Therapeutic effect of perinatal exogenous melatonin on behavioral and histopathological changes and antioxidative enzymes in neonate mouse model of cortical malformation

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\textbf{A R T I C L E   I N F O}

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\textbf{A B S T R A C T}

\textbf{Background:} Melatonin, which is an antioxidant and neuroprotective agent, can be an effective treatment for neurological disorders. We assessed the effect of melatonin administration on histological changes, antioxidative enzyme levels, and behavioral changes in a neonate mouse model of cortical malformation.

\textbf{Materials and methods:} Cortical malformation was induced by two injections of 15 mg/kg methylazoxymethanol (MAM) on gestational day 15 (E15). Pregnant Balb/c mice were randomly divided into the following six groups: Control (CO), Melatonin (MEL), Luginbile (LUG), MAM, MEL + MAM1 (co-treatment), and MEL + MAM2 (pretreatment). Melatonin was intraperitoneally injected at a dose of 10 mg/kg daily (from E15 until delivery of from E6 for 20 days after delivery). On postnatal day 31, the activity and anxiety of mice were assessed by open field and elevated plus maze tests, respectively. Histopathological changes in the neonate cortex were studied using hematoxylin and eosin staining and neurofilament immunohistochemistry. Enzyme-linked immunosorbent assays were used to measure the activity of nitric oxide (NO), malondialdehyde (MDA), and antioxidant enzymes, including catalase (CAT), super oxide dismutase (SOD), and glutathione peroxidase (GPX).

\textbf{Results:} In the behavioral assessment of neonate mice, a significant increase in the crossing activity and decrease in anxiety were recorded in groups treated with MAM plus melatonin. In histological examination, heterotopic, dysmorphic, and ectopic cells, as well as dyslamination, were seen in the MAM and LUG groups. However, these defects were attenuated in the MAM plus melatonin groups. Significant reductions were recorded in the SOD and GPX levels in the MAM and LUG groups compared to the control, while the NO level was increased in these groups. Groups that received MAM plus melatonin showed significant increases in the levels of SOD and GPX and a significant decrease in the level of NO, compared to the MAM group.

\textbf{Conclusion:} Melatonin increased the crossing activity and decreased the anxiety in the treated mice of the neonate mouse model of cortical malformation. Histologically, the administration of exogenous melatonin in pregnant mice and their neonates had a protective effect on the cerebral cortex of neonates. Also, this effect is elicited by decreasing NO and increasing antioxidative enzymes.

1. Introduction

Cortical malformation occurs following impairments in intrauterine development. For the natural formation of cortex, neurons and glial cells should progress through the proliferation, migration, and differentiation phases. Impairments during any of these phases during fetal

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