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Title : CLONIDINE POTENTIATION OF HALOTHANE ANESTHESIA AND REVERSAL

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Introduction. The antihypertensive agent clonidine is a potent central -adrenergic receptor agonist. Sedation and sleep are the most noticeable side effects in animals and man[1]. Acute clonidine abolishes paradoxical sleep and increases total sleep fraction in the EEG of rats and increases the arousal threshold of reticular stimulation in the rabbit EEG. Antinocioceptive and antianxiety effects have been reported[2]. Tolerance to the above side effects is developed rapidly. Chronically administered clonidine potentiates halothane anesthesia by only 15%[3]. Since tolerance is achieved to clonidine-induced sedation and sleep, it was felt important to examine the effects of acute clonidine on halothane anesthesia.

Methods. Eleven mongrel dogs were induced with halothane by mask. They were intubated under deep halothane anesthesia, ventilated with oxygen to maintain normal pCO_2, and instrumented. ECG, heart rate and mean arterial pressure were recorded on a direct writing polygraph. Blood temperature was maintained within 0.5°C at about 39°C. Halothane concentrations were monitored by infrared spectroscopy and measured by gas chromatography. Standard methods were used to determine minimun alveolar concentration of halothane anesthesia (MAC) necessary to prevent movement in response to painful stimulus[4]. MAC was determined for a 2 hour (hrs) control period. Single dose clonidine 20 ug/kg was given i.v. MAC was determined up to 8 hrs post clonidine. For the reversal studies three dogs were stabilized at a halothane level 0.1% above control MAC about 3.5 hrs post clonidine and given tolazoline 5 mg/kg, an α-adrenergic antagonist.

Results. Control halothane MAC was 0.784±.04% (X±SE). This dose of clonidine in an unanesthetised dog was found to cause sedation, however, the animals could be aroused. Clonidine 20 ug/kg i.v. produced a marked potentiation in halothane anesthesia as determined by MAC. One hour post clonidine MAC was reduced 34±5% from control ($p<.05$). Peak effect occured at about 2.5 hrs where MAC was reduced 48.6 ±3% from control ($p<.01$). These values returned to control over 6-8 hrs post clonidine. Tolazoline 5 mg/kg resulted in an immediate reversal of the clonidine induced halothane anesthesia potentiation (see figure 1).

Discussion. It is well known that sedative and antinociceptive agents facilitate anesthesia. This may be said to be the basis for the combination of halothane and clonidine. Furthermore, it is known that agents which increase the synaptic availability of catecholamines such as dextroamphetamines and monoamine oxidase inhibitors increase anesthetic requirement. Conversely, depletion of central catecholamines stores by adminstration of reserpine or alpha-methyl tyrosine(AMPT) has been reported to potentiate anesthetic action. The suggested conflict, ie. clonidine an adrenergic agonist potentiating anesthesia, might be explained by clonidines selectively stimulating the "auto-inhibition" receptor believed to be present in the central nervous system. Thus the α-adrenergic agonist clonidine would have the same result as the depleting agent. This high degree of selectivty might also explain the increased effectiveness of clonidine (48% clonidine, 20-30% reserpine and AMPT).

Conclusions. Clonidine appears to be a potent and reversable potentiator of halothane anesthesia. The resulting potentiation is greater than any previously reported for an adrenergic agent.

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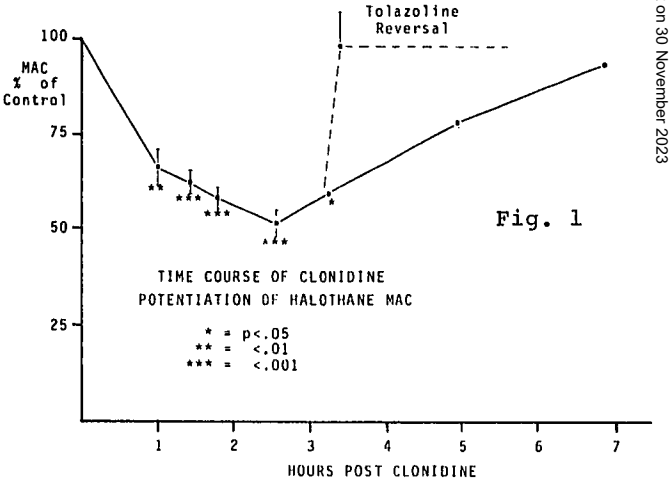

Fig. 1