

Title : ANESTHETIC DOSE THAT BLOCKS ADRENERGIC RESPONSE TO INCISION

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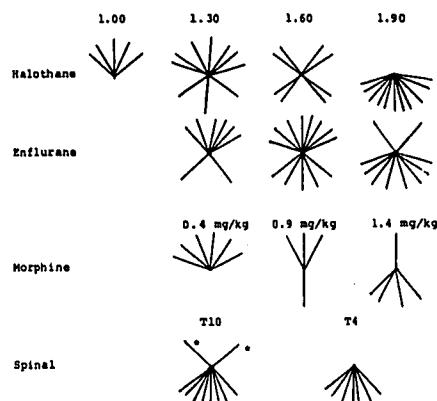
The cardiovascular response to surgery may be an important determinant of patient morbidity. For example, tachycardia and hypertension may compromise myocardial oxygenation in the presence of coronary artery occlusive disease. By blocking the neuroendocrine response to stress, anesthesia may protect against this and similar potentially deleterious effects of surgery. To assess the protective action of different anesthetics and anesthetic doses, we studied the plasma norepinephrine, pupillary dilatation, muscle movement, and cardiovascular responses to skin incision with several anesthetic techniques.

Methods. Informed consent based on a protocol approved by the UCSF Committee on Human Research was obtained in all cases. 97 unpremedicated ASA I or II adults were randomly assigned to one of the following anesthetic groups: 60% nitrous oxide and oxygen with an age adjusted halothane MAC value (halothane plus nitrous oxide) of 1.0, 1.3, 1.6 or 1.9; or 60% nitrous oxide and oxygen with an age adjusted enflurane MAC value of 1.3, 1.6, or 1.9; or 60% nitrous oxide with 0.4, 0.9 or 1.4 mg/kg morphine sulfate; or spinal anesthesia to either T4 or T10 level. Anesthesia was induced via face mask or with 1 mg/kg thiopental at least 25 minutes prior to the first sample in the volatile agent group, or with 3/4 of the morphine dose followed by 4 mg/kg thiopental with 3 mg curare followed by 1.5 mg/kg succinylcholine in the morphine group, or with lumbar puncture in the spinal group. The tracheas of all patients given general anesthesia were intubated after a 2 mg/kg lidocaine spray, and ventilation subsequently was controlled. End tidal anesthetic concentrations were held constant thereafter until the study was completed. Fifteen minutes after intubation, 18 minutes after intubation (= 1 minute prior to skin incision), and again 3 and 10 minutes after skin incision, 10 ml of blood were drawn from an indwelling venous line. Oscillatory blood pressure, heart rate, and pupillary diameter were recorded. Blood acid-base status and plasma catecholamine concentrations (radioenzymatic analysis) were determined. A pH not between 7.33 and 7.45, a P_vCO_2 not between 30 and 44, a P_vO_2 below 40 on any sample excluded the patient from the study. A 10 percent or greater difference in any pair of preincision measurements excluded the patient from the study. An increase of 10 percent or more from mean baseline values to mean postincision values in heart rate,

blood pressure, pupillary diameter, or norepinephrine level constituted an all or none positive response. Statistical analysis was performed by the Waud technique.

Results. The ED₅₀ for blocking adrenergic response to skin incision was 1.47±.07 MAC for halothane, 1.63±0.10 MAC for enflurane and 1.10±.17 mg/kg for morphine. No patient with adequate spinal anesthesia had a norepinephrine increase with skin incision. Individual responses are given in the table. Pupillary and norepinephrine responses were directly correlated. 2 of 5 patients in the 1.0 MAC halothane group and 12 of 14 patients given morphine moved with incision.

Discussion. Enflurane, halothane, morphine and spinal anesthesia all can prevent the neuroendocrine response to skin incision at clinically attainable doses. Thus, comparisons of neuroendocrine stress during surgery require quantitation of anesthetic dose. Using the all or none response, pupillary dilatation was as good as plasma norepinephrine in assessing stress. Cardiovascular and movement responses to incision were not as good; all patients save one who received 1.4 mg/kg morphine moved after incision while only one had a 10 percent or greater increase in plasma norepinephrine level. If adverse effects of surgery (metabolic, hepatic, renal, myocardial, etc.) are related to the neuroendocrine stress surgical (and anesthetic) manipulations induce, then the hypothesis, "the less anesthetic the better" may be wrong. Perhaps morbidity is decreased by using enough anesthetic to block myocardial or splanchnic sympathetic stimulation.



Note: Each line indicates an individual patient; an upward line indicating increased norepinephrine levels and a downward line indicating unchanged or decreased levels.

*Patients who reported a sensation of pain on incision, and who required additional anesthesia to allow surgery to proceed.