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Title : Anesthetics Alter the Response of Cerebral Metabolism to Catecholamines

Authors : Alan A. Artru, M.D., Michael Nugent, M.D., and John D. Michenfelder, M.D.

Affiliation: Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota 55901

INTRODUCTION:

In certain clinical situations it may be desirable to use anesthetics which decrease the cerebral metabolic rate for oxygen ($CMRO_2$). Recent evidence suggests, however, that catecholamines may alter the $CMRO_2$ response expected with certain anesthetics. Siesjo and his colleagues reported that in rats, $CMRO_2$ increases during nitrous oxide anesthesia with conditions likely to evoke a stress response (e.g. hypoxia[1] and hypercarbia[2]) and with intravenous infusion of epinephrine (E) or norepinephrine (N)[3]. In previous canine studies from this laboratory it was reported that $CMRO_2$ did not increase with hypercarbia[4] or hypoxia[4] during nitrous oxide anesthesia, but did increase in a single dog with E or N infusion during cyclopropane anesthesia.[5] The present study was undertaken to determine if potentially undesirable increases in $CMRO_2$ with E or N infusion would consistently occur in dogs anesthetized with nitrous oxide, cyclopropane, or other inhalational or intravenous anesthetics (halothane, thiopental, or ketamine).

METHOD:

Eighteen dogs were anesthetized with one of the above agents and $CMRO_2$ was determined during infusion of E or N via a central vein at doses ranging from 0.1 to 25 μg/kg/min. $CMRO_2$ was derived from the product of cerebral blood flow (CBF) (timed collection and electromagnetic flowmeter measurement of cannulated sagittal sinus outflow) and arterial-sagittal sinus blood oxygen content ($C_{(a-v)}O_2$) difference. At each dose plasma E and N levels were determined fluorometrically by the trihydroxy indole method. For each dose of E or N, the desired dose was reached by gradually increasing the infusion rate over several minutes thereby preventing excessive hypertension and consequent increased permeability of the BBB. At the end of the study, Evans blue dye was circulated systemically for 30 min and the integrity of the BBB was determined by sectioning the excised brain and inspecting it for evidence of parenchymal staining with the dye.

RESULTS:

Intravenous infusion of each dose of either E or N during cyclopropane was associated with a 17-23% increase in $CMRO_2$ which returned to control levels within 20 min after discontinuing E or N. With the other anesthetics no significant increase in $CMRO_2$ occurred during E or N infusion. Cyclopropane produced marked staining of cerebral tissue with Evans blue dye representing a substantial increase in BBB permeability, whereas with the other agents no increased BBB permeability to Evans blue dye was noted. At each dose, plasma E and N levels were not significantly different between any of the anesthetics.

DISCUSSION:

With cyclopropane the increased $CMRO_2$ likely relates to passage of E or N across the BBB. It has been previously reported that when the BBB is circumvented $CMRO_2$ increases in response to N.[6] In the present study, the 17-23% increase in $CMRO_2$ is in excellent agreement with the 21% increase in $CMRO_2$ reported by MacKenzie et al in phencyclidine anesthetized baboons when N was given either as 40 μg/kg directly into the cerebral ventricles or as 50 ng/kg/min into the carotid artery following osmotic disruption of the BBB with hypertonic urea.[6] With halothane, thiopental, nitrous oxide, and ketamine, $CMRO_2$ does not increase during exogenous catecholamine administration provided excessive hypertension is avoided and the permeability of the BBB is not otherwise increased. Thus, during aneshtesia with these agents no deleterious cerebral metabolic effects should occur when endogenous catecholamines are increased or when exogenous catecholamines are administered.

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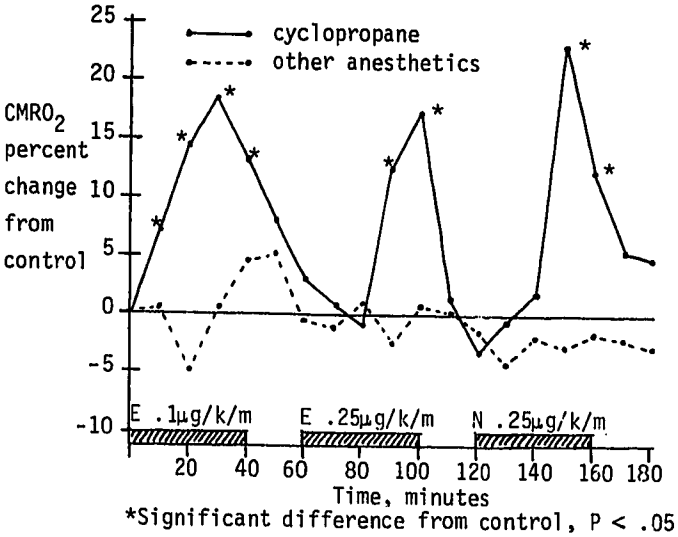

*Significant difference from control, $P < .05$