Title : EEG AROUSAL BY DOXAPRAM, NALOXONE, AND PHYSOSTIGMINE

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Introduction. Induction of general anesthesia produces an abrupt change in EEG pattern from posterior to anterior amplitude dominance. This EEG pattern shift is coincident with loss of awareness in humans[1] and with a marked decrease in $CMRO_2$ in dogs.[2] It occurs at sub-MAC levels of inhalational anesthesia. This study was designed to determine whether doxapram, naloxone, and physostigmine produce EEG evidence of arousal by causing an anterior to posterior change in EEG amplitude dominance.

Methods. Eight fasted mongrel dogs were anesthetized with halothane. Succinylcholine (3mg/kg IV) facilitated endotracheal intubation and mechanical ventilation with halothane and oxygen. Arterial pressure, 4 lead bipolar EEG (anterior, anterolateral, posterolateral, and posterior), temperature, EKG, and end-tidal halothane concentrations were continuously recorded with a Grass 78-D polygraph. Pressures were measured via a Statham P23AC transducer. End-tidal halothane concentrations were measured with an infrared analyzer (Beckman). Arterial blood gases were repeatedly sampled. $PaCO_2$ was maintained at 40±2.5 torr and PaO_2 at greater than 200 torr. Nasopharyngeal temperature was maintained at 37.0±0.5°C. After induction, EEG shift points were determined for each dog as previously described. Halothane concentration was then increased to 20% above the shift point and doxapram (1mg/kg IV) administered. The duration of drug induced EEG arousal was noted. After doxapram effects were dissipated and 1 hour for reequilbration allowed, 4 dogs were given naloxone (0.006mgm/kg IV) and 4 physostigmine (0.03mg/kg IV). EEG patterns and shift point changes were again followed.

Results. Induction of anesthesia with halothane produced an abrupt EEG change from posterior to anterior amplitude dominance in all dogs. This shift occurred at end-tidal halothane concentrations of 0.61±0.03 percent. Doxapram administration abruptly shifted the EEG from an asleep pattern to posterior amplitude dominance (awake) within 20±3.5 sec. (Figure 1) The EEG shift coincided with increases in arterial pressure (27±7 percent) and heart rate (18±9 percent). The duration of EEG arousal was 50±7 min while cardiovascular changes were of shorter duration (8±3 min). Placebo injections of saline in 8 dogs produced no EEG or cardiovascular effects.

After recovery from doxapram administration and 1 additional hour of halothane anesthesia at 20% above the shift point, 4 dogs were given naloxone and 4 were given physostigmine. Both drugs shifted the EEG to a posterior dominant awake pattern; naloxone in 80±8 sec and physostigmine in 225-37 sec. Times for return of an anterior dominant asleep pattern were 18±7 min for naloxone and 38±9 min for physostigmine.

Discussion. Doxapram, naloxone, and physostigmine are frequently given at the end of an anesthetic to arouse patients. However, many other maneuvers are usually being performed at the same time that these drugs are being administered. These variables were eliminated by maintaining constant end-tidal halothane concentration, by controlling ventilation, and by minimizing external stimulation. If the observed EEG shift from posterior amplitude dominance does indeed indicate loss of awareness, then doxapram, naloxone, and physostigmine, reverse this effect of halothane. At clinically-used concentrations they shift EEG in the unstimulated dog receiving sub-MAC concentrations of halothane from anterior amplitude dominance to posterior amplitude dominance.

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References.

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