Effect of thimerosal on the neurodevelopment of premature rats

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Original article

Background: **This study was undertaken to determine the effect of thimerosal on the neurodevelopment of premature rats.**

Methods: **Thimerosal was injected into premature SD rats at a dose of 32.8, 65.6, 98.4 or 131.2 μg/kg on postnatal day 1. Expression of dopamine D4 receptor (DRD4) and serotonin 2A receptor (5-HT2AR), apoptosis in the prefrontal cortex on post-injection day 49, and learning and memory function were studied and compared with those in a control group injected with saline.**

Results: **Expression of DRD4 and 5-HT2AR and learning function decreased, and apoptosis increased significantly in the 131.2 μg/kg group (P<0.001). Memory function was significantly impaired by 65.6 (P<0.05), 98.4 and 131.2 μg/kg (P<0.001).**

Conclusions: **The negative adverse consequences on neurodevelopment observed in the present study are consistent with previous studies; this study raised serious concerns about adverse neurodevelopmental disorder such as autism in humans following the ongoing worldwide routine administration of thimerosal-containing vaccines to infants.**

World J Pediatr 2013;9(4):356-360

Key words: **dopamine D4 receptor; neurodevelopment; serotonin 2A receptor; thimerosal**

Introduction

Neurological alterations that may result from thimerosal exposure have recently become a hot topic. Thimerosal exposure via vaccination is thought to cause brain disorder.[1] Since there is no appropriate agent to replace, thimerosal is used as a preservative in vaccines. Therefore, it is necessary to determine the appropriate levels of thimerosal for neurodevelopment. Studies[2,3] have been focused on neurological alterations after exposure to thimerosal in rats, but further study is required to demonstrate the acceptable levels of exposure for neurodevelopment.

Rat model is considered feasible for research in intoxication following metal exposure. Learning and memory are important brain functions. And the prefrontal cortex is a critical region receiving stimulation for the development of learning and memory function,[4] which is mainly executed by neurotransmitters. The variants of dopamine D4 receptor (DRD4) are reported to be associated with memory function of rats,[5] whereas serotonin 2A receptor (5-HT2AR) is correlated with impaired episodic memory performance.[6] It was reported that in the human neuroblastoma cell line, thimerosal induced mitochondria-mediated apoptosis.[7]

In the present study, we investigated whether thimerosal could induce alterations in expression of DRD4 and 5-HT2AR, apoptosis of the prefrontal cortex, and learning and memory functions in the premature rats.

Methods

The protocol of this study was approved by the Institutional Ethics Committee of Xi'an Jiaotong University Health Science Center, Xi'an, China. Thirty premature Sprague-Dawley rats (Laboratory Animal Center of Xi'an Jiaotong University Health Science Center) were delivered on day 20 of gestation (term=day 22) by hysterotomy, and they were randomly divided into five groups, with six rats in each group. Thimerosal (Sigma-Aldrich, St. Louis, MO, USA) was dissolved in saline and injected into the gluteus maximus of four

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doi: 10.1007/s12519-013-0443-z