A620

TITLE: ISOFLURANE PRESERVES BRAIN POTASSIUM HOMEOSTASIS DURING INDUCED HYPOTENSION AND HYPOCAPNIA IN RATS

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Introduction. Combined hypocapnia and induced hypotension as used in neuroanesthesia involves a potential risk of cerebral ischemia. We studied the effect of isoflurane and halothane on cell membrane function, as reflected by interstitial potassium concentration $[K^+]_e$, and local blood flow (l-CBF) in two brain regions.

Methods. Twentyfour male Wistar rats were anesthetized with isoflurane (n = 12) or halothane. A tail arterial catheter was used for monitoring of mean arterial pressure (MAP) and blood sampling. Each experiment included 6 consecutive combinations of MAP and $PaCO_2$: (I) normotension/normocapnia, (II) normotension/$PaCO_2$ = 20 mm Hg, (III) MAP = 50 mm Hg/$PaCO_2$ = 20 mm Hg, (IV) MAP = 30 mm Hg/$PaCO_2$ = 20 mm Hg, (V) normotension/$PaCO_2$ = 20 mm Hg, and (VI) normotension/normocapnia. In each anesthetic group potassium (n = 6) or platinum microelectrodes (n = 6) (hydrogen clearance) were positioned in parietal cortex as well as dorsal hippocampus.

Results. Potassium: In isoflurane-treated animals there was no change of $[K^+]_e$ during the 6 stages of the experiment. In halothane-treated animals a statistically significant increase to 5.6 mmol/l was observed during hypotension/hypocapnia (stage IV). This increase was reversed during the subsequent normotension/hypocapnia (stage V).

Flow: In both groups and in both regions, l-CBF decreased by 30-40% during hypocapnia (II); however, the decrease was only statistically significant in hippocampus using halothane. Changes in MAP during the subsequent stages (III-V) did not appear to influence l-CBF. In the final stage (VI, normotension/normocapnia) marked flow increases (150-200% of the initial values) were observed in both groups.

Discussion. Brain potassium homeostasis appeared to be well preserved during hypocapnia combined with hypotension induced with either isoflurane or halothane. Increased interstitial potassium was observed only in the cortex of halothane-treated animals and only so during severe hypotension/hypocapnia. Our findings support the concept that during extreme conditions, isoflurane may offer some protection of cellular homeostasis, possibly due to its lowering of cellular metabolism.

A621

TITLE: EFFECT OF ALLOPURINOL ON MYOCARDIAL PURINE RELEASE AFTER TOTAL ISCHEMIA AND REPERFUSION IN ISOLATED RAT HEART

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Purine salvage,i.e. reutilization of purine base to synthesize ATP, is believed to be important to protect ischemic myocardium. However,little is known whether allopurinol,an inhibitor of xanthine oxidase,enhances purine salvage. The purpose of this study was to determine how allopurinol changes the excretion pattern of purine compounds (adenosine, inosine, hypoxanthine, xanthine and uric acid) and also the total amount of excretion of these compounds from reperfused myocrdium.

METHOD: With institutional approval, 17 Wistar rats (control group,n=9;allopurinol group,n=8) were sacrificed under ether anesthesia. Hearts were quickly isolated and perfused by Langendorff technique at a perfusion pressure of 50 mmHg with Krebs-Ringer bicarbonate solution (pH 7.4,37°C). Heart rate was maintained at 300 bpm by electric stimulation except for the ischemic period. Left ventricular pressure was monitored by using a water filled latex balloon placed in the left ventricle. After 30 min of equilibration period, hearts were subjected to 7 min of total ischemia and then reperfused for 40 min. In allopurinol group, hearts were perfused with medium containing 10 μM of allopurinol from 10 min prior to ischemia and during reperfusion. Perfusate from pulmonary artery was collected and used to determine the purine compounds. These compounds were determined by HPLC with UV detection method. Data was expressed as mean ±SEM and analyzed by ANOVA with subsequent Newman-Keuls testing. $P<0.05$ was accepted as significant.

RESULTS: Allopurinol significantly reduced uric acid (Fig.1) and xanthine release from reperfused heart. On the contrary, hypoxanthine (Fig.2) and inosine release were significantly increased. Allopurinol did not change adenosine release (Fig.3). No statistical difference was observed in total purine release between control and allopurinol treated hearts (Fig.4). Coronary flow and peak systolic pressure of left ventricle did not change with allopurinol treatment.

DISCUSSION: Previous study [1] suggested that the protective effect of allopurinol on ischemic myocardium was due to the preservation of purine bases. Our data show that allopurinol did not change the total amount of purine excretion. However, purine excretion pattern was alterd by allopurinol. This might indicate that allopurinol plays a role in regulating the intracellular purine metabolic pathway during myocardial ischemia. Further studies as to whether an increased amount of hypoxanthine ,a substrate for phosphoribosylation, can contribute to purine salvage will be required.

REFERENCE:1.J.Clin.Invest. 81:16-20,1988