

Comparison of organic and inorganic mercury distribution in suckling rat

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ABSTRACT: Thiomersal is used as a preservative in vaccines given to small children. The metabolic product of thiomersal is ethylmercury and its distribution and kinetics are still not known, especially at this early age. The purpose of this study was to compare the body distribution of two forms of mercury: organic (thiomersal) and inorganic (mercury(2+) chloride) in very young, suckling rats. Mercury was applied subcutaneously three times during the suckling period on days 7, 9 and 11 of pups age, imitating the vaccination of infants. A single dose of mercury was equimolar in both exposed groups, i.e. $0.81 \mu\text{mol Hg kg}^{-1}$. At 14 days of age the animals were killed and the total mercury analysed in blood and organs (kidney, liver and brain). The analytical method applied was total decomposition, amalgamation, atomic absorption spectrometry. The results showed that the level of mercury was higher in the liver and kidney of the inorganic mercury group than in the thiomersal exposed group. However, the brain and blood concentrations of mercury were higher in the thiomersal exposed group. These results need to be clarified by additional data on the kinetic pathways of ethylmercury compared with inorganic mercury. Copyright © 2006 John Wiley & Sons, Ltd.

KEY WORDS: thiomersal; ethylmercury; mercury(2+) chloride; suckling rat; distribution; blood; kidney; liver; brain

Introduction

Thiomersal (Thiomerosal, Merthiolat) is an organic compound of mercury added as a preservative to the childhood vaccines diphtheria-tetanus-pertussis (DTP) or diphtheria-tetanus (DT). The vaccine is given subcutaneously to infants several times during their first 6 months of life, up to the age of 6 years. The metabolite of thiomersal is ethylmercury and its absorption, distribution and excretion is similar to methylmercury. The similarity of metabolic pathways and actions are due to similar reactions as organic molecules. Both substances increase oxidative stress and are neurotoxic (Ueha-Ishibashi *et al.*, 2004; ATSDR, 1999). Ethylmercury is, however, less toxic than methylmercury due to the lower clearance half-time and the lower possibility to pass the blood–brain barrier (Magos, 2003) than methylmercury. Due to unknown toxicity from low-dose exposures to ethylmercury, there has been concern that this exposure to mercury may be of some detriment to young children. Autistic spectrum disorders and neurodevelopmental disorders have been a controversial topic since 1999

connected with thiomersal-containing vaccines (Parker *et al.*, 2004). Therefore, the American Academy of Pediatrics and the US Public Health Service issued a joint statement calling for the removal of thiomersal from vaccines. However, in our country and probably in many other countries such vaccines are still in use.

Data on the difference between ethylmercury and inorganic mercury distribution in newborns are, however, limited. In this study the distribution of the two chemical forms of mercury, organic (thiomersal) and inorganic (mercury(2+) chloride) was measured and compared in very young, suckling rats. Application of substances was subcutaneous three times during the suckling period, imitating the vaccination of infants.

Methods

Animals and Experimental Protocol

Adult animals used in the experiment were Wistar rats raised in the Institute's breeding farm (Institute for Medical Research and Occupational Health, Zagreb, Croatia). They were fed standard rat diet (Mucedola, Milano, Italy) and tap water *ad libitum*. The rats were kept in the animal facility at a constant room temperature of 20–22 °C, constant humidity ($40 \pm 10\%$) and 12 h light/dark cycle. Females were mated with males in the ratio of 3 : 1. Pregnant females were kept in individual

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