

Title: LACK OF EFFECT OF CIMETIDINE AND RANITIDINE ON LIDOCAINE DISPOSITION IN THE PARTURIENT

Authors: Flynn, R.J., F.F.A.R.C.S., Moore, J., Ph.D.

Affiliation: Department of Anaesthetics, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL

Introduction. Acid aspiration is a common cause of maternal morbidity and mortality and the routine use of H₂ receptor antagonists has been recommended as prophylaxis¹. Reports that cimetidine decreases the hepatic clearance of lidocaine and increases the risk of toxicity² cause particular concern especially as lidocaine is often used in large doses to provide satisfactory analgesia for epidural Cesarean section. Hodgkinson³ has stated that until further studies are carried out the administration of H₂ receptor blockers prior to epidural analgesia is inadvisable since toxic levels may occur. In view of this an investigation into the effect of oral cimetidine and ranitidine on lidocaine disposition seemed indicated.

Methods. Only healthy women at term who selected epidural analgesia for elective Cesarean section were included. They had no relevant past history and were not on any medication. Patient and Research Ethical Committee approval were obtained.

Patients were randomly allocated to receive either cimetidine 400 mg, ranitidine 150 mg or no pretreatment. The H₂ blockers were given 90-120 min prior to instituting the epidural block. Lidocaine 2% with freshly added epinephrine 1:200,000 was the local anesthetic used. All patients received 20 ml given over 5 min. This provided satisfactory analgesia in all cases to the level of T6. Any patients requiring supplementary doses were eliminated from the study. Statistical analysis was by independent 't' test and analysis of variance (ANOVA). Venous blood was collected from an antecubital vein in the non-infused arm via a 16G cannula. Samples were obtained before any local anesthetic was given (control) and then at 5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80, 90 min and at 2, 3, 4 and 5 h after local anesthetic administration. A sample was taken from the umbilical vein at delivery. The samples were centrifuged and the supernatant plasma stored at -20°C until analysis. Lidocaine estimations were by HPLC with mepivacaine as the internal standard.

Results. Seventeen patients were included in the study. Seven patients received ranitidine, five received cimetidine and five had no pretreatment with H₂ blockers. All groups were comparable in terms of age, weight and parity. Figure 1 shows that pretreatment with oral cimetidine or ranitidine has no effect on plasma lidocaine levels when compared to the control

group. In addition there was no significant difference between groups in umbilical vein levels, UV/MV ratios or Apgar scores.

Discussion. The anesthesiologist has to be aware that lidocaine elimination is dependent on hepatic blood flow. Controversy exists in the literature regarding reports that H₂ receptor antagonists decrease hepatic blood flow because the methods of estimation used have a significant margin of error.

The results of this study suggest that the use of oral cimetidine or ranitidine prior to epidural Cesarean section does not increase the risk of local anesthetic toxicity and is therefore quite acceptable for use in clinical practice.

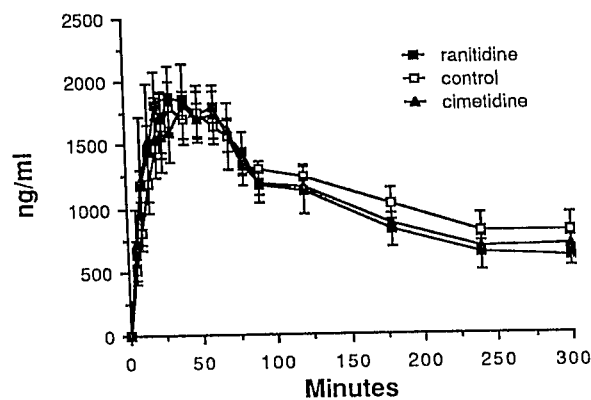


Figure 1. Mean plasma lidocaine levels (+ SE)

References.

- 1 Moir DD, Thorburn J: Obstetric Anaesthesia and Analgesia, 3rd edition. London, Bailliere Tindall, p. 171, 1986.
- 2 Feely J, Wilkinson GR, McAllister CB, Wood AJJ: Increased toxicity and reduced clearance of lidocaine by cimetidine. *Ann Int Med* 96: 592, 1982.
- 3 Hodgkinson R: Potential interactions between cimetidine and amide local anaesthetics in obstetrics. *Anesthesiology* 60: 508, 1984.