A608

TITLE: DEXMEDETOMIDINE IMPROVES OUTCOME FROM INCOMPLETE CEREBRAL ISCHEMIA IN THE RAT

AUTHORS: W.E. Hoffman, Ph.D., E. Kochs, M.D., C. Werner, M.D., R.F. Albrecht, M.D.

AFFILIATION: Anes. Dept., University of Illinois-Chicago/Humana Hospital-Michael Reese, Chicago, IL 60616

The purpose of this study was to determine whether dexmedetomidine, an α_2-adrenoreceptor agonist, decreases sympathetic activity and improves outcome from incomplete ischemia in the rat.

Methods: After institutional animal care committee approval, 45 male Sprague Dawley rats (350-450 g) were intubated and anesthetized with isoflurane. Femoral artery and vein catheters were inserted. At the end of surgery the isoflurane was replaced with an iv infusion of 25 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ fentanyl and 70% N_2O ventilation in oxygen. There were four treatment groups. Group 1 (n=15) served as controls. Group 2 (n=10) received an intraperitoneal (ip) injection of 10 µg/kg dexmedetomidine (DEXMED) 15 minutes before the start of ischemia. Group 3 (n=10) received an ip injection of 100 µg/kg dexmedetomidine. Group 4 (n=10) received 100 µg/kg dexmedetomidine and 1 mg/kg atipamezole (ATIPAM), an α_2-adrenoreceptor antagonist. Ischemia was produced by right carotid ligation combined with hemorrhagic hypotension to 35 mmHg for 30 minutes. Arterial PCO_2 and pH were maintained at control levels and skull temperature at 37°C during ischemia. Plasma glucose and catecholamines were measured during ischemia. After ischemia, the rats were recovered and neurologic outcome measured daily for 3 days using an 18 point scale (0 = normal, 18 = stroke related death).

Result: Total catecholamines (epi+norepi) during ischemia were: group 1 = 2.33±.24 ng/ml, group 2 = 0.57±.17 ng/ml (P<0.05), group 3 = 0.21±.07 ng/ml (P<0.05), group 4 = 2.50 ng/ml. Neurologic outcome was improved by dexmedetomidine and this effect was reversed by atipamezole (fig 1). Neurologic outcome was correlated with plasma catecholamines (r=0.67, P<0.05) but not plasma glucose (r=0.02).

Discussion: These results show that dexmedetomidine decreases catecholamines and improves outcome from ischemia by stimulation of α_2-adrenoreceptors.

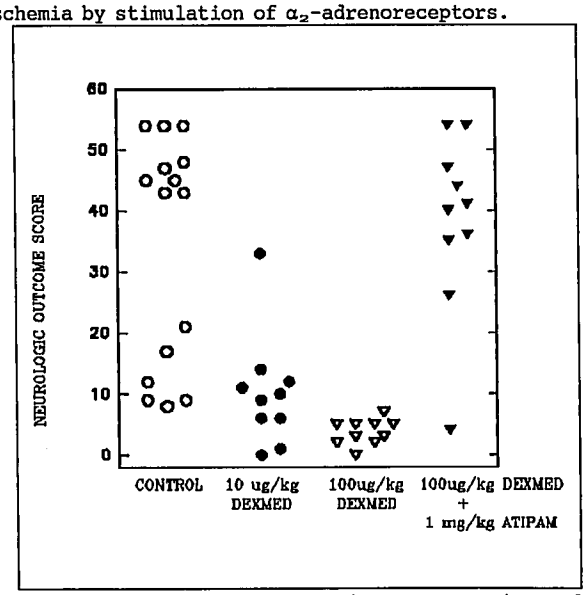

Figure 1. Total score for 3 days. DEXMED (10 and 100 ug/kg) improved outcome vs control (P<0.05)

A609

TITLE: EFFECTS OF MK-801 ON CEREBRAL REGIONAL OXYGEN CONSUMPTION IN FOCAL CEREBRAL ISCHEMIA

AUTHORS: O.Z. Chi, M.D., M. Anwar, M.D., A.K. Sinha, Ph.D., H.R. Weiss, Ph.D.

AFFILIATION: Depts. of Anesthesia, Ped. & Physiol-Biophysics, UMDNJ-Robert Wood Johnson Med. Sch., New Brunswick, NJ 08903

The purpose of this investigation was to test whether MK-801, an N-methyl-D-aspartate (NMDA) receptor antagonist, would improve the balance of O_2 supply and consumption in the focal ischemic area of the brain induced by occlusion of the middle cerebral artery (MCA).

Adult male long Evans rats were anesthetized with pentobarbital (50 mg/kg ip) and the MCA was ligated. Fifteen min after MCA occlusion, 5 mg/kg of MK-801 was administered iv over 2 min to the MK-801 group (N=12) and normal saline was given to the control group (N=12). One hour after MCA occlusion in each group, the regional cerebral blood flow (rCBF) was determined in 6 rats using ^{14}C-iodoantipyrine, while the regional arterial and venous O_2 saturation were determined using a microspectrophotometric technique in the other 6 rats. O_2 extraction and consumption were calculated from rCBF, A-V O_2 saturation difference and Hb.

Blood pressure, heart rate, $PaCO_2$, hemoglobin concentration and temperature were not different between the two groups at the time of determination of CBF and O_2 saturation. rCBF was not affected by MK-801 in all the brain regions studied including the ischemic cortex (Table 1). O_2 extraction was significantly higher in the ischemic cortex than in the contralateral cortex for the control group. However for the MK-801 group, there was no significant difference between these cortices. O_2 extraction in the ischemic cortex of the MK-801 group was significantly lower than that of the control group. The regional O_2 extraction was not significantly different among the various non-ischemic brain regions of both the control and the MK-801 group. The distribution of venous O_2 saturations in the ischemic cortex of the MK-801 group was significantly shifted toward higher O_2 concentrations when compared with that of the same region in the control group. Calculated ischemic regional O_2 consumption was similar to the non-ischemic values in the control group, while the ischemic value was reduced to 61% of the value of the contralateral cortex in the MK-801 group (Figure 1).

Our study demonstrated that MK-801 improved the O_2 supply to consumption ratio by decreasing the O_2 consumption without a significant change in the O_2 supply of the ischemic region. Inhibition of the increase of O_2 extraction in the ischemic cortex of the MK-801 group may be related to the ability of MK-801 to block the NMDA receptors.

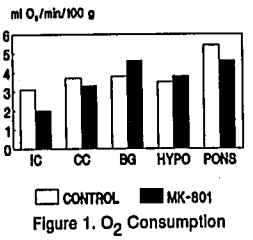

Figure 1. O_2 Consumption

Table 1. Cerebral blood flow, O_2 extraction and O_2 supply to consumption ratio one hour after MCA occlusion (Mean ± SD).

Brain Region	Group	Blood Flow (ml/min/100g)	O_2 Extraction (ml O_2/100 ml blood)	O_2 Supply to Consumption Ratio
Ischemic Cortex (IC)	Control	36±16+	8.8±2.1+	2.1±0.3+
	MK-801	33±10+	6.1±1.0*	2.9±0.7*
Contralateral Cortex (CC)	Control	67±14	5.6±0.3	3.3±0.3
	MK-801	58±11	5.7±1.1	3.2±0.4
Basal Ganglia(BG)	Control	67±15	5.6±0.5	3.2±0.2
	MK-801	70±23	6.5±1.0	2.8±0.6
Hypothalamus (HYPO)	Control	67±14	5.3±0.5	3.4±0.6
	MK-801	66±14	5.8±1.2	3.2±0.6
Pons (PONS)	Control	84±16+	6.5±1.5	2.9±0.7
	MK-801	72±15	6.4±1.3	2.7±0.4

+ Significantly different from the contralateral cortex ($p < 0.05$).
* Significantly different from the control ($p < 0.05$).