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Effect of Cimetidine and Ranitidine on Lidocaine Concentrations during Epidural Anesthesia for Cesarean Section

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Aspiration of gastric contents is a leading cause of anesthesia-related maternal mortality during cesarean section.[1] Consequently, premedication to reduce the acidity of gastric contents has become standard practice. The agents most commonly administered are clear oral antacid agents, such as sodium citrate. To reduce both the volume and the hydrogen ion content of gastric fluid, histamine H_2-receptor antagonists (*i.e.*, cimetidine or ranitidine) have been administered prior to anesthesia and proven popular for all types of surgery, including cesarean section.[2–4] However, cimetidine interferes with the cytochrome P-450-mediated metabolism of several drugs, including lidocaine, propranolol, phenytoin, diazepam, theophylline, and warfarin-type anticoagulants.[5,6] Ranitidine has a different chemical structure, and does not appear to influence the metabolism of these drugs as does cimetidine. Accordingly, we compared the effect of cimetidine and ranitidine on maternal venous and umbilical arterial and venous whole blood lidocaine concentrations after administration of 2% lidocaine for lumbar epidural anesthesia for cesarean section.

MATERIALS AND METHODS

With approval from the Committee on Human Research and consent from each patient, we studied 34 healthy nonlaboring patients who required epidural anesthesia for elective cesarean section. Patients with major complications during pregnancy, major organ diseases, pre-eclampsia, or fetal distress were excluded from the study. Indwelling intravenous catheters were inserted in both arms, one for sampling of venous blood and the other for administering drugs and fluids. Patients were randomly assigned to one of three groups for antacid therapy. The control group were given only sodium citrate (n = 12); the ranitidine group received ranitidine, 150 mg po, at least 120 min prior to anesthesia and sodium citrate (n = 11); and the cimetidine group received cimetidine, 300 mg im, at least 60 min prior to anesthesia and sodium citrate (n = 11). Within 15 min of beginning anesthesia, all patients were given 0.3 M sodium citrate, 30 ml po, and an intravenous infusion of at least 1000 ml of a glucose-free, balanced salt solution. An epidural catheter was then inserted *via* the L2-3 or L3-4 interspace and patients were positioned supine with left uterine displacement. Twenty-five milliliters of 2% lidocaine with epinephrine 1:200,000 were injected over a 5-min period (3-ml test dose, 3-min observation, followed by 5-ml q 30 s). Hypotension, defined as a systolic blood pressure of <100 mmHg or a greater than 30% decrease from baseline, was promptly treated with rapid infusion of balanced salt solution, additional uterine displacement, and intravenous ephedrine.

Venous whole blood samples for determination of lidocaine concentrations were obtained from the mother prior to lidocaine administration and 3, 9, 12, 15, 18, 21, 30, 40, 50, and 60 min after the injection was completed. If needed, an additional dose of 12.5 ml of 2% lidocaine with epinephrine 1:200,000 was administered through the epidural catheter 60 min after the initial injection. Sampling intervals were the same after administration of the additional epidural lidocaine dose. Maternal venous whole blood specimens were also obtained at delivery and 75, 90, 105, 120, 135, 150, 165, 180, 210, and 240 min after the final epidural lidocaine dose, when possible. Umbilical venous (UV) and umbilical arterial (UA) whole blood samples were withdrawn from a doubly clamped segment of umbilical cord to determine lidocaine concentrations and perform blood gas analyses. Samples for whole blood lidocaine determinations were frozen until analyzed by a gas-liquid chromatographic technique.[7] This

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TABLE 1. Study Patients' Characteristics

	Control (n = 9)	Ranitidine (n = 8)	Cimetidine (n = 9)
Age (yr)	28.4 ± 4.9	32.8 ± 7.4	26.4 ± 5.2
Height (cm)	156.1 ± 7.1	159.1 ± 6.1	155.3 ± 5.8
Weight (kg)	81.0 ± 12.0	84.1 ± 13.3	73.0 ± 13.4
Body surface area (M^2)	1.81 ± 0.14	1.88 ± 0.17	1.73 ± 0.16
Incidence of hypotension	78%	88%	67%
Time from H_2 antagonist to lidocaine (min)	NA	198.6 ± 57	103.0 ± 32.4*
Duration of anesthetic prior to delivery (min)	36.2 ± 11.5	29.2 ± 9.5	34.0 ± 9.9
Time from H_2 antagonist to delivery (min)	NA	226.9 ± 62.5	137.0 ± 33.9*

Values are expressed as mean ± SD; NA = not applicable.

* $P < 0.05$, ranitidine *vs.* cimetidine, unpaired *t* test.

technique has a relative standard deviation of 10% over the range of 0.5–5.0 μg/ml. The area under the concentration-time curve (AUC) for the first 60 min after lidocaine administration was calculated using the trapezoidal rule.[8]

The condition of the newborn was evaluated using Apgar scores at 1 and 5 min, analyses of umbilical cord blood gases, Neurologic and Adaptive Capacity Scores (NACS)[9] at 0.25, 2, and 24 h after birth, and time-to-sustained respirations. The examiner of the newborn was unaware of the antacid therapy administered to the mother prior to surgery.

Data were analyzed using one-way analysis of variance and the Student-Newman-Keuls' test for patient height, weight body surface area, whole blood lidocaine concentrations, AUC, duration of anesthesia before delivery, and umbilical cord blood gas values at delivery. The times from H_2 antagonist administration to lidocaine administration and delivery were compared using Student's unpaired *t* test. Values are presented as mean ± SD. Apgar scores and NACS were compared using Fisher's exact test. A P value of <0.05 was considered significant.

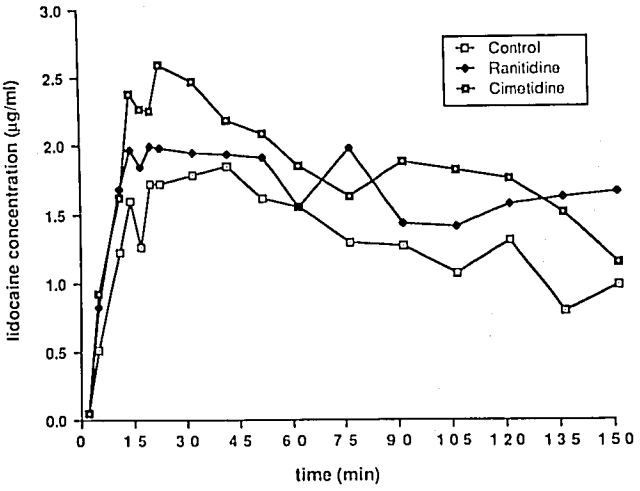

FIG. 1. Effect of no H_2-receptor antagonist (control), cimetidine 300 mg im, and ranitidine 150 mg po, on whole blood lidocaine concentration during epidural anesthesia with 25 ml of 2% lidocaine with 1: 200,000 epinephrine. For clarity, standard deviation bars have been deleted.

RESULTS

Data were collected from 34 patients. However, three patients in the control group and one patient in the cimetidine group were excluded from analysis because lidocaine (3.30–45.4 μg/ml) was present in the specimen obtained prior to epidural lidocaine administration. This occurred when skin was infiltrated with lidocaine prior to inserting the indwelling intravenous catheter used for sampling; 2-chloroprocaine was used for skin infiltration in all other patients. Three patients in the ranitidine group also were excluded from analysis. One required additional lidocaine before delivery of the infant, one received ranitidine only 89 min before administration of lidocaine, and the third weighed 138 kg. One additional patient given cimetidine was excluded because she received cimetidine only 43 min before injection of lidocaine. For data analysis, there were nine patients in the control group, eight in the ranitidine group, and nine in the cimetidine group. The groups did not differ significantly in age, height, weight, body surface area, or incidence of hypotension (table 1). At 20 min, all patients obtained a sensory block to pinprick at a level of T4 or higher.

All patients were delivered less than 60 min after lidocaine administration, with no significant difference among groups in mean time from administration to delivery (table 1). Maternal lidocaine concentrations after epidural administration of 25 ml of 2% lidocaine with epinephrine 1:200,000 did not differ significantly among groups (fig. 1) at any time, nor did the ratios of UV/maternal venous and UA/UV lidocaine concentrations at delivery (table 2). There was no significant difference among groups in AUC for the first 60 min after lidocaine administration (control 88.7 ± 22 μg/ml, ranitidine 101.9 ± 44.6 μg/ml, cimetidine 118.2 ± 50.1 μg/ml). Peak

TABLE 2. Lidocaine Concentrations and Ratios at Delivery after Epidural Administration of 25 ml of 2% Lidocaine with Epinephrine (1:200,000)

	Control (n = 9)	Ranitidine (n = 8)	Cimetidine (n = 9)
MV* (μg/ml)	1.85 ± 0.36	1.84 ± 0.67	2.10 ± 0.97
UV (μg/ml)	1.44 ± 0.53	1.26 ± 0.55	1.54 ± 0.58
UA (μg/ml)	0.86 ± 0.39	0.91 ± 0.43†	0.93 ± 0.49‡
UV/MV	0.81 ± 0.30	0.68 ± 0.12	0.78 ± 0.19
UA/UV	0.59 ± 0.13	0.67 ± 0.17†	0.72 ± 0.26‡

Values are expressed as mean + SD. There were no significant differences among groups.
* MV = maternal venous.
† n = 7.
‡ n = 6.

TABLE 3. Peak Lidocaine Concentrations after Epidural Administration of 25 ml of 2% Lidocaine with Epinephrine (1:200,000)

	Control (n = 9)	Ranitidine (n = 8)	Cimetidine (n = 9)
Mean maternal peak lidocaine concentration (μg/ml)	2.18 ± 0.64	2.35 ± 0.97	2.91 ± 1.23
Highest lidocaine concentration (μg/ml)	3.26	3.91	4.80

Values are expressed as mean ± SD; there were no significant differences among groups.

lidocaine concentrations after 25 ml of 2% lidocaine with epinephrine also did not differ significantly among groups (table 3). The highest maternal lidocaine concentration was 4.80 μg/ml. This occurred 21 min after the administration of lidocaine in a patient given cimetidine.

Thirty-one percent of patients required an additional dose of 12.5 ml of 2% lidocaine with epinephrine 1:200,000 60 min after the initial 25-ml dose; there was no difference in incidence among groups. The highest lidocaine concentration measured after administration of the additional 12.5 ml of lidocaine was 2.98 μg/ml in the control group, 1.88 μg/ml in the ranitidine group, and 4.31 μg/ml in the cimetidine group.

The condition of newborns did not differ among groups when comparing the time to sustained respirations, Apgar scores, NACS, or umbilical cord blood gas values (table 4).

DISCUSSION

Maternal lidocaine concentrations tended to be higher, though not significantly so, in patients given cimetidine, as opposed to ranitidine or no H_2-receptor antagonist. One patient given cimetidine had lidocaine concentrations approaching toxic values, but did not complain of any symptoms of toxicity such as dizziness or tinnitus. In studies demonstrating cimetidine-related increases in lidocaine concentrations, patients were given more than one dose of cimetidine.[6,10] However, our patients received only one dose of cimetidine or ranitidine. It has been suggested that inhibition of drug metabolism by cimetidine may be dose-related[11] and may depend on the duration of pretreatment with cimetidine.[12] Patients given cimetidine, 300 mg q 6 h, during lidocaine iv infusion experienced a 56% increase in serum lidocaine concentrations 6 h after the first cimetidine dose and an additional 43% increase after the second dose.[10] Had we administered cimetidine or ranitidine the night before and the morning of surgery, we might have seen a greater effect of cimetidine on lidocaine concentrations.

Based on the comparative pharmacodynamics and pharmacokinetics of cimetidine and ranitidine,[13] we administered cimetidine, 300 mg im, or ranitidine, 150 mg po, at least 1 h or 2 h, respectively, before anesthesia. These doses have been shown to increase the *p*H of gastric contents to >2.5 at the time of induction of anesthesia, particularly when given in combination with sodium citrate.[2,4,14,15] The bioavailability of ranitidine, 150 mg po, is 50% with a mean peak plasma concentration of 360–650 ng/ml occurring ~90 min after administration.[13] The ED_{50} for ranitidine (plasma concentration producing 50% inhibition of acid) is 73–165 ng/ml and plasma ranitidine concentrations following a dose of 150 mg po maintain or exceed this level for ~8 h. The ED_{50} for cimetidine is 0.5 μg/ml and plasma cimetidine concen-

TABLE 4. Condition of the Neonate

	Control	Ranitidine	Cimetidine
TSR < 90 s	9/9	8/8	9/9
Apgar scores of 8–10*			
1 min	7/9	8/8	7/9
5 min	9/9	8/8	9/9
NACS of 35–40*			
15 min	4/9	6/8	5/8
2 h	4/7	6/8	5/7
24 h	7/8	7/8	6/8
UV blood gas	(n = 9)	(n = 8)	(n = 9)
*p*H (units)	7.35 ± 0.05	7.37 ± 0.03	7.34 ± 0.03
P_{CO_2} (mmHg)	43.5 ± 5.4	40.8 ± 5.7	41.3 ± 4.6
P_{O_2} (mmHg)	26.2 ± 5.5	29.9 ± 4.4	31.6 ± 5.8
BE (mEq/l)	−1.5 ± 1.7	−1.1 ± 1.6	−3.0 ± 2.4
UA blood gas	(n = 8)	(n = 7)	(n = 7)
*p*H (units)	7.28 ± 0.05	7.31 ± 0.06	7.25 ± 0.05
P_{CO_2} (mmHg)	55.9 ± 7.1	52.3 ± 6.9	54.4 ± 5.3
P_{O_2} (mmHg)	18.8 ± 3.4	19.3 ± 4.3	14.0 ± 2.6
BE (mEq/l)	−1.2 ± 1.6	−0.5 ± 2.2	−3.4 ± 4.3

There were no significant differences among groups. Umbilical cord blood-gas values are expressed as mean ± SD.
* Apgar scores of 8–10 and Neurologic and Adaptive Capacity Scores (NACS) of 35–40 denote a vigorous baby.

trations following a dose of 300 mg immediately achieve or exceed this level for ~4 h.[16] Therefore, based on the ED_{50}, bioavailability, and plasma concentrations after administration, we administered comparable doses of cimetidine and ranitidine. Parenteral ranitidine was not available when this study was initiated.

Several studies have reported impairment of lidocaine elimination by cimetidine, but not by ranitidine. Both agents interact with cytochrome P-450 as ligands, but the affinity for cimetidine is approximately tenfold greater than that for ranitidine.[17] In a placebo-controlled study of healthy subjects, 300 mg of cimetidine administered orally four times over 24 h decreased systemic clearance of lidocaine (1 mg/kg iv) by 25% and produced significantly higher peak concentrations of lidocaine.[6] Ranitidine, 150 mg po, administered orally twice over 24 h did not alter the elimination half-life, systemic clearance, or distribution of lidocaine.[18] Cimetidine also decreases the systemic clearance of antipyrine (a marker of hepatic enzyme activity) and theophylline, while ranitidine does not.[19]

Lidocaine is highly cleared by the liver.[20] Consequently, any decrease in blood flow to the liver is likely to decrease the clearance of lidocaine. Feely *et al.*[21] studied the effect of hypotension on hepatic blood flow and lidocaine clearance in patients with idiopathic autonomic dysfunction. After an iv dose of lidocaine (61 ± 4 mg), hypotension (25% decrease in mean arterial pressure maintained for 6 h by tilting the patient) resulted in significant reductions in hepatic blood flow (30%), lidocaine clearance (24%), and volume of distribution at steady state (39%).[21] Peak lidocaine concentrations were 80 ± 45% higher during hypotension. While there was a high incidence of hypotension in our patients, prompt treatment made it unlikely that hypotension significantly affected the lidocaine concentrations. Mather *et al.*,[22] who administered epidural lidocaine to two subjects and measured cardiovascular effects and lidocaine concentrations, allowed their subjects to become severely hypotensive (systolic blood pressure 60 mmHg) and bradycardic before treatment with ephedrine. When blood pressure was lowest, lidocaine concentration changed only slightly, possibly due to decreased uptake of lidocaine from the site of injection at the same time hepatic blood flow was decreased.

When cimetidine is used as premedication prior to epidural anesthesia with lidocaine, lidocaine concentrations may reach toxic levels, particularly in the absence of epinephrine in the lidocaine solution and the presence of repetitive dosing or preeclampsia. In nonpregnant subjects, the mean peak concentration of lidocaine following epidural administration of 20 ml of 2% lidocaine with epinephrine (1:200,000) is approximately 3 μg/ml.[23] If epinephrine is not added, the peak concentration is approximately 5 μg/ml. Plasma accumulation of lidocaine has been demonstrated following epidural administration of 16–21 ml of 2% lidocaine (without epinephrine) followed by 60% of the initial dose q 35–55 min.[24] The peak concentration of lidocaine increased from 2.30 μg/ml following the first dose to 3.34 μg/ml after the second dose, and 4.11 μg/ml after the third. Total body clearance of lidocaine is prolonged in preeclampsia.[25] This may be due to the vasospasm of the splanchnic bed, liver dysfunction, and increased alpha-1 acid glycoprotein levels associated with preeclampsia.

In summary, there were no statistically significant differences in whole blood lidocaine concentrations in patients given ranitidine or cimetidine *versus* no H_2-receptor antagonist. However, lidocaine concentrations tended to be higher in patients given cimetidine, one of whom had lidocaine concentrations approaching toxic values. The inability to detect an effect of cimetidine or ranitidine on lidocaine concentrations may be due to the small sample size as well as the small treatment effect with respect to the population standard deviation (Type II error). Although we do not routinely administer H_2-receptor antagonists to patients undergoing cesarean section with epidural lidocaine anesthesia, we recommend the use of ranitidine rather than cimetidine when an H_2-receptor antagonist is selected.

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References

1. Kaunitz AM, Hughes JM, Grimes DA, Smith JC, Rochat RW, Kafrissen ME: Causes of maternal mortality in the United States. Obstet Gynecol 65:605–612, 1985
2. McCaughey W, Howe JP, Moore J, Dundee JW: Cimetidine in elective caesarean section. Effect on gastric acidity. Anaesthesia 36:167–172, 1981
3. Hodgkinson R, Glassenberg R, Joyce TH III, Coombs DW, Ostheimer GW, Gibbs CP: Comparison of cimetidine (Tagamet™) with antacid for safety and effectiveness in reducing gastric acidity before elective cesarean section. ANESTHESIOLOGY 59: 86–90, 1983
4. Johnston JR, Moore J, McCaughey W, Dundee JW, Howard PJ, Toner W, McClean E: Use of cimetidine as an oral antacid in obstetric anesthesia. Anesth Analg 62:720–726, 1983
5. Bauman JH, Kimelblatt BJ: Cimetidine as an inhibitor of drug metabolism: Therapeutic implications and review of the literature. Drug Intell Clin Pharm 16:380–386, 1982
6. Feely J, Wilkinson GR, McAllister CB: Wood AJJ: Increased toxicity and reduced clearance of lidocaine by cimetidine. Ann Intern Med 96:592–594, 1982
7. Asling JH, Shnider SM, Wilkinson GR, Way EL: Gas chromatographic determination of mepivacaine in capillary blood. ANESTHESIOLOGY 31:458–461, 1969
8. Gibaldi M, Perrier D: Appendix D Estimation of areas, Pharmacokinetics. New York, Marcel Dekker, 1982, pp 445–449
9. Amiel-Tison C, Barrier G, Shnider SM, Levinson G, Hughes SC,

Stefani SJ: A new neurologic and adaptive capacity scoring system for evaluating obstetric medications in full-term newborns. ANESTHESIOLOGY 56:340–350, 1982
10. Knapp AB, Maguire W, Keren G, Karmen A, Levitt B, Miura DS, Somberg JC: The cimetidine-lidocaine interaction. Ann Intern Med 98:174–177, 1983
11. Feely J, Wilkinson GR, Wood AJJ: Reduction of liver blood flow and propranolol metabolism by cimetidine. N Engl J Med 304: 692–695, 1981
12. Jensen JC, Gugler R: Cimetidine interaction with liver microsomes *in vitro* and *in vivo*. Involvement of an activated complex with cytochrome P-450. Biochem Pharmacol 34:2141–2146, 1985
13. Richards DA: Comparative pharmacodynamics and pharmacokinetics of cimetidine and ranitidine. J Clin Gastroenterol 5(Suppl 1):81–90, 1983
14. McAuley DM, Moore J, McCaughey W, Donnelly BD, Dundee JW: Ranitidine as an antacid before elective caesarean section. Anaesthesia 38:108–114, 1983
15. Morison DH, Dunn GL, Fargas-Babjak AM, Moudgil GC, Smedstad K, Woo J: A double-blind comparison of cimetidine and ranitidine as prophylaxis against gastric aspiration syndrome. Anesth Analg 61:988–992, 1982
16. Walkenstein SS, Dubb JW, Randolph WC, Westlake WJ, Stote RM, Intoccia AP: Bioavailability of cimetidine in man. Gastroenterology 74:360–365, 1978
17. Rendic S, Ruf HH, Weber P, Kajfez: Cimetidine and ranitidine: Their interaction with human and pig liver microsomes and with purified cytochrome P-450. Eur J Drug Metab Pharmacokinet 9:195–200, 1984
18. Feely J, Guy E: Lack of effect of ranitidine on the disposition of lignocaine. Br J Clin Pharmacol 15:378–379, 1983
19. Breen KJ, Bury R, Desmond PV, Mashford ML, Morphett B, Westwood B, Shaw RG: Effects of cimetidine and ranitidine on hepatic drug metabolism. Clin Pharmacol Ther 31:297–300, 1982
20. Nies AS, Shand DG, Wilkinson GR: Altered hepatic blood flow and drug disposition. Clin Pharmacokinet 1:135–155, 1976
21. Feely J, Wade D, McAllister CB, Wilkinson GR, Robertson D: Effect of hypotension on liver blood flow and lidocaine disposition. N Engl J Med 307:866–869, 1982
22. Mather LE, Tucker GT, Murphy TM, Stanton-Hicks M d'A, Bonica JJ: Hemodynamic drug interaction: Peridural lidocaine and intravenous ephedrine. Acta Anaesthesiol Scand 20:207–210, 1976
23. Scott DB, Jebson JR, Braid DP, Ortengren B, Frisch P: Factors affecting plasma levels of lignocaine and prilocaine. Br J Anaesth 44:1040–1048, 1972
24. Inoue R, Suganuma T, Echizen H, Ishizaki T, Kushida K, Tomono Y: Plasma concentrations of lidocaine and its principal metabolites during intermittent epidural anesthesia. ANESTHESIOLOGY 63:304–310, 1985
25. Ramanathan J, Bottorff M, Jeter JN, Khalil M, Sibai BM: The pharmacokinetics and maternal and neonatal effects of epidural lidocaine in preeclampsia. Anesth Analg 65:120–126, 1986

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High Thoracic Epidural Sufentanil for Post-thoracotomy Pain: Influence of Epinephrine as an Adjuvant—A Double Blind Study

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A previous study in which epinephrine was added to morphine administered epidurally resulted in analgesia of a more intense nature, more rapid in onset, and of longer duration than when plain morphine solutions were used.[1] It was also noted that the adverse effects of pruritus, nausea, vomiting, and difficulty of micturation were intensified by the addition of epinephrine. Furthermore, respiratory depression as reflected by diminished responsiveness to inhaled CO_2 between 6 and 16 h after morphine injection was greater following morphine-epinephrine solution. However, these studies were performed in human volunteers using a poorly lipid soluble drug. Results from three recent studies suggest that epinephrine added to highly lipid soluble opioids for lumbar epidural analgesia not only reduces their unwanted side effects, but also confers a longer duration and intensity of analgesia.[2–4] Sufentanil has a lipid solubility 1000 times greater than morphine, is even more selective than fentanyl for the μ-receptor,[5] and is clinically more potent[6] than fentanyl or morphine. In addition, it has not yet been associated with delayed respiratory depression after epidural administration.[7,8] A previous study in which plain sufentanil was administered for thoracic epidural analgesia revealed a peak plasma level of sufentanil within 10 min of the initial and subsequent injections.[9] Respiratory rate,

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