Title: NALOXONE REVERSES THE POTENTIATION OF INHALATIONAL ANESTHESIA AND HEMODYNAMIC CHANGES INDUCED BY THE ACUTE ADMINISTRATION OF CLONIDINE.

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Introduction. Acutely administered clonidine (CLON), a centrally acting alpha-2 adrenergic agonist, has been shown to reduce halothane requirement by 40-50%[1] and has been used to augment narcotic anesthesia while stabilizing patient hemodynamics during cardiac anesthesia.[2] It has been shown that naloxone (NLX) reverses the antihypertensive action of CLON[3] but not CLON induced analgesia. Also NLX can potentially cause dramatic hemodynamic changes when given to antagonize opiates[4]. Since NLX may be used clinically to reverse narcotic anesthesia in the presence of CLON, interactions of NLX and CLON need study. We determined the effects of NLX on MAC and hemodynamics during CLON potentiation of isoflurane (ISO) anesthesia.

Methods. ISO was administered by mask to unpremedicated mongrel dogs to produce deep anesthesia. Following i.v. succinylcholine (0.5 mg/kg), the dog was intubated and ventilated to normocarbia with 2% ISO in oxygen during the period of instrumentation.

All drugs and fluids were administered through a catheter in the femoral vein. Arterial, central venous, pulmonary arterial, and left ventricular pressures were monitored. Cardiac outputs were determined by thermodilution. Each dog was stabilized for one hour, breathing spontaneously at 1.5% end-tidal ISO concentration. MAC was determined as published.[1]

Two groups of dogs were studied. Four MAC determinations were made sequentially in each dog. In group A, control ISO MAC, CLON MAC following CLON (20 μg/kg), NLX MAC following NLX (25 μg/kg bolus and 25 μg/kg/hr infusion) and finally tolazoline (TOL) MAC after TOL 5 mg/kg were determined. In group B, the sequence was altered. NLX was administered prior to CLON and infused until CLON MAC was determined. Hemodynamic parameters were recorded at each test concentration of ISO. Statistical methods included analysis of variance for repeated measure and Bonferroni modified t-test.

Results. In group A, the acute administration of CLON reduced the ISO anesthetic requirement by 38%. NLX partially reversed ($p<0.01$) this effect to 21%. Heart rate (HR) and cardiac output (CO) were significantly decreased by CLON. NLX reversed the CLON-induced HR change but not the CO. In Group B, NLX alone had no effect on anesthetic requirement, HR or CO. All parameters returned to control levels following the administration of tolazoline.

Discussion. NLX can cause dramatic hemodynamic changes when used to reverse narcotics in patients. This may reflect interactions between the central opiate and adrenergic pathways. Our results demonstrate such an interaction. The CLON induced reductions in ISO MAC and hemodynamic parameters are due in part to a decrease in central adrenergic outflow, an alpha-2 effect. NLX, an opiate antagonist, partially antagonized these effects.

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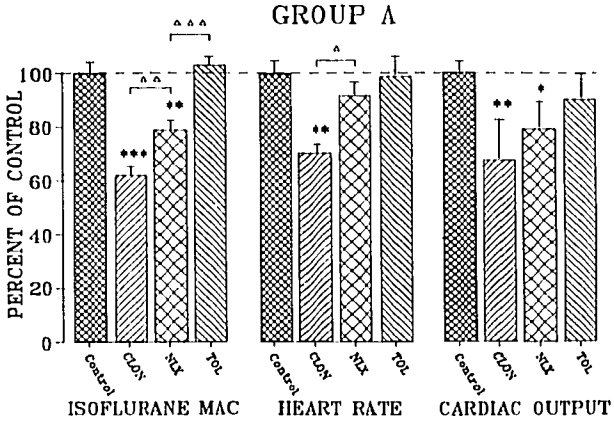


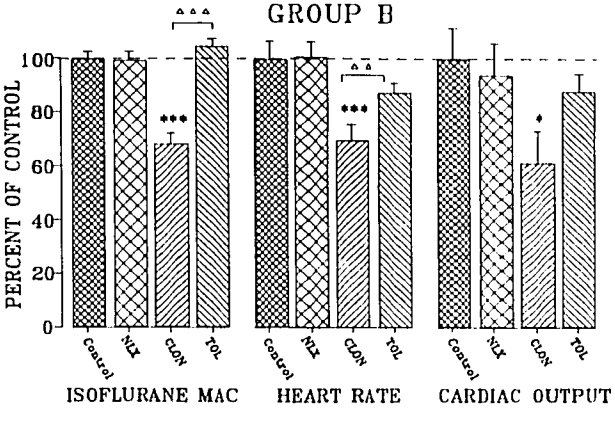


| p | < 0.05 | < 0.01 | < 0.001 |
|---|---|---|---|
| Difference from control | * | ** | *** |
| Difference between values | Δ | ΔΔ | ΔΔΔ |