abstracts

Methoxyflurane Anesthesia in Pediatric Patients: Evaluation of Anesthetic Metabolism and Renal Function.

"Serum ionic fluoride concentrations during and following low-dose methoxyflurane anesthesia and elective operation were measured in 13 pediatric patients. Possible explanations for lower serum ionic fluoride concentrations in pediatric patients compared with adults include (1) slower metabolism of methoxyflurane; (2) increased renal clearance of ionic fluoride from the blood; (3) greater storage of ionic fluoride in bone; (4) more rapid methoxyflurane elimination in the postoperative period.

"Dose-related polyuric renal dysfunction may follow methoxyflurane anesthesia. The amount of ionic fluoride produced depends on the amount of methoxyflurane metabolized and the levels of serum ionic fluoride determine the extent of renal impairment. A knowledge of the changes in serum ionic fluoride levels after methoxyflurane anesthesia may be of predictive value in determining the potential for renal dysfunction. For example, low-dose methoxyflurane anesthesia administered to nonobese patients resulted in peak measured serum ionic fluoride concentrations of 43.9 ± 5.7 µmol/1 (mean ± SE) 24 hours after anesthesia. This ionic fluoride concentration was well below the 90-120 µmol/1 levels present when polyuric renal dysfunction occurred after methoxyflurane anesthesia.

"Serum ionic fluoride data following methoxyflurane administered to pediatric patients are not available. This study reports serum ionic fluoride concentrations and renal function during and following low-dose methoxyflurane anesthesia administered to pediatric patients.

"Thirteen patients undergoing elective noncardiac operations were studied. Premedication was with morphine and atropine intramuscularly 60 minutes preoperatively. Anesthetic induction was with thiamylal followed by succinylcholine and tracheal intubation. Anesthetic maintenance was with nitrous oxide and methoxyflurane in oxygen. Total flows were 5 l/min in all patients. Methoxyflurane was vaporized from a Copper Kettle and the delivered concentrations adjusted to the least amount necessary to maintain systolic blood pressure near the awake preoperative level. After 3 hours methoxyflurane was discontinued and any additional necessary anesthesia provided with nitrous oxide and fentanyl. Ventilation was controlled with a volume ventilator. Competitive neuromuscular blockers were administered when necessary for skeletal muscle paralysis.

"Serum ionic fluoride concentrations increased significantly after 3 hours of methoxyflurane-nitrous oxide anesthesia. Blood urea nitrogen, serum creatinine, and osmolality did not change from control levels during the first 48 postoperative hours. Peak measured serum ionic fluoride concentrations occurred 24 hours after discontinuing methoxyflurane in both adult and pediatric patients. In contrast, serum ionic fluoride levels were significantly less in pediatric patients during and after anesthesia the measured peak being about half that in adults.

"Since serum ionic fluoride parallels renal dysfunction after methoxyflurane anesthesia, the low measured peak serum ionic fluoride in children may imply
greater safety for methoxyflurane in pediatric patients. ... Possible reasons for lower serum ionic fluoride concentrations in children compared with adults include: (1) slower rates of methoxyflurane metabolism; (2) increased renal clearance of ionic fluoride from the blood; (3) greater storage of ionic fluoride in bone; (4) more rapid methoxyflurane elimination in the postoperative period....

As with adults, there was marked variability in the extents of methoxyflurane metabolism in the children as reflected by serum ionic fluoride concentrations. ... Renal clearance of fluoride would influence serum ionic fluoride concentrations. Evidence in man suggests that the kidney efficiently and rapidly eliminates fluoride by glomerular filtration. ... Serum uric acid increased transiently after methoxyflurane but never exceeded normal levels. No evidence of renal dysfunction was suggested by blood urea nitrogen or serum creatinine or osmolality measurements....

"Greater skeletal deposition of fluoride could account for lower serum ionic fluoride levels in pediatric patients compared with adults."

**Effects of Morphine—Nitrous Oxide Anesthesia on Cerebral Autoregulation.**

Jobes, David R.; Kennell, Eric; Bitner, Richard; Swenson, Eldon; and Wollman, Harry: Anesthesiology 42:30-34 (Jan.) 1975.

"We know the effects of many anesthetics on human cerebral blood flow (CBF) and are aware of some effects on cerebral autoregulation. The effects of morphine sulfate-nitrous oxide anesthesia on autoregulation are not known. This knowledge is important, since large doses of morphine plus nitrous oxide anesthesia are widely used for cardiopulmonary bypass and other procedures during which large variations of arterial pressure may occur. This study measures the effects of morphine-nitrous oxide on human cerebral autoregulation....

"Eight fully informed, healthy, male volunteers were accepted for the study after history, physical and laboratory examinations were performed. On the day of the study, peripheral venous, central venous, and radial artery catheters were inserted and electrocardiogram leads attached while the subject was awake. Preanesthetic medication was atropine sulfate, 0.4 mg, administered intravenously 5 minutes before induction. Nitrous oxide-oxygen (70:30 percent) was administered, along with d-tubocurarine, 0.7 mg/kg. The trachea was intubated and ventilation controlled with a Bird ventilator set to deliver 125 ml/kg/min through a nonrebreathing circuit.... Morphine was given intravenously at approximately 10 mg/min to a total dose of 2 mg/kg.

"Each subject was studied after morphine at his awake level of mean arterial blood pressure (MABP). The MABP was then raised to 120 torr and lowered to 60 torr in a randomly assigned balanced order and CBF measured at each level. Last, in five subjects, CBF was measured again at the awake level of MABP.... Our data show no statistically significant change in CBF over the range of MABP studied....

"It is known that nitrous oxide alone or in combination with morphine does not affect CBF or cerebral autoregulation. Halothane, on the other hand, increases CBF and probably disrupts cerebral autoregulation.... Morphine and/or nitrous oxide may be unique, in that they
can afford the patient a stable CBF with an intact autoregulatory mechanism to deal with wide swings in blood pressure. One must keep in mind, however, that patients with pre-existing neurologic disease such as intracerebral hemorrhage or infarction may have altered cerebral autoregulation mechanisms and respond differently.

Clinical Studies of Induction Agents XLIII: Recovery From Althesin — A Comparative Study with Thiopentone and Methohexitone


"Hans Selye (1941) observed during his early investigations that, following the administration of suitable doses of active steroids . . . anaesthesia was produced from which animals recovered without ill effects. However . . . it was not until 1955 that a suitable i.v. steroid anaesthetic, in the form of hydroxydione, was available for use in man. One of the advantages claimed for this form of anaesthesia was a rapid, uncomplicated recovery with minimum postanaesthetic depression . . .

"The advent of Althesin, a new steroid i.v. anaesthesia agent, the clinical features of which have been widely investigated and reported . . . has prompted a comparison with the standard barbiturate anaesthetic agents thiopentone and methohexitone . . .

"The techniques employed to evaluate recovery are numerous and vary greatly in their degree of sophistica-
tion . . .

"The evaluation of recovery in this study was in two phases: firstly, a preliminary investigation of Althesin, in the form of a dose-duration study, was performed to obtain some impressions of the characteristics of recovery following Althesin-induced anaesthesia. 310 unselected patients, male and female, undergoing minor surgery were given different doses of Althesin. Neither pre-
medication nor i.v. atropine was given before the administration of Althesin . . .

"A second group of patients underwent a detailed recovery and follow-up assessment . . . 150 co-operative and reasonably intelligent, fit female patients undergoing minor gynaecological surgery of short duration received various doses of Althesin, methohexitone or thiopentone. Intravenous Atropine 0.6 mg was administered to each patient as standard premedication . . .

"During the preliminary investigation certain critical end-points were determined and these were noted accurately during the recovery phase from the different anaesthetic agents. The times of all end-points were measured from the end of injection. The recovery end-points measured in each patient were as follows:

(i) the return of the eyelash reflex;

(ii) the time to opening of eyes . . .

(iii) the patient's first verbal response;

(iv) neglecting involuntary movements, the time when the patient was first capable of making a purposeful limb movement in response to a com-
mand;

(v) the rapidity of the patient's orientation in person, time and place;

(vi) the time for the patient to sit up in bed unaided;

(vii) as a result of the previous findings, when the observer thought that the patient was "fit" to stand at the side of the bed, she was tested for Rombergism and the time noted when it became absent.

"When the patient could sit up unaided she was asked to attempt the peg-board performance test. This was repeated until each subject regained her preoperative control time. This end-point was described as the "time to full re-
cover". The patient's appetite was assessed 1 hr after waking and the inci-
cence of emetic sequelae was noted . . .

"The patient's own assessment of her recovery was determined by asking
her what she felt like doing 30, 60, and 120 min after wakening. In this way it was possible to discover whether the subject overestimated her degree of recovery.

“In a review comparing the newer i.v. barbiturates with thiopentone, methohexitone alone appeared to offer any advance. However, this short-acting barbiturate was not free from certain disadvantages itself, and it was suggested that any further progress in i.v. anaesthesia would come from the non-barbiturate drugs.

“Althesin, a new steroid anaesthetic agent, like propanidid is rapidly metabolized and excreted rather than being redistributed in body tissues as are the barbiturates.

“Published opinions on the speed of recovery following Althesin are widely divergent. This investigation confirmed the low incidence of emetic sequelae following Althesin anaesthesia enabling 48% of patients to retain a “good” appetite 1 hr after waking. Nausea and vomiting were much less common than after thiopentone.

“In conclusion, using the detailed method described for investigating the recovery period, it has been possible to compare the postanaesthetic phase of the steroid anaesthetic agent, Althesin, with methohexitone and thiopentone. The method itself was not intended to determine a definite end-point consistent with “street-fitness”. However, it has been possible to establish the fact that Althesin is a suitable anaesthetic agent for outpatient practice. Those patients to whom Althesin has been administered should be retained in a recovery ward, like those receiving propanidid or methohexitone, for 2 hr after surgery.

“From a medicolegal view, it is doubtful if any patient should be allowed home unaccompanied following treatment involving an anaesthetic agent, regardless of how brief the duration of action of the drug administered.”

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