MELATONIN TREATMENT PREVENTS GLYCINE-INDUCED IMPAIRMENT OF REDOX AND ENERGY HOMEOSTASIS IN CEREBRAL CORTEX OF NEWBORN RATS

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Introduction and objectives: Non ketotic hyperglycinemia (NKH) is an aminoacidopathy biochemically characterized by the accumulation of glycine (GLY) in body fluids and tissues of affected patients. The most severe presentation of NKH is the classic neonatal form that is characterized by mental retardation and seizures that can lead to early death. Since the pathophysiology of brain damage observed in affected individuals is not totally established, we investigated the ex vivo effects of a single intracerebroventricular (ICV) GLY administration (0.2 μmol/g) on energy and redox homeostasis in cerebral cortex of 1-day-old rats. Material and Methods: The biochemical parameters were analyzed in cerebral cortex homogenates from rats euthanized 1, 5 or 10 days after GLY injection. The cerebral cortex was dissected, homogenized and used to measure thiobarbituric acid-reactive substances (TBA-RS), glutathione (GSH) concentrations, and the activities of creatine kinase (CK) and respiratory complex IV (CIV). Results and Discussion: We verified that GLY decreased GSH concentrations 1, 5 and 10 days after its injection in rat cerebral cortex. Lipid peroxidation reflected by increased TBA-RS levels was observed 5 days after GLY exposure, whereas CK and CIV activities were altered 1, 5 and 10 days after treatment. We also observed that melatonin (intraperitoneally injected once daily during 5 days at a dose of 20 μmol/g) prevented the effects on TBA-RS levels, GSH and the CK and CIV activities 5 days after GLY injection, reinforcing the view that GLY induces reactive species generation. Finally, GLY injection increased S100β staining in cerebral cortex, implying induction of gliosis. Conclusions: Our findings demonstrate that GLY elicits oxidative stress, energy metabolism impairment and histopathological alterations in rat brain. It may be presumed that these pathomechanisms are involved in the neurological dysfunction found in NKH. Acknowledgements: Research grant from CNPq, PRONEX, FINEP, IBN-Net #01.06.0842-00 and INCT-EN.

Keywords: Non ketotic hyperglycinemia, glycine toxicity, cerebral cortex.