Increased Susceptibility of Brain Acetylcholinesterase Activity to Methylmalonic Acid in young Rats with Acute Kidney Failure

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INTRODUCTION: Tissue methylmalonic acid (MMA) accumulation is the biochemical hallmark of methylmalonic acidemia. Clinically, the disease is characterized by progressive neurological deterioration and renal failure, whose pathophysiology is still undefined. In the present study we investigated the effect of acute MMA administration on some important parameters of brain neurotransmission in cerebral cortex of rats, namely Na⁺, K⁺-ATPase, ouabain-insensitive ATPases and acetylcholinesterase activities, in the presence or absence of kidney injury induced by gentamicin administration.

MATERIAL AND METHODS: Initially, thirty-day old Wistar rats received one intraperitoneal injection of saline or gentamicin (70 mg/kg). One hour after, the animals received three consecutive subcutaneous injections of MMA (1.67 µmol/g) or saline, with an 11 hours interval between each injection. One hour after the last injection the animals were killed and the cerebral cortex isolated.

RESULTS AND DISCUSSION: MMA administration by itself was not able to modify Na⁺, K⁺-ATPase, ATPases ouabain-insensitive or acetylcholinesterase activities in cerebral cortex of young rats. In rats receiving gentamicin simultaneously with MMA, it was observed an increase in the activity of acetylcholinesterase activity in cerebral cortex, without any alteration in the activity of the other studied enzymes. CONCLUSIONS: Therefore, it may be speculated that cholinergic imbalance may play a role in the pathogenesis of the brain damage. Furthermore, the pathophysiology of tissue damage cannot be exclusively attributed to MMA toxicity, and control of kidney function should be considered as a priority in the management of these patients, specifically during episodes of metabolic decompensation when MMA levels are higher.

Keywords: methylmalonic acid, renal failure, acetylcholinesterase activity, brain

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