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Title: HEPATORENAL INDICES AMONG GENERAL ANESTHETICS IN OBESITY

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Concern has been expressed regarding the use of highly lipid soluble inhalational anesthetic agents in morbidly obese patients.[1,2] Increased biotransformation of these agents is known to occur, with possible resultant viscerotoxicity.[3] To address this concern, a randomized prospective study was designed to compare indices of hepatorenal function pre- and postoperatively in morbidly obese patients receiving general anesthesia with nitrous oxide/pancuronium combined with either fentanyl, enflurane, or halothane. Ionic fluoride was measured as a marker of possible hepatorenal toxicity in those patients receiving either halothane or enflurane.

Methods: Following approval by the Human Subjects Committee, consenting morbidly obese patients scheduled for elective gastric stapling were studied. All patients were in good general health preoperatively. Maintenance anesthesia was with N_2O/O_2 (60:40) plus: 1) fentanyl-thiopental (n = 20), 2) enflurane (n = 24), or 3) halothane (n = 23). End-tidal anesthetic (enflurane, halothane) concentrations were assayed by gas chromatography to calculate anesthetic dose (MAC hrs). Blood samples were collected preoperatively and at various intervals intra- and postoperatively for 24 hours for ionic fluoride determination by an ion specific electrode. Both pre- and postoperatively, determinations were made of creatinine clearance, creatinine, BUN, SGOT, SGPT. Urine output has monitored in all patients for 24 hours postoperatively with an indwelling catheter. Analysis of variance and the Bonferroni t-test were used to compare observations among the groups. Student t-test for paired data was used to make preoperative, postoperative comparisons. Significance was defined at $p < 0.05$.

Results: Characteristics of the 67 patients (female/male = 55/12) studied were as follows (mean ± SE): age, 38 ± 1 yr; weight, 126 ± 2.7 kg; height 166 ± 1 cm. Dosages of volatile anesthetic in MAC hours ± SE were as follows: enflurane = 1.38 ± 0.09 and halothane = 1.8 ± 0.13 respectively. Among the randomly assigned groups (fentanyl, enflurane, halothane), hepatorenal indices demonstrated no statistical differences pre- or 24 hours postoperatively. However, pre- to postoperative comparisons were significantly different for each index of hepatorenal function. BUN and serum creatinine were decreased at 24 hours in all anesthetic groups ($p < .001$). In contrast, at 24 hours postop there was in increase in SGOT, SGPT, and creatinine clearance ($p < .05$) in all three groups. Twenty-four hour urine output was the same in all groups. There was a statistically significant increase in serum ionic fluoride in both the enflurane group (mean peak, ± SE: 24.9 ± 1.5 μM, $p < 0.01$) and halothane group (mean peak, ± SE: 3.2 ± 0.5 μM, $p < 0.01$). Anesthesia time was longer in the N_2O narcotic group ($p < .04$) and MAC hours greater in the halothane patients ($p < .01$).

Discussion/Conclusions: Despite the fact that both enflurane and halothane demonstrated significant metabolism to ionic fluoride, no indices of hepatorenal dysfunction were found in morbidly obese subjects. The operative procedure itself produced a significant change in hepatorenal indices when preop to postop comparisons were determined for each anesthetic group. Three key conclusions from this randomized prospective clinical study are:

1. Considering early (24 hours) indices of hepatorenal function in morbidly obese patients, there is little to commend one anesthetic agent over another.
2. Impairment of creatinine clearance could not be demonstrated in obese patients at mean peak ionic ionic fluoride levels of 24.9 ± 1.5 μM.
3. Statistically significant metabolism of halothane (following 1.8 MAC hours) to ionic fluoride was demonstrated in morbidly obese patients.

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