TITLE: EPIDURAL MORPHINE REDUCES THE MAC OF HALOTHANE IN HUMANS.
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INTRODUCTION: Systemic, and intrathecal[1], administration of opioids such as morphine (M) reduces halothane (H) MAC (HMAC) in humans. Epidural (epi) M is routinely used in the control of postoperative (postop) pain and the maximum pain relief is reported to appear 60-90 min after its administration[2]. The purpose of this study was to examine the effect of epi M on HMAC in humans in a blinded randomized fashion.
METHODS: After institutional approval and informed consent, 16 patients (pts) undergoing upper abdominal surgery were enrolled and randomized into 1 of 2 groups (n=8 each). Pts receiving medication known to affect MAC were excluded from the study. An epi catheter was placed in the L3-L4 or L2-L3 space prior to induction of anesthesia in all unpremedicated pts and its correct position verified by the a 3 ml saline-epinephrine 1:200000 test dose administered through the catheter. Five min later, M sulphate 4 mg in 10 ml or saline 10 ml (Control) was injected blindly through the catheter. MAC was determined as previously described ("gross purposeful" movement to skin incision). Anesthesia was induced with H, O2 and N2O. Following induction, succinylcholine 1 mg/kg was injected, N2O discontinued, the pt's trachea sprayed with 4 ml 4% lidocaine and intubated, and a temperature (T) probe and esophageal stethoscope inserted. After intubation, the H concentration (conc) was adjusted (Capnomac, Datex) to maintain a preselected end-tidal conc corrected to account for pt age related differences in MAC, for a minimum of 20 min before skin incision (the result of each trial dictated the conc used on the subsequent trial). Blood pressure (BP) was measured noninvasively, and ventilation adjusted to maintain an end-tidal PCO2 between 30 and 38 mmHg. A nerve-stimulator was used to ensure that no residual effect of succinylcholine persisted at the time of skin incision. The presence or absence of "gross purposeful" movement was determined by an observor blinded to the nature of the epidurally injected drug. End-tidal CO2, BP, heart rate (HR) and T were recorded prior to skin incision. After skin incision anesthetic management was left to the discretion of the anesthesiologist. At the end of the surgical procedure, all pts spent the next 24h in the recovery room where epi M was used for analgesia. Statistical analysis included logistic regression and t-test with $p<0.05$ considered significant.
RESULTS: Compared to epi saline, epi M reduced HMAC by 30% when injected 91±31min before skin incision (0.74% vs 0.52% respectively, $p<0.05$; Figure). There were no significant differences between the groups in the pts' age, weight, time from injection to incision, or preincision T, end-tidal PCO2, systolic BP, or HR.
DISCUSSION: This study demonstrated that epi M decreases the anesthetic requirements of halothane in our patient population when the pharmacodynamic properties (time between injection and stimulus) are respected. This decrease in HMAC is similar to that obtained by an intrathecal administration of M (0.75mg)[1]. Epidural morphine may prove beneficial perioperatively in patients who cannot tolerate the deleterious effects of volatile anesthetics.
REFERENCES: 1. Anesthesiology 69:310-312, 1988
2. Anesthesiology 67:877-888, 1987

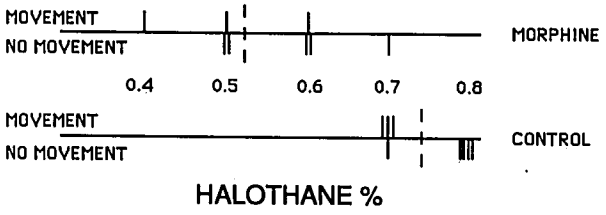

Fig: Individual pt responses to skin incision. The x axis represents alveolar halothane conc at the time of skin insicion. An upward deflection = movement, a downward deflection = no movement to the stimulus. Dashed line indicates calculated MAC values.

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TITLE: MAC-AWAKE OF ISOFLURANE EVALUATED BY SLOW AND FAST ALVEOLAR WASH-OUT
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MAC-awake is defined as the alveolar concentration of an anesthetic gas,which allows eye opening to a verbal command for the first time during awakening from anesthesia (Ref.1).It has been hypothesized that the MAC-awake value of different inhalation anesthetics uniformly corresponded to approximately 0.5 MAC,if slow alveolar wash-out was applied,allowing for brain and alveolar gas equilibration (Ref.1).MAC-awake of isoflurane was only measured recently by fast alveolar wash-out,and was found to be far lower (0.15 MAC; Ref. 2) as compared to halothane (0.33 MAC; Ref. 1).This difference may be due to the lower lipid solubility of isoflurane compared to halothane,which leads to a greater decrease in MAC-awake values when measured by fast alveolar wash-out (Ref.1).The present study was conducted in order to clarify the discrepancy between measured and predicted (Ref.1) MAC-awake values of isoflurane, by comparing slow and fast alveolar wash-out.

Sixteen ASA I patients ,scheduled for elective septoplasties, were examined after informed consent and approval by the local institutional research committee had been obtained.No premedication was given.Anesthesia was induced by propofol (2 mg/kg i.v.) and maintained with isoflurane (1.1-1.3 Vol %) in air/oxygen by normoventilation (PaCO2 4.7-5.1 kPa). Prior to intubation, vecuronium bromide (0.1 mg/kg i.v.) was given and topical anesthesia of larynx and upper trachea performed (lidocaine 4%,3ml).In-and endexpiratory concentrations of isoflurane ,CO2 and O2 were continuously measured (Capnomac,Datex).After termination of surgery,all patients received regularly (every 20 sec) a standardized verbal command by ear phones, to open their eyes .Normoventilation with a fresh gas flow of 10 l/min was maintained throughout the awakening period.In group I (slow wash-out,n=8),the inspiratory isoflurane concentration was decreased in 15 min steps of 0.2 vol % to achieve brain-alveolar equilibration,whereas in group II (fast wash-out, n=8),isoflurane administration was immediately stopped at the end of surgery, and the system flushed with pure oxygen.The endexpiratory isoflurane concentration on first eye opening was recorded in both groups,and devided by the age adjusted MAC value (Ref.3).

The two groups did not differ with regard to age,weight,body temperature, duration of operation and hemodynamic variables.The MAC-awake value in group I (0.31± 0.01 Vol %,mean ±SE) was significantly higher than in group II (0.23 ± 0.2 Vol %).These values corresponded to 0.25 ± 0.01 and 0.19 ± 0.01 MAC,respectively.The ratio between slow and fast wash-out MAC-awake values was 1.3.

Present data confirm the importance of brain and alveolar equilibration to identify the true MAC-awake value.There was only a slight difference in the MAC-awake value obtained by fast alveolar wash-out in the present (0.19 MAC) versus a previous study (0.15 MAC) (Ref. 2),which may be explained by the use of a longer lasting induction agent (thiopental) and hyperventilation in the latter study (Ref. 2).The MAC-awake value obtained by slow alveolar wash-out was markedly lower than hypothesized from data obtained with other inhalation agents (Ref.1).The ratio of MAC-awake by slow versus fast wash-out was lower for isoflurane (1.3) than observed for halothane (1.7; Ref.1); though,based on lipid solubility,this ratio should have been higher for isoflurane (Ref.1). These data ,therefore, do not support the idea of an uniform ratio of MAC-awake to MAC values for different inhalation anesthetics (Ref.1),and indicate that other factors than lipid solubility are important in brain-alveolar gas equilibration.
References: 1) Anesthesiology,33:5-9,1970
2) Anesth.Analg. 67:27-30,1988
3) Anesthesiology,42:197-200,1975