3 Azithromycin-based extended spectrum antibiotic prophylaxis for non-elective cesarean delivery: a pragmatic multicenter placebo-controlled double-blind rct

Alan Tita[1], Jeff Szychowski[1], Kim Boggess[2], George Saade[3], Sherri Longo[4], Erin Clark[5], Sean Esplin[5], Kirsten Cleary[6], Ron Wapner[7], Kellett Letson[8], Michelle Owens[9], Adi Abramovici[10], Namasivayam Ambalavanan[11], Gary Cutter[12], William Andrews[1]

[1]University of Alabama at Birmingham, Center for Women's Reproductive Health, Birmingham, AL, [2]University of North Carolina - Chapel Hill, Chapel Hill, NC, [3]University of Texas Medical Branch, Galveston, TX, [4]Ochsner, New Orleans, LA, [5]University Of Utah and Intermountain Health Care, Salt Lake City, UT, [6]Columbia University, New York City, NY, [7]Columbia University, New York, NY, [8]Mission Hospital, Ashville, NC, [9]University of Mississippi, Jackson, MS, [10]UT Houston, Houston, TX, [11]University of Alabama at Birmingham, Division of Neonatology, Birmingham, AL, [12]University of Alabama at Birmingham, Birmingham, AL

OBJECTIVE: Standard antibiotic prophylaxis (AP) for Cesarean delivery (CD) does not cover some organisms such as Ureaplasmas, which are frequently associated with post-CD infections. We evaluated the effect of adding azithromycin (AZI) to usual AP on post-CD infections in women undergoing non-elective CD.

STUDY DESIGN: The multicenter double-blind C/SOAP RCT (CT.gov NCT01235546), included women with singletons ≥24 wks' GA who had CD during labor or at least 4 hrs after membrane rupture. All women received standard AP. Subjects were randomized to also receive either AZI (500mg in 250ml saline) or identical placebo (250ml saline) by a center-stratified computer-generated scheme. Study medication was given preferably up to 1 hr pre-incision (or as soon as possible after). The centrally adjudicated primary outcome was a composite of endometritis, wound infection, or other infection (abdominopelvic abscess, sepsis, pelvic septic thrombophlebitis, pyelonephritis, pneumonia or meningitis) within 6 wks. Secondary outcomes included neonatal morbidities and reported adverse events. We estimated that N=2000 would be needed to show a ≥33% reduction in the primary outcome from a baseline of 8-12% with 80% power and 2-sided alpha of 0.05. Analysis was by intent-to-treat.

RESULTS: Of 17,790 women screened from 04/2011 to 11/2014, 2013 were randomized to AZI (n=1019) or placebo (n=994) at 14 sites. Groups were similar at baseline (35% Caucasian, 34% Black, 29% Latino and mean BMI of 29.9). Drug was administered before incision in 88% per group. The primary outcome occurred significantly less in the AZI group compared to placebo (Table; 6 vs 12%, p <.0001). Postpartum readmissions or emergency visits for any reason were also lower in the AZI group (Table). Neonatal outcomes were similar. Severe adverse maternal events (1.5% vs. 2.9%; p=.026) but not neonatal were less frequently reported with AZI.

CONCLUSION: Adding AZI to usual AP for non-elective CD reduced post-CD infections (NNT=17) and severe adverse maternal events with no difference in neonatal outcomes.

Table: The incidence of the outcomes by study group and RR (95% CI)

	Azithromycin n=1019	Placebo n=994	RR (95% CI)	P-value*
Maternal Outcomes	n (%)	n (%)		
Primary Composite Outcome	**62 (6.1)**	**119 (12.0)**	**0.51 (0.38-0.68)**	**<0.0001**
Endometritis	39 (3.8)	61 (6.1)	**0.62 (0.42-0.92)**	**0.017**
Wound infection	24 (2.4)	66 (6.6)	**0.35 (0.22-0.56)**	**<0.0001**
Other infections	3 (0.3)	6 (0.6)	0.49 (0.12-1.94)	0.337
Postpartum fever	51 (5.0)	81 (8.2)	**0.61 (0.44-0.86)**	**0.004**
Postpartum admission or unscheduled visit	83 (8.1)	123 (12.4)	**0.66 (0.51-0.86)**	**0.001**
Neonatal Outcomes				
Suspected sepsis	120 (11.8)	124 (12.5)	0.94 (0.75-1.19)	0.630
Confirmed sepsis	1 (0.1)	1 (0.1)	0.98 (0.06-15.6)	>0.99
Composite neonatal morbidity*	45 (4.4)	34 (3.4)	1.29 (0.83-2.0)	0.250
Neonatal death	3 (0.3)	1 (0.1)	2.93 (0.30-28.1)	0.624
NICU admission	171 (16.8)	169 (17.0)	0.99 (0.81-1.20)	0.894

*Composite neonatal morbidity =RDS, BPD, NEC, IVH 3 or 4 and SIRS

4 Chlorhexidine-alcohol compared with iodine-alcohol for preventing surgical-site infection at cesarean: a randomized controlled trial

Methodius Gamuo Tuuli[1], Jingxia Liu[1], Molly J. Stout[1], Shannon Martin[1], Alison G. Cahill[1], Graham Colditz[1], George A. Macones[1]

[1]Washington University in St. Louis, St. Louis, MO

OBJECTIVE: Optimizing preoperative skin antisepsis has the potential to decrease surgical-site infections (SSI) given that the skin is a major source of pathogens. Unfortunately, there is a paucity of evidence to guide the choice of antiseptic at cesarean - the most common major surgical procedure in women in the United States. We tested the hypothesis that preoperative skin antisepsis with chlorhexidine-alcohol is superior to iodine-alcohol for preventing SSI after cesarean.

STUDY DESIGN: This was a randomized controlled trial. Pregnant women undergoing cesarean were randomly assigned to preoperative skin preparation with either chlorhexidine-alcohol or iodine-alcohol. The primary outcome was SSI within 30 days after cesarean based on the Centers for Disease Control Nosocomial Infections Surveillance System definitions. Secondary outcomes were individual subtypes of SSI, other wound complications and adverse skin reactions. Analysis was by intention-to-treat. We estimated *a priori* that 1084 subjects would afford 80% power to detect a 50% difference in SSI (baseline rate 8%, 2-tailed, α=0.05).

RESULTS: 1082 subjects (538 in the chlorhexidine-alcohol group and 544 in the iodine-alcohol group) were included in the intention-to-treat analysis. The primary outcome, overall rate of SSI, was significantly lower in the chlorhexidine-alcohol group than in the iodine-alcohol group (4.3% vs. 7.7%; P=0.017; relative risk [RR], 0.55; 95% confidence interval [CI], 0.34 to 0.91) (**Table/Figure**). Chlorhexidine-alcohol was more protective than iodine-alcohol against superficial (3.2% vs. 5.2%) and deep (1.1% vs. 2.6%) infections, although the within-subtype differences were not statistically significant. Other wound complications and adverse skin reactions were similar in the two groups. Similar findings were observed in the as-treated analysis of 1068 subjects (4.1% vs. 7.6%; P=0.015; RR, 0.54; 95% CI, 0.33 to 0.90).

CONCLUSION: Preoperative skin antisepsis with chlorhexidine-alcohol is superior to iodine-alcohol for preventing SSI after cesarean.

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Table: Proportion of subjects with primary and secondary outcome by treatment group in intention-to-treat analysis (N=1082)

	Chlorhexidine-alcohol (n=538)	Iodine-alcohol (n=544)	Relative Risk (95% CI)	P
Primary outcome, n (%)				
Surgical site infection	23 (4.3)	42 (7.7)	0.55 (0.34 – 0.91)	0.017
Superficial incisional	17 (3.2)	28 (5.1)	0.61 (0.34 – 1.11)	0.102
Deep incisional	6 (1.1)	14 (2.6)	0.43 (0.17 – 1.12)	0.075
Secondary outcomes, n (%)				
Other wound complications				
Skin separation	65 (12.1)	66 (12.1)	1.00 (0.72 – 1.37)	0.980
Seroma	24 (4.5)	28 (5.2)	0.87 (0.51 – 1.48)	0.598
Hematoma	7 (1.3)	5 (0.92)	1.42 (0.45 – 4.43)	0.549
Cellulitis	5 (0.9)	10 (1.8)	0.51 (0.17 – 1.47)	0.201
Endometritis	8 (1.5)	11 (2.0)	0.74 (030 – 1.81)	0.503
Adverse skin reaction, n (%)				
Pruritus at operative site	0 (0)	3 (0.6)	-	0.249
Erythema at operative site	13 (2.4)	11 (2.0)	1.19 (0.54 – 2.64)	0.685
Allergic skin reaction	2 (0.4)	1 (0.2)	2.02 (0.18 – 22.20)	0.623

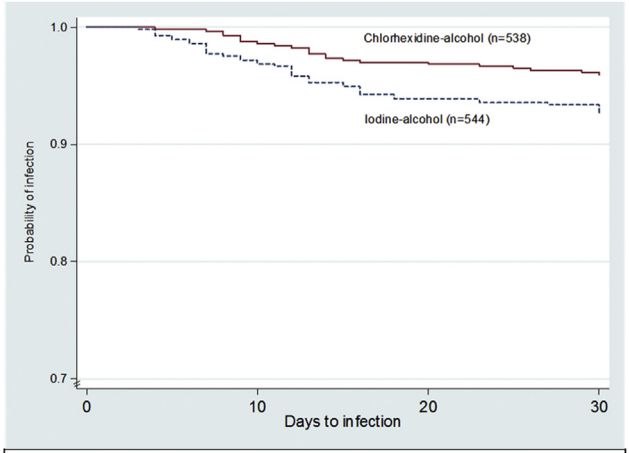


Figure: Kaplan-Meier Curves for Freedom from Surgical site Infection. Subjects allocated to skin preparation with chlorhexidine-alcohol were significantly more likely to remain free of surgical site infection than those allocated to iodine-alcohol (P=0.018 by log-rank test). In the chlorhexidine-alcohol group, 23 subjects had surgical site infection (4.3%) and the data from 515 were censored. In the iodine-alcohol group, 42 subjects had surgical site infection (7.7%) and data from 502 subjects were censored.

5 Foley or Misoprostol for the Management of Induction (The 'FOR MOMI' trial): A four-arm randomized clinical trial

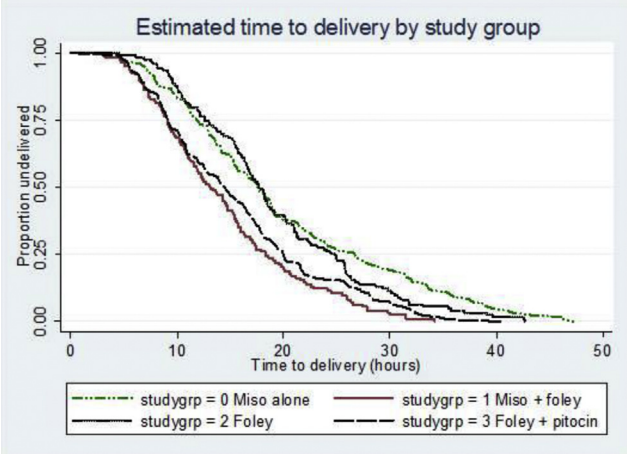
Lisa Danielle Levine[1], Mary D. Sammel[2], Samuel Parry[1], Catherine T. Williams[2], Michal A. Elovitz[1], Sindhu K. Srinivas[1]
[1]Maternal and Child Health Research Program; University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, [2]Department of Biostatics and Epidemiology, Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA

OBJECTIVE: Induction of labor occurs in over 20% of women, yet there is no clear evidence demonstrating which induction method achieves the shortest labor. The use of combined agents to decrease labor length is an understudied, novel approach to shortening the time to delivery. Our objective was to evaluate the difference in time to delivery among four different induction methods, including two combination methods.

STUDY DESIGN: A four-arm randomized clinical trial was conducted from May 2013-June 2015 comparing the use of: Misoprostol/Cervical foley (MF) concurrently, foley/Pitocin concurrently (FP), misoprostol alone (M), and foley alone (F). Randomization was stratified by parity. Labor management was standardized among participants. Term (≥37 weeks) singletons with intact membranes undergoing an induction with bishop score ≤6 were included. Our primary outcome was median [IQR] time to delivery and secondary outcome was cesarean delivery (CD) rate. Kruskal-Wallis, Pearson chi-square and Cox survival analyses with intent-to-treat principles were performed.

RESULTS: 492 women were randomized. Both combined methods (MF, FP) had a significantly shorter time to delivery (hours) than individual methods (M, F): (MF: 13.1 [9.1-18.3], FP: 14.5 [9.3-20.0], M: 17.6 [12-26.7], F: 17.7 [12.6-24.9], p=0.0001), see Figure. When adjusting for parity and mode of delivery, women induced with MF delivered 2.5 times faster than women who received M (Hazard ratio (HR): 2.5 (95%CI: 1.9-3.3), p<0.0001) and 2 times faster than women who received F (HR: 2.0 (95% CI: 1.6-2.6), p<0.0001). Results were similar when FP was compared to M and to F. There was no difference in time to delivery between MF and FP (p=0.2). CD rates were similar (MF: 27.6%, FP: 30.4%, Mo: 24.0%, Fo: 28.5%, p=0.7). A non-significant increase in neonatal morbidity was noted for the groups with a longer labor (MF: 0.8%, FP: 0.8%, M: 3.3%, F: 2.4%, p=0.4).

CONCLUSION: This randomized trial is one of the first of its kind to compare four different induction methods in a head-to-head trial. We found that combination induction methods resulted in delivery in half the amount of time as single agents with no difference in CD rates. Therefore, combined methods should be used for induction to achieve the shortest delivery time.



6 The use of serial cervical length and quantitative fetal fibronectin to identify nulliparous women at risk of subsequent spontaneous preterm birth

Michael Esplin[1]
[1]for the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development NuMoM2b Network, Bethesda, MD

OBJECTIVE: To assess whether universal screening using transvaginal cervical length (TVCL) and quantitative fetal fibronectin (fFN) can be used to accurately predict spontaneous preterm live birth (sPTB) in nulliparous women.

STUDY DESIGN: We recruited nulliparous women with singleton pregnancies at 8 clinical sites to identify markers of adverse pregnancy outcomes. Women had a quantitative fFN performed at 3 time