The Novel Potential Therapeutic Utility of Montelukast in Alleviating Autistic Behavior Induced by Early Postnatal Administration of Thimerosal in Mice

Lobna A. Abdelzaher, Ola A. Hussein, I. E. M. Ashry

Abstract:

Background and Aim Thimerosal (THIM) is a mercury-containing preservative widely used in many biological and medical products including many vaccines. It has been accused of being a possible etiological factor for some neurodevelopmental disorders such as autistic spectrum disorders (ASDs). In our study, the potential therapeutic effect of montelukast, a leukotriene receptor antagonist used to treat seasonal allergies and asthma, on THIM mice model (ASDs model) was examined.

Methodology Newborn mice were randomly distributed into three groups: (Group 1) Control (Cont.) group received saline injections. (Group 2) THIM-treated (THIM) group received THIM intramuscular (IM) at a dose of 3000 μg Hg/kg on postnatal days 7, 9, 11, and 15. (Group 3) Montelukast-treated (Monte) group received THIM followed by montelukast sodium (10 mg/kg/day) intraperitoneal (IP) for 3 weeks. Mice were evaluated for growth development, social interactions, anxiety, locomotor activity, and cognitive function. Brain histopathology, alpha 7 nicotinic acetylcholine receptors (α7nAChRs), nuclear factor kappa B p65 (NF-κB p65), apoptotic factor (Bax), and brain injury markers were evaluated as well. Results THIIM significantly impaired social activity and growth development. Montelukast mitigated THIM-induced social deficit probably through α7nAChRs upregulation, NF-κB p65, Bax, and brain injury markers were evaluated as well. Results THIIM significantly impaired social activity and growth development. Montelukast mitigated THIM-induced social deficit probably through α7nAChRs upregulation, NF-κB p65, Bax, and brain injury markers downregulation, thus suppressing THIM-induced neuronal toxicity and inflammation. Conclusion Neonatal exposure to THIM can induce growth retardation and abnormal social interactions similar to those observed in ASDs. Some of these abnormalities could be ameliorated by montelukast via upregulation of α7nAChRs that inhibited NF-κB activation and significant suppression of neuronal injury and the associated apoptosis.

Keywords:

Autistic spectrum disorders · Thimerosal · Montelukast · α7nAChRs · S100b · Synaptophysin

Published In:

Cellular and Molecular Neurobiology