Title: GASTRIC FLUID pH AND VOLUME AFTER PREOPERATIVE ACID ASPIRATION PROPHYLAXIS WITH 15(R)-15 METHYL PGE_2 (ARBACET)

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Introduction. Prostaglandin E_2 (PGE_2) is a prostanoid produced by the gastric mucosa. Both PGE_2 and its dimethyl analogues decrease gastric acid secretion while conveying "cytoprotection" against mucosal injury by noxious stimuli.[1,2] The purpose of this research is to determine if the novel PGE_2 analogue, 15(R)-15 methyl prostaglandin E_2 (ARBACET - Upjohn Company, Kalamazoo, MI) is an effective preoperative oral prophylactic agent to decrease perioperative risk of acid induced pulmonary aspiration injury. This double blind randomized trial was approved by Dartmouth's IRB; all patients gave written and oral informed consent.

Methods. Forty predominately ASA I-II elective surgical patients, ages 19 to 78, were randomized into two groups of 20. Pregnant females and unsterilized women of child bearing age were excluded. Group I (GI) patients received gelatin capsules containing 50 mcg Arbacet in triacetin vehicle p.o. HS the evening before surgery. Group II (GII) patients (placebo group) were given an identical appearing gelatin capsule containing equal amount of triacetin, same HS and on call schedule; all patients received IM 0.1 mg/kg morphine and 1 mg/kg IM pentobarbital on call. After endotracheal intubation, a #18 oral gastric tube was positioned by insufflation and auscultation. The stomach was aspirated dry and acidity and volume were measured. Serial gastric fluid volumes were aspirated and pooled every 30 minutes til extubation. Maintenance anesthesia was balanced nitrous oxide-fentanyl-relaxant technique or isoflurane nitrous oxide-O_2 inhalation per attending anesthesiologist. Gastric fluid quantity was ascertained by visual inspection (1 ml increment graduated container). Gastric acidity was ascertained using a Corning 112 digital pH meter; titratable acidity was obtained by titration to pH 7.0. Difference between groups was analyzed nonparametrically (Wilcoxan Rank Sum Test) ($p \leq 0.05$ considered significant).

Results. Mean age of GI was 44.6 ± 12.6 and 46.4 ± 18.1 in GII. Ten patients (6 in GI, 4 in GII) were eliminated from pH analysis (reasons included failure to receive both capsules-2, gastric aspirate QNS-5, surgery postponement-3. Seven patients (4 GI, 3 GII) were eliminated from volume analysis for similar reasons. Sex distribution in Groups I and II was 13 male, three female and 6 male, 11 female respectively. Mean duration (min.) from ingestion of on call preop dose to induction was 94.3 ± 34.3 GI and 87.3 ± 35.3 GII. Mean gastric volumes and pH at induction are shown in Table I. Four GI and 10 GII patients had a gastric pH < 2.5. Only three GII patients had pH > 3.0 at induction. One Arbacet treated patient experienced bronchospasm at induction (history of significant asthma). Subendocardial myocardial infarction occurred in one Arbacet treated patient during a stressful induction. Neither event was felt related to Arbacet. Incidence of perioperative nausea or vomiting was similar in GI and GII.

Discussion. Arbacet produces a significant increase in gastric pH at induction of anesthesia compared to placebo. Since aspiration of gastric fluid with pH < 2.5 is associated with increased mortality, by extrapolation preoperative Arbacet would reduce the risk attributed to gastric acid injury if aspiration occurs at induction.[3] Though Arbacet failed to show a significant reduction in gastric volume at induction, volume decreased significantly compared to placebo over the subsequent 90 minutes. Thus, risk of pulmonary injury by aspiration occurring at extubation might decrease up to 90 minutes post induction. In contrast to cimetidine, Arbacet is not known to inhibit hepatic mixed function oxidase.[4] Further, such dimethyl PGE_2 analogues convey cytoprotection against stress ulceration irrespective of any effects on gastric acid secretion.[2] In view of these considerations, further study is planned of Arbacet's dose response and its comparative safety and efficacy versus other prophylactic agents.

References.

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3. Coombs DW: Aspiration pneumonia prophylaxis. Anesth Analg 62:1055, 1983.
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TABLE I - GASTRIC pH AT INDUCTION OF ANESTHESIA

GROUP	N	MEAN ± S.D.	MEDIAN	PROB
I-Arbacet	14	4.49 ± 2.29	4.00	p=0.02
II-Placebo	16	2.81 ± 1.82	2.01	

GASTRIC VOLUME AT INDUCTION OF ANESTHESIA

I-Arbacet	16	10.1 ± 10.8	6.5	p=0.21(NS)
II-Placebo	17	22.1 ± 31.2	14.0	