes were perinatal death, Apgar score <3 at 5 minutes, umbilical artery acidemia, NICU admission, and a severe composite adverse outcome. Analysis was by intention to treat with $p<0.05$ considered significant. We planned to enroll 501 women per group to achieve 80% power to demonstrate a 6.6% absolute difference in cesarean, assuming a baseline incidence of 20% in the SDO group.

RESULTS: 1003 women were randomized from 9/28/15 to 9/1/20. The incidence of cesarean was not significantly different between the groups. However, there was a significantly lower median labor duration, and a significant reduction in the incidence of chorioamnionitis in the HDO group compared with SDO (Table). There were no significant differences in other outcomes, specifically no increased risk of adverse neonatal outcomes (e.g., cesarean for non-reassuring fetal status, umbilical artery acidemia, severe perinatal composite) with HDO.

CONCLUSION: The use of HDO for labor management did not result in a change in the incidence of cesarean. However, HDO was associated with a significant reduction in chorioamnionitis and duration of labor augmentation, without increases in neonatal complications.

	High-dose oxytocin (n=502)	Standard-dose oxytocin (n=501)	RR (95% CI)	p-value*
Maternal/Obstetric Outcomes				
Cesarean delivery	73 (14.4)	72 (14.5)	1.01 (0.75-1.37)	0.94
Arrest of dilation	27	25		
Arrest of descent	23	23		
Non-reassuring fetal status	19	23		
Maternal request	0	1		
Failed operative vaginal attempt	4	0		
Labor duration - hr				
Median duration of stay in labor and delivery unit (IQR)	10.6 (7.6-14.6)	11.4 (8.4-16.4)		**<0.01****
Median time interval from randomization to delivery (IQR)	6.9 (4.4-10.9)	8.0 (5.5-12.9)		**<0.01****
Chorioamnionitis	52 (10.4)	78 (15.6)	0.66 (0.48-0.92)	**0.01**
Postpartum endometritis	3 (0.6)	5 (1.0)	0.60 (0.14-2.49)	0.51
Postpartum hemorrhage	29 (5.8)	23 (4.6)	1.25 (0.74-2.14)	0.40
Perinatal Outcomes				
Stillbirth or neonatal death	0	0	NA	NA
5-minute Apgar score ≤3	3 (0.6)	4 (0.8)	0.75 (0.17-3.33)	0.72
Umbilical artery pH <7.0 or base excess >12 mmol/L (n=381, 382)	14 (3.7)	26 (6.8)	0.54 (0.28-1.02)	0.05
Admission to neonatal intensive care unit	29 (5.8)	33 (6.6)	0.88 (0.54-1.42)	0.59
Severe morbidity composite§	5 (1.0)	7 (1.4)	0.71 (0.23-2.23)	0.56

All data are presented in n (%) unless otherwise indicated
*Chi square or Fisher's exact tests unless otherwise indicated
**Wilcoxon rank sum test
§Severe morbidity composite included any of the following: stillbirth, neonatal death, severe respiratory distress requiring cardiorespiratory support and/or ventilation (intubation, continuous positive airway pressure, high- flow nasal cannula) for more than 12 hours, major birth injury (brachial plexus injury, bone fractures, other neurologic injury, facial nerve injury), neonatal encephalopathy, neonatal seizure, need for hypothermic treatment (cooling), or neonatal sepsis (positive blood, urine, or cerebrospinal fluid culture; or in the absence of positive culture(s), clinical evidence of cardiovascular collapse or an unequivocal X-ray confirming infection).

7 Oral azithromycin ± amoxicillin to prevent peripartum infection in laboring high-risk women: A 3-Arm RCT

Akila Subramaniam[1], Ye Yuanfan[1], Rahel Mbah[2], Jodie Dionne-Odom[1], Lorie M. Harper[3], Waldemar Carlo[1], Gregory Halle-Ekane[4], Jeff M. Szychowski[1], Pius Tih[2], Alan Tita[5]
[1]Center for Women's Reproductive Health, University of Alabama at Birmingham, Birmingham, AL, [2]Cameroon Baptist Convention Health Services, Nord-Ouest, Cameroon, [3]University of Texas at Austin, Dell Medical School, Austin, TX, [4]University of Buea, Cameroon, Africa, Sud-Ouest, Cameroon, [5]University of Alabama at Birmingham, Birmingham, AL

OBJECTIVE: In low-income countries (LICs), maternal peripartum infections are a major cause of maternal mortality and mostly occur after vaginal birth. We compared the effectiveness of single dose azithromycin (AZI) ± amoxicillin (AMOX) vs placebo to prevent peripartum infection in laboring women.

STUDY DESIGN: Multicenter 3-arm double-blind RCT (NCT3248297) of women with viable term non-anomalous gestations with prolonged labor >18 hrs or ROM >8 hrs in Cameroon, Africa (2018-2020). Women with chorioamnionitis, study drug contraindications, or planned cesareans were excluded from enrollment. Women were randomized to: Arm 1) AZI 1g PO/Placebo, Arm 2) AZI 1g PO/AMOX 2g PO or Arm 3) Placebo/Placebo. All groups received "usual care" including antibiotics (abx) given at provider discretion. The primary outcome was composite maternal peripartum infection/death up to 6 wks postpartum. Two comparisons (Arm 1 vs 3; Arm 2 vs 3) were planned. We estimated 250 women/group (750 total) would provide 80% power at two-sided α=0.05 (0.025 per comparison) to detect a 50% effect size with 20% baseline composite infection rate.

RESULTS: Of 6531 women screened, 756 were randomized (Figure). Baseline characteristics (BMI, duration of ROM, labor, etc) were balanced except women were younger in the placebo arm (p=0.04). Over 60% of women in each arm received "usual care" abx: >90%