

A1244

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Room Hall B1-Area C

Cognitive and Neurodegenerative Effects of the Medetomidine/Ketamine Anesthesia Combination in Mice

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Background: Medetomidine (MED)/Ketamine (KET) is a commonly used combination in laboratory animals. Several studies have shown that KET can enhance neuronal death in neonates (1). Nevertheless, little is known about its effect in combination with Med and in adult. The aim of this work was to study the effect of different concentrations of MED/KET in cognition and its potential neurodegenerative effect in adult mice.

Methods: Fifty-two mice males, inbred C57BL/6, with 28 weeks old, were divided into 4 different groups (I- saline, II-1mg/kg MED, III-1mg/kg MED + 25mg/kg KET, IV-1mg/kg MED + 75mg/kg KET). Drugs were administered intraperitoneally (i.p.). After one hour, anesthesia was reversed with atipamazole 1mg/kg (i.p.). Thirty-two animals (n=8 per group) were behavioral tested with the T-maze task (28 h, 1 and 2 weeks after anesthesia) and open field (24 h after anesthesia). The remaining 20 animals (n=5 per group) were sacrificed 3 hours after anesthesia by cervical dislocation followed by decapitation and their brains analyzed by hemotoxylin-eosin staining and caspase-3 activation to assess neurodegeneration in the retrosplenial cortex, visual cortex, pyramidal cell layer from CA1 and CA3 areas of the hippocampus, and in the granular layer of the dentate gyrus. Death cells (H&E) and cells showing clear positive immunoreactions (caspase-3) were counted. Statistical analysis was performed using univariate ANOVA.

Results: No significant differences were detected between groups on the behavior performance of the T-maze and open field. These observations were supported by similar results with histopathological studies (H&E and caspase 3 activation, Figure 1). [figure1] Figure 1- Caspase-3 activation (C3A) positive profile per mm² (number of apoptotic cells) in retrosplenial cortex, visual cortex, pyramidal cell layer of the CA1 (CA1) and CA3(CA3) fields from the hippocampus and granular layer of the dentate gyrus (gyrus). Data showed as average + standard deviation per mm²; n= 5. Group I- saline; Group II - 1mg/kg medetomidine; group III- 1 mg/kg medetomidine + 25mg/kg ketamine; group IV- 1mg/kg medetomidine + 75 mg/kg ketamine.

Conclusion: This study showed no cognitive impairment or neurodegenerative differences induced by different concentrations of MED/KET anesthesia in the brain of adult mice.

References:

1- Scallet, AC et al. Toxicological Sciences 2004 81(2):364-370

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From Proceedings of the 2010 Annual Meeting of the American Society Anesthesiologists.

Figure 1

