Journal of Immunology
Research and Therapy
JIRT, 6(1): 221-223
www.scitcentral.com

ISSN: 2472-727X

Mini Review: Open Access

The Role of Thimerosal-Containing Vaccines in Impairments of Brain and Behavior

Namvarpour Z[1], Amini A[2*] and Namvarpour M[3]

[1]*Institute for Cognitive Science Studies (ICSS), Tehran, Iran*

[*2]*Department of Biology and Anatomical Sciences, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[3]*Department of Immunology, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran.*

Received December 09, 2019; Accepted January 06, 2020; Published June 06, 2021

INTRODUCTION

Thimerosal, (THIM; sodium ethylmercurithiosalicylate), has been applied as a preservative agent in the manufacture of many vaccines and other medicinal productions for years [1-3]. The possibility of neuropathological alterations following a long use of THIM has become a hot topic in the medical area. For a long time, it was thought that THIM was the main source of organic mercury exposure in many infants. In developing nations, because there is no suitable substance to replace, THIM is still in use in many biological and drug products. Thus, the special effects of this substance should be taken into consideration [1,4]. THIM accumulates in the central nervous system and other organs as inorganic mercury combinations. As we know, mercury has many harmful effects on the brain. It reduces the amount of glutathione and antioxidants, impairs antioxidant systems, destroys receptor and enzymes functions and makes widespread alterations in the 3D structure of many proteins and makes them suitable antigens for the immune system [5,6]. Therefore, it is predictable that THIM accumulation in early stages of brain development may result in developmental deficiencies, peripheral neuropathies, and higher neurodegenerative changes, especially in prenatal and neonatal life. However, due to the lack of data about pharmacokinetic properties and toxicity of ethyl-mercury, methyl-mercury has been applied to instate of ethyl-mercury toxicity based on the theory that both of them has the same toxic effect. Though, the present studies have shown that methyl-mercury differs from ethyl-mercury because they have extensive dissimilarities in terms of tissue distribution and rates of clearance in the brain [7]. Nowadays, many studies have reported brain biochemical and neurological alternations after THIM exposure. For example, Burbacher et al. in 2015 [8] showed that exposure of monkey infants into THIM-containing vaccines led to the accumulation of mercury in their brain than in other parts, such as blood. These accumulations may persist for months or even years in their brain. Magos et al. [9] showed that ethyl mercury crosses the cell membrane and transform into inorganic mercury (Hg^{2+}) in the cells, and accumulate in the central nervous system. These accumulations in the brain cells were more for ethyl mercury than methyl mercury. Earlier research showed that the injection of THIM containing radioactive mercury into rabbits led to fallen about 75% of radioactive mercury level in the blood cells after 1 to 6 h post-injection, while in this time there was significantly improved radioactivity levels in the fetal brain. In another way, this study explained that this quick drop in blood mercury levels from THIM injection is because of uptake by other tissues of the body and not excretion [10]. Any delay in detoxification of mercury causes serious damage in methylation reactions, which negatively disrupts growth factor derived development of the brain [11]. The amount of mercury accumulated in the brain of infants is so high that can create neurotoxic effects and may destroy nerve cells. Moreover, much evidence suggests that THIM has adverse effects on neuro-immune cells, which result in neurogenic inflammatory responses [12]. For example, Rampersad et al. [13] showed that THIM is a strong inhibitor of phagocytosis, which is the main phase of the natural immune system and it is possible that this agent inhibits an infant's immune system. Another study on immune cells including mast cells (MCs) and microglia and the pro-neuroinflammatory cytokines (Interleukin-1b (IL-1b) and tumor necrosis factor-α (TNF-α)) in the prefrontal cortex of rat brain exposed to THIM showed that ethyl-mercury causes an undesired neurogenic

Corresponding author: Abdollah Amini, Department of Biology and Anatomical Sciences, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, Tel: +9821-23872577; E-mail: d.amini2008@yahoo.com

Citation: Namvarpour Z, Amini A & Namvarpour M. (2021) The Role of Thimerosal-Containing Vaccines in Impairments of Brain and Behavior. J Immunol Res Ther, 6(1): 221-223.

inflammatory reaction and that these alterations in neuro-immune cells can stay for longer time in brain than blood [14]. These findings revealed that THIM can lead to a strong autoimmunity and this situation may play undesirable main role in neuro-inflammation and neuro-immune reaction in the brain [14]. In addition to its hurtful effects on the autoimmune system, THIM also disrupts the tissue and brain function, so, it is known as one of the main factors in the pathogenesis of many types of central nervous system disorders. Different studies have tested this hypothesis and were detected several neuropathological variations after exposure to THIM: (1) the degeneration of the nerve cells in the prefrontal, temporal cortex, hippocampus formation, and the cerebellum; (2) blood vessel defects in the temporal cortex; (3) reduced reaction of synaptophysin in the hippocampus formation; (4) related astroglial atrophy and astrogliosis in the hippocampus and cerebellum cortex; (5) apoptosis in Bergmann astroglia (positive caspase-3 response); (6) decreased opioid receptors (morphine, MOR) in the caudate nuclei, periaqueductal gray maters, putamen nuclei, and hippocampus formation; (7) decrease in the number of Purkinje cells in cerebellum; (8) reduce the number of cerebellum cells, demyelination of axonal neoplasms, Purkinje and granular cells necrosis and glycemia in all layers of the cerebellum [3,15,16]. This amount of destruction in brain structure is also expected to cause extensive behavioral and functional deficits.

Extensive findings have approved this hypothesis. For example, in a study by Hornig et al. [17] a number of neurological disorders were discovered in an autoimmune disease-sensitive mouse strain exposed to THIM. Similarly, Hewitson et al. [18] explained that monkeys infant exposed to THIM-containing hepatitis B vaccine showed a delay in getting of some survival, motor and sensorimotor reflexes. In another behavioral study, it was revealed that neonatal exposure to THIM can make abnormal social interactions, stereotyped behaviors and locomotors activity comparable to those detected in neurodevelopmental disorders [6].

CONCLUSION

In conclusion, all these findings support a theory that THIM has many negative effects on CNS and immune system and may reason neurotoxic changes in the developing brain, which is a powerful reason for eliminating this unnecessary component from vaccines and other medicinal products.

REFERENCES

1. Bernard S, Enayati A, Roger H, Binstock T, Redwood L (2002) The role of mercury in the pathogenesis of autism. Mol Psychiatry 7: 42.
2. Duszczyk-Budhathoki M, Olczak M, Lehner M, Majewska MD (2012) Administration of thimerosal to infant rats increases overflow of glutamate and aspartate in the prefrontal cortex: Protective role of dehydroepiandrosterone sulfate. Neurochem Res 37: 436-447.
3. Olczak M, Duszczyk M, Mierzejewski P, Meyza K, Majewska MD (2011) Persistent behavioral impairments and alterations of brain dopamine system after early postnatal administration of thimerosal in rats. Behav Brain Res 223: 107-118.
4. Chen YN, Wang J, Zhang J, Li SJ, He L, et al. (2013) Effect of thimerosal on the neurodevelopment of premature rats. World J Pediatr 9: 356-360.
5. Kern JK, Geier DA, Audhya T, King PG, Sykes LK, et al. (2012) Evidence of parallels between mercury intoxication and the brain pathology in autism. Acta Neurobiol Exp 72: 113-153.
6. Namvarpour Z, Nasehi M, Amini A, Zarrindast MR (2018) Protective role of alpha-lipoic acid in impairments of social and stereotyped behaviors induced by early postnatal administration of thimerosal in male rat. Neurotoxicol Teratol 67: 1-9.
7. Barrett JR (2005) Thimerosal and animal brains: New data for assessing human ethyl mercury risk. Environ Health Perspect 113: A543A544.
8. Burbacher TM, Shen DD, N. Liberato N, Kimberly SG, Elsa C, et al. (2005) Comparison of blood and brain mercury levels in infant monkeys exposed to methyl mercury or vaccines containing thimerosal. Environ Health Perspect 113: 1015-1021.
9. Magos L, Brown AW, Sparrow S, Bailey E, Snowden RT, et al. (1985) The comparative toxicology of ethyl and methyl mercury. Arch Toxicol 57: 260-267.
10. Gasset AR, Itoi M, Ishii Y (1975) Teratogenicities of ophthalmic drugs: II. Teratogenicities and tissue accumulation of thimerosal. Arch Ophthalmol 93: 52-55.
11. Mutter J, Naumann J, Schneider R, Walach H, Haley B (2005) Mercury and autism: Accelerating evidence? Neuroendocrinol Lett 26: 439-446.
12. Olczak M, Duszczyk M, Mierzejewski P, Bobrowicz T, Majewska MD, et al. (2010) Neonatal administration of thimerosal causes persistent changes in mu opioid receptors in the rat brain. Neurochem Res 35: 1840-1847.
13. Rampersad GC, Suck G, Sakac D, Fahim S, Foo A, et al. (2005) Chemical compounds that target thiol-disulfide groups on mononuclear phagocytes inhibit immune mediated phagocytosis of red blood cells. Transfusion 45: 384-393.
14. Afsordeh K, Sadeghi Y, Amini A, Zahra N, Amin M, et al. (2019) Alterations of neuroimmune cell density and pro-inflammatory cytokines in response to thimerosal in

prefrontal lobe of male rats. Drug Chem Toxicol 42: 176-186.

15. Laurente J, Remuzgo F, Ávalos B, Chiquinta J, Ponce B, et al. (2007) Neurotoxic effects of thimerosal at vaccines doses on the 'encephalon and development in 7 days old hamsters. An Fac Med Lima 68: 222-237.
16. Namvarpour Z, Amini A, Nasehi M, Zarrindast MR (2018) The effects of early exposure to thimerosal on impairments of social and stereotyped behaviors and the number of Purkinje cells of cerebellum in rats. Appl Biotechnol Rep 5: 105-111.
17. Hornig M, Chian D, Lipkin WI (2004) Neurotoxic effects of postnatal thimerosal are mouse strain dependent. Mol Psychiatry 9: 833.
18. Hewitson L, Lopresti BJ, Stott C, Mason NS, Tomko J (2010) Influence of pediatric vaccines on amygdala growth and opioid ligand binding in rhesus macaque infants: A pilot study. Acta Neurobiol Exp 70: 147-164.