Extended Abstract The Neurologist: Clinical & Therapeutics Journal 2020
Vol.4 No.1

Neurosurgery 2020: Melatonin ameliorates oxidative damage induced by maternal lead exposure in rat pups - Maryam Bazrgar - Damghan University

Maryam Bazrgar,
Damghan University, Iran

During the period of cerebellum development, exposure to lead decreases cerebellum growth & can result in selective loss of neurons. The detection & prevention of Pb toxicity is a major international public health priority. This research study was conducted to evaluate the effects of melatonin, an effective antioxidant & free radical scavenger, on Pb induced neurotoxicity & oxidative stress in the cerebellum. Pb exposure was initiated on gestation on day 5 with the addition of daily doses of 0.2% lead acetate to distilled drinking water & Continues until weaning. Melatonin (10mg/kg) was given only once daily at the same time. 21 days after birth, several antioxidant enzyme activities including superoxide dismutase (SOD) & glutathione peroxidase (GPx) were assayed. Thiobarbituric acid reactive substance (TBARS) levels were measured as a marker of lipid peroxidation. Rotarod & locomotor activity tests were performed on postnatal days (PDs) 31–33 & a histological study was performed after the completion of behavioral measurements on PD 33. The results of present work demonstrated that the Pb could induce lipid peroxidation, increase TBARS levels & decrease GPx & SOD activities in the rat cerebellum. We also observed that the Pb impaired performance on the rotarod & locomotor activities of rats. However, the treatment with melatonin significantly attenuated themotoric impairment & lipid peroxidation process & restored the levels of antioxidants. The Histological analysis indicated that the Pb could decrease Purkinje cell count & melatonin prevented this toxic effect. These results suggest that treatment with melatonin can improve motor deficits & oxidative stress by protecting the cerebellum against Pb toxicity. Administration of ethanol significantly increased TBARS levels in the cerebellum compared to control pups ($P< 0.01$). The treated pups with ethanol exhibited a marked decrease in the GPx activity ($P< 0.01$) whereas, despite decrease in the activities of SOD & CAT, when compared to control, there were not significant differences. The spherical cell bodies of Purkinje cells in control rats are aligned nicely between the granular & molecular layers. In ethanol treated pups, Purkinje cells scattered within the Purkinje cell layer & shrinkage of the cell somata is seen. Perhaps, psychologic stress disrupts oxidant-antioxidant balance within the brain, causing impairment of antioxidant enzyme function. This leads to glutathione depletion & increases oxidative stress. Simultaneously occurring glutamate toxicity, calcium imbalance, & mitochondrial impairment collectively intensify oxidative stress, causing biochemical distress in the brain. This disrupts neurocircuitry & weakens hippocampal, amygdalar & cortical connections, ultimately causing behavioral & cognitive deficits. It seems reasonable to suggest that, perhaps, tight regulation of oxidative stress, either by enhancing the activity of enzymes of antioxidant defense or by directly quenching pro-oxidants, offers the potential to limit psychiatric symptoms. Thus, data discussed in this review provides a basis for a biologically plausible oxidative stress hypothesis that would explain how oxidative damage might cause psychiatric symptoms. Melatonin is one of the strongest antioxidants hormones whereas, it is considered as free radical scavenger leading to attenuation of oxidative stress. Thus, it has a strong chemoprotective, immunostimulatory effect to neurons. In the present study, examination of stained cerebellar sections of deltamethrin rats that simultaneously supplemented with melatonin displayed apparently reversed most of the immunohistochemical & histopathological alterations induced by deltamethrin. Generally, most organisms widely use antioxidants like GSH, SOD, catalase & other antioxidants to protect themselves against liberated free radicals. In the current work a remarkable decrease in the levels of serum glutamate & serotonin was noticed among the deltamethrin treated mothers & their offspring in comparing with control.

Serotonin or 5-hydroxytryptamine (5-HT) is an essential monoamine neurotransmitter that plays a crucial role in regulation of several behavioral & physiological functions like mood, sleep, body temperature, appetite, aggression, & sexual behavior. In cerebellum, serotonin plays a role in regulation of neuronal activity, synaptic transmission & cerebellar development. In the current study, the decreased level of serum serotonin under the influence of deltamethrin may be due to the potential role of deltamethrin to stimulate calcium influx in cerebellar neurons through prolonged open calcium channels. Moreover, the reduced level of serotonin may be implicated in loss of appetite for deltamethrin treated-mother's rats & their offspring leading to their weight loss which in accordance with the obtained result.

Glutamate is the anion form of glutamic acid. It plays a major role in neuro- transmission of signals in some area of brain, especially in the Purkinje & granular cells of cerebellum. Also, glutamate plays critical role in the regulation of synaptogenesis during early brain development. The remarkable reductions in glutamate

Note: This work is partly presented at 26th International Conference on Neurosurgery and Neuroscience Webinar on June 17-18 2020

level under the influence of deltamethrin in this study may be attributed to loss of Purkinje cells under the influence of oxidative stress induced by deltamethrin. McKimm confirmed that developmental loss of cerebellar Purkinje cells leads to reductions in glutamate release in cerebellar efferent pathways that subsequently influence dopamine release.

Dopamine is released by some nerve terminals & functions as a neurotransmitter among nerve cells of the brain. Dopamine deficiency leads to Parkinson's disease & schizophrenia. In the current work a highly significant decrease in the level of cerebellar tissue dopamine was recorded among deltamethrin-treated mother's rats & their offspring if compared with control. Similar finding was recorded by Kirby who explained that deltamethrin & other pyrethroid are potent neurotoxins for dopaminergic nerve terminals through their exerting augmentation from nerve terminals into the blood.

In contrast to our results, it has been found that exposure can decrease dopamine uptake by the nerve of mice to deltamethrin resulted in an elevation in dopamine uptake which possibly indicative of an up-regulation of dopamine transmission. Such conflict of results may be attributed to the variation in exposed dose of deltamethrin or to the condition of experiment.

The results of the present work demonstrated that ethanol exposure during the vulnerable window could increase TBARS levels (lipid peroxidation) & decrease GPx levels in pup's cerebellum. Also, the results confirmed ethanol-induced microencephaly, cerebellar Purkinje cell loss. These findings suggest that Purkinje cell loss is, in part through decrease in the activity of GPx & increase of lipid peroxidation in the rat cerebellum.

Note: This work is partly presented at 26th International Conference on Neurosurgery and Neuroscience Webinar on June 17-18 2020