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Vascular Response To Isoproterenol In Pregnancy

R Landau, MD, AJJ Wood, MD, V Dishy, MD, CM Stein, MD, RM Smiley, MD, PhD. Dept. of Anesthesiology, Columbia University, New York, NY, and Dept. of Medicine, Vanderbilt University, Nashville, TN

It is widely believed that pregnant women have a diminished response to vasoactive drugs (1), but this has been difficult to study in humans. We used the dorsal hand vein/linear variable displacement transformer (LVDT) method of Aellig (2) to assess the vascular response to isoproterenol (ISO) during and after pregnancy.

Methods: After IRB approval and informed, written consent, 20 healthy pregnant women were studied between 32 and 37 weeks gestation and again at >12 weeks postpartum (PP). A dorsal hand vein was cannulated with a 25G IV catheter. Maternal SpO2, ECG and BP, and FHR were monitored. The LVDT was mounted on the back of the hand over the vein under investigation, 10 mm proximal to the cannula. A sphygmomanometer was inflated intermittently to a congestion pressure of 60 mm Hg resulting in a vertical displacement of the core of the LVDT. The amplitude of the core displacement at baseline (BL) and under drug infusion conditions is directly proportional to the size of the vein and was recorded for each drug dose studied. Phenylephrine (PE) was infused at an increasing rate until 50% constriction, or to a maximum of 9600 ng/min. The PE infusion was continued at that rate and a graded infusion of ISO was started (1-480 ng/min). Total infusion rate was kept constant at 24 ml/hr. Dilatation of the vein with ISO was recorded until a maximum response was achieved and a full dose-response curve was obtained. The concentration of ISO resulting in 50% of the maximal dilatation observed (ED50) and the maximal effect (Emax) were determined by non-linear regression. The log of the ED50 was used for statistical analysis and results are expressed as geometric means (95% confidence interval). Pregnant versus PP values were compared by paired t-test. The number of subjects in each group for which ISO dilatation restored the vein to BL was compared by Fisher's exact test.

Results: Two pregnant women did not achieve 50% vasoconstriction, thus ISO dilatation was not studied in these subjects. No changes in maternal BP nor FHR tracings occurred during ISO infusion; one PP subject became tachycardic at the maximal dose (480 ng/min). ED50 and Emax did not differ between pregnant and PP subjects (n=7). However, return of the vein to BL was achieved in only 4/18 pregnant women and in all PP studies completed so far.

	Pregnant (n=18)	Pregnant (n=7)	Postpartum (n=7)
ED50 (ng/min)	20 (11,35)	16 (3,78)	10 (4,30)
Emax (%)	82 (65,99)	93 (65,122)	114 (106,121)

Discussion: We have demonstrated that the LVDT/hand vein technique can be used to study vascular responses in pregnant women. With the majority of subjects still to be studied post-partum, firm conclusions about ISO effects in pregnancy compared to PP cannot yet be made.

Refs: 1. Am J Kidney Dis 1987; 9:303-7; 2. Br J Clin Pharmac 1981. 11: 237-43

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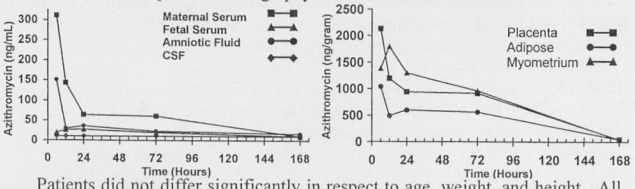
Does Oral Azithromycin Have A Role In Prophylaxis For Regional Anesthesia?

M. Vaules, M.D.; P. S. Ramsey, M.D.; G.M.S. Vasdev, M.D.; K. D. Ramin, M.D. Anes and MFM Depts., Mayo Clinic, Rochester, MN and UAB, Birmingham, AL.

The risk of central neuro-axial infections may preclude the use of regional anesthesia in febrile parturients. Macrolides are an attractive choice for prophylaxis due to their broad spectrum of activity. Azithromycin (AZ) has a favorable side effect profile, long half-life, and deep tissue penetration[1,2]. However, the pharmacokinetics of AZ are unknown in parturients. The aim of this study was to determine if AZ reached minimum inhibitory concentration (MIC_{90}) in maternal fat, blood, and cerebrospinal fluid (CSF).

After IRB approval and written informed consent, 21 ASA-1 parturients scheduled for an elective c-section under spinal anesthesia were enrolled. Each patient was assigned to receive an oral dose of 1g AZ at either 6, 12, 24, 72, or 168 hrs. preoperatively. 3 ml CSF; 10 ml each of maternal blood, urine, amniotic fluid, and cord blood; 5 gm each of placenta, myometrium and adipose tissue were obtained from each patient at the time of surgery. All specimens were collected within 20 min. of each other and frozen. AZ concentration was determined using high-performance liquid chromatography with electrochemical detection.



Patients did not differ significantly in respect to age, weight, and height. All patients tolerated the preoperative AZ without any side effects. Maternal serum and adipose levels of AZ peaked at 6 hrs and plateaued at 24-72 hrs. Myometrial levels peaked at 12 hrs, with drug levels >500 ng/gm for 72 hrs. AZ concentration of <20 ng/ml was found in the maternal CSF across all the time points.

Our study demonstrates that AZ penetrates maternal tissue, however the CSF concentrations are well below MIC_{90} for *Strep.* and *Staph.* species (100 ng/ml)[3] after 1g oral dose. Adipose levels are higher than MIC_{90} and therefore AZ may be effective in preventing an epidural infection. CSF penetration is below MIC_{90}, and AZ may not be useful in treating meningitis unless penetration improves with inflammation. Optimal dosing needs to be established before AZ can be recommended for use as a prophylactic agent. This study was supported in part by an unrestricted grant from Pfizer Corp.

References: 1. Annals of Pharmacotherapy 1992, 26:1253-1261. 2. Eur J Clin Microbiol Infect Dis 1991;10:807-812. 3. Mayo Clin Proc 1999, 74:613-634.

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Is a Trial of Labor in a Patient Who Has Had a Previous Cesarean Delivery Cost-effective?

A.. Chung, M.D., A. Macario, M.D., Y. El-Sayed, M.D., E.T. Riley, M.D., B. Duncan, M.D., D. Sheinberg B.S.
Departments of Anesthesia, Gynecology and Obstetrics, Health Research and Policy, and Economic Systems and Operations Research, Stanford University School of Medicine, Stanford, California.

It is unknown whether it is cost-effective for women who have had a previous cesarean delivery to have a trial of labor. These parturients have a small risk of uterine rupture with the potential for significant maternal and neonatal adverse outcomes. The goal of this study was to complete a cost-effectiveness analysis of vaginal birth after cesarean (VBAC).

We created a cost-effectiveness decision model from society's perspective incorporating published data on incidences of maternal outcomes and expert opinion on probabilities of neonatal outcomes. We also measured actual hospital cost data for patients having vaginal or cesarean delivery and then computed incremental costs of adverse outcomes.

The incremental cost-effectiveness of an elective repeat cesarean delivery relative to a trial of labor equaled $51,200 per quality-adjusted life-year. The model was extremely sensitive to the probability of successful vaginal delivery. If the probability of successful VBAC was less than 69%, elective repeat cesarean is both less costly and more effective. If the probability of successful VBAC was greater than 76%, trial of labor was then more cost effective.

The cost-effective selection of a delivery method in patients with one previous, low transverse cesarean depends on the a priori estimate of the likelihood of successful trial of labor. Maternal preferences for the method of delivery also need to be included. Improved algorithms for computing the likelihood of a particular patient having a successful vaginal delivery after a cesarean are necessary.

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Gastric Emptying in Term Parturients: Is NPO after Midnight Necessary?

M Loffredi, MD, CA Wong, MD, JN Ganchiff, RN, J Zhao, BS, Z Wang, MD, M Avram, PhD
Dept. of Anesthesiology, Northwestern University Medical School, Chicago, IL

Introduction: Studies in healthy, non-pregnant patients suggest that ingestion of clear liquids up until 2 h before induction of anesthesia does not adversely affect gastric pH and volume. The present study compared gastric emptying in term, non-laboring parturients after ingestion of 50 mL (control) and 300 mL of water.

Methods: Eleven healthy, non-obese, term pregnant volunteers participated in this IRB approved, cross-over study. Gastric emptying was assessed using serial gastric ultrasounds and acetaminophen absorption. Volunteers were NPO overnight. After obtaining a baseline blood sample and gastric ultrasound, volunteers swallowed liquid acetaminophen, 1.5 g in 15 mL, followed by 50 mL or 300 mL of water (in a random order on two different study days). Gastric ultrasounds were performed every 10 min for 1 h, gastric antral cross section area was determined, and $t_{½}$ for gastric emptying was calculated. Blood was obtained every 10 min to 1 h, then every 30 min to 2 h for plasma acetaminophen concentration analysis by HPLC. Areas under the acetaminophen concentration *vs.* time relationships (AUC), peak concentrations (C_{max}), and times to peak (t_{max}) were determined. Control (50 mL) and treatment (300 mL) data were compared by paired t-test. The criterion for rejection of the null hypothesis was $P < 0.05$.

Results: Gastric emptying $t_{½}$ was significantly shorter after 300 mL water compared to 50 mL (24 ± 6 min vs. 34 ± 8 min). There were no differences between 50 and 300 mL in AUC at 60, 90, or 120 min, or in C_{max} (Table). T_{max} was longer for 50 mL.

Conclusion: Healthy, term, non-obese, non-laboring parturients may safely drink clear liquids up until 2 h prior to the induction of anesthesia without risk of delayed gastric emptying or increased gastric volume.

Table. Acetaminophen Gastric Absorption Data (mean ± SD)

Water Ingested	$AUC_{0\text{-}60min}$ µg·min/mL	$AUC_{0\text{-}90min}$ µg·min/mL	$AUC_{0\text{-}120min}$ µg·min/mL	C_{max} µg/mL	t_{max} min
50 mL	1018 ± 397	1529 ± 501	1949 ± 606	33 ± 11	41 ± 19
300 mL	1091 ± 306	1587 ± 424	1988 ± 520	31 ± 13	25 ± 12*

*$P < 0.05$.

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