Title: ENDOTOXEMIA CAUSES A NALOXONE-REVERSIBLE DECREASE IN THE ALVEOLAR CONCENTRATION OF ISOFLURANE REQUIRED FOR ANESTHESIA

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Introduction. The death rate with septic shock is high (approximately 50%) even after aggressive medical management (1). Although septic shock is not uncommon in patients suffering trauma, burns, gastrointestinal injury, etc., little is known about the relations between this type of shock and anesthetic requirements. One aim in the present experiments was to determine if endotoxin administration to rabbits alters the minimal alveolar concentration (MAC) of isoflurane needed to prevent withdrawal from a noxious stimulus. Secretion of endogenous opioid peptides has been linked to septic shock (2). The opioid antagonist naloxone may (3) or may not (4) lessen some physiological parameters of septic shock in man. When the MAC was found to be reduced by endotoxin, the effects of naloxone pretreatment on this change was investigated.

Methods. After approval by the internal Animal Research Board, a 2.5 French endotracheal tube was placed via tracheostomy and sutured in place in New Zealand white rabbits (3-5 kg) anesthetized with ketamine (100 mg/kg). The animals were ventilated with isoflurane and oxygen and the end-tidal concentration of isoflurane was determined with an Engstrom analyzer or a mass spectrometer connected to a rebreathing circuit. The MAC of isoflurane required to prevent withdrawal responses to application of a hemostat to the ear 50% of the time was determined every 10 minutes using standard procedures. Endotoxemia was induced by i.v. infusion of lipopolysaccharide obtained from Salmonella minnesota (4 μg/kg). Body temperature was controlled via a rectal thermistor probe and an automatic heating/cooling blanket. Arterial blood pressure was monitored and decreases were counteracted by infusions of D5RL. 2-3 hours after endotoxin injection, when MAC was stable, 0.4 mg of naloxone was given i.m.

Results. Before endotoxin was given the average MAC for 9 rabbits was 1.61%, a level that was stable for over 4 hours in 1 animal that did not receive endotoxin. Endotoxin injection caused a major decrease (43%, 16-73% range) in the average MAC value. The nadir of the decrease in MAC occurred approximately 1.5 hours (range 40-170) minutes) after endotoxin injection in the 8 rabbits tested. In 3 of these animals the changes in MAC were biphasic - 2 decreases separated by a spontaneous increase that peaked approximately 2.5 hours after endotoxin. In these latter animals the second nadir occurred approximately 30 minutes after the rise. In all 6 rabbits tested with naloxone, there was a rapid increase in MAC, to within an average of 19% of the pre-endotoxin levels.

Discussion. The results indicate that endotoxemia has a substantial effect on the MAC of isoflurane and that this influence can be inhibited by naloxone. The basis of the decrease in MAC caused by endotoxin is unknown. Although early conceptions of the role of endogenous opioid peptides in pain control and anesthetic action are now believed to be oversimplified, there is evidence that endotoxin increases the concentration of endorphins in the circulation (2). It is well known that such endogenous opioids can act centrally to promote analgesia. Therefore it may be that endotoxin decreases MAC via release of endogenous peptides. The results with naloxone, a classic antagonist at opioid receptors, support this idea. Whatever the eventual interpretation of these results, in terms of opioid peptides or other factors, they open interesting questions about anesthetic requirements and altered mechanisms of anesthesia in septic patients.

References.

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