TITLE: METABOLIC AND EICOSANOID PROFILES IN HEPATIC ISCHEMIA-ANOXIC AND REPERFUSION INJURY.

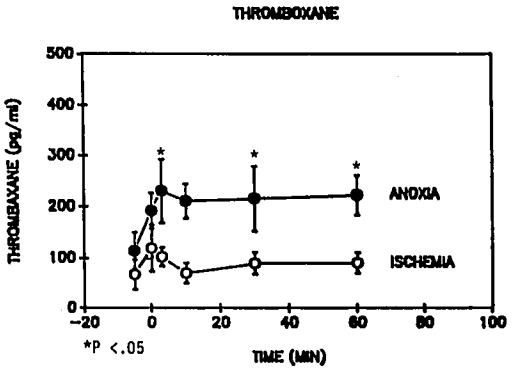
AUTHORS: E. Pretto, M.D., and R. Evans, Ph.D.

AFFILIATION: International Resuscitation Research Center and Department of Anesthesiology/CCM, University of Pittsburgh, 3434 Fifth Avenue, Pittsburgh, PA 15260

In this study, our aim was to determine whether hepatic ischemia or anoxia and reperfusion injury of similar duration would result in the same degree of hepatic failure as measured by metabolic indices and eicosanoid levels.

35 male Sprague-Dawley rats (300-350g) were used as organ donors. Livers were studied in vitro using an isolated perfused rat liver preparation, maintained at 38°C in a temperature controlled chamber oxygenated with a Hamilton lung and perfused with a modified Krebs-Henseleit buffer and 2% Bovine albumin. Two groups of livers were studied, Group 1 (n=10) and Group 2 (n=15) experiments consisted of livers exposed to 90 min of global ischemia or global anoxia at 38°C, respectively, followed by 60 min of reperfusion. LFTs, ABGs, electrolytes, TxB_2, 6 Keto-prostaglandin F ($PGF_1\alpha$), and leukotriene C4 (LTC_4) were measured, the latter by radioimmunoassay, at Baseline (-5,0) and 3,10, 30 and 60 min during reperfusion only. Results indicate that ischemia or anoxia-induced hepatic failure result in a similar degree of hepatic metabolic dysfunction. However, TxB_2 levels during reperfusion differed significantly between Groups 1 (anoxia) and 2 (ischemia) (Fig.). We conclude that there may be subtle differences in TxB_2 levels between hepatic ischemia and anoxia which will require further elucidation using more sophisticated biochemical analyses.

FIGURE



A739

TITLE: ONDANSETRON, A SELECTIVE SEROTONIN TYPE 3 ($5\text{-}HT_3$) ANTAGONIST, REDUCES NAUSEA AND VOMITING IN FEMALES FOLLOWING MAJOR GYNECOLOGIC SURGERY

AUTHORS: R.McKenzie, M.D., S. Odell, S.N.A. T. Rudy, Ph.D., A.F. Joslyn, Ph.D.

AFFILIATION: Anes. Dept., Magee-Womens Hospital, University of Pittsburgh, Pittsburgh, PA 15213 and Glaxo Inc., Research Triangle Park, NC 27709

Nausea and vomiting (N/V) continue to be a major source of postoperative morbidity following major gynecologic surgery. Ondansetron (OND; GR38032F, Glaxo) a selective $5\text{-}HT_3$ antagonist has previously been shown to effectively control chemotherapy-induced N/V. This study was designed to evaluate the prophylactic antiemetic efficacy and safety of OND in females undergoing major gynecologic surgery. IRB approved informed consents were obtained from 56 healthy (ASA I-II) subjects scheduled for elective inpatient gynecologic surgery. Unpremedicated patients were randomized to receive, in a double-blind manner, either OND 8 mg IV or placebo (PLA) infused over 2-5 min prior to general anesthesia induction, with a second dose infused 8 hr after the first dose. General anesthesia consisted of induction with thiopental followed by sufentanil, $N_2O:O_2$ (70/30%) isoflurane, and muscle relaxant as indicated.

Postoperative pain relief was provided by patient controlled analgesia using meperidine or morphine. Hematologic, hepatic and renal parameters were evaluated prior to and 24 hr post study drug infusion. Droperidol 0.625 mg IV was given as a rescue antiemetic when indicated. There were no significant differences in demographic data or type and amount of postoperative narcotic given for pain relief between the two groups. Antiemetic efficacy is defined as complete response - no emetic episodes and no droperidol administration for 24 hr after anesthesia. The complete response rate for OND (16/30; 53%) was significantly ($p=0.047$) greater than PLA (7/26; 27%) for the 24 hr post-anesthesia period. Treatments were compared using the Mantel-Haenszel test.

Nausea was assessed on a numerical scale of 0 (no nausea) to 10 (worst nausea) pretreatment, on awakening, and at 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, and 24 hour. OND was significantly ($P < 0.05$) better than PLA at preventing nausea at 3, 4, 5, 6, and 8 hr post study drug infusion. Treatments were compared using the Wilcoxon rank sum test.

No significant differences were found between groups with respect to study drug related adverse events. There were no study drug related changes in hematologic, hepatic or renal parameters 24 hr post treatment.

OND is a safe and effective antiemetic for the prophylactic control of N/V following major gynecologic surgery.