Homozygous gene deletions of the glutathione S-transferases M1 and T1 are associated with thimerosal sensitization

Received: 8 September 1999 / Accepted: 25 March 2000

Abstract Objective: Thimerosal is an important preservative in vaccines and ophthalmologic preparations. The substance is known to be a type IV sensitizing agent. High sensitization rates were observed in contact-allergic patients and in health care workers who had been exposed to thimerosal-preserved vaccines. There is evidence for the involvement of the glutathione system in the metabolism of thimerosal or its decomposition products (organomercury alkyl compounds). Thus detoxification by polymorphically expressed glutathione S-transferases such as GSTT1 and GSTM1 might have a protective effect against sensitization by these substances. Methods: To address this question, a case control study was conducted, including 91 Central European individuals with a positive patch-test reaction to thimerosal. This population was compared with 169 healthy controls and additionally with 114 individuals affected by an allergy against para-substituted aryl compounds. The latter population was included in order to test whether possible associations were due to substance-specific effects, or were a general feature connected with type IV immunological diseases. Homozygous deletions of GSTT1 and GSTM1 were determined by polymerase chain reaction. Results: Glutathione S-transferase M1 deficiency was significantly more frequent among patients sensitized to thimerosal (65.9%, \( P = 0.013 \)) compared with the healthy control group (49.1%) and the “para-compound” group (48%, \( P = 0.034 \)). Glutathione S-transferase T1 deficiency in the thimerosal/mercury group (19.8%) was barely elevated versus healthy controls (16.0%) and the “para-compound” group (14.0%). The combined deletion (GSTT1−/GSTM1−) was markedly more frequent among thimerosal-sensitized patients than in healthy controls (17.6% vs. 6.5%, \( P = 0.0093 \)) and in the “para-compound” group (17.6% vs. 6.1%, \( P = 0.014 \)), revealing a synergistic effect of these enzyme deficiencies (healthy controls vs. thimerosal GSTM1 negative individuals, \( OR = 2.0 \) [CI = 1.2–3.4], GSTT1−, OR = 1.2 [CI = 0.70–2.1], GSTM1/T1−, OR = 3.1 [CI = 1.4–6.5]). Conclusions: Since the glutathione-dependent system was repeatedly shown to be involved in the metabolism of thimerosal decomposition products, the observed association may be of functional relevance.

Key words  Glutathione S-transferase · Polymorphism · Thimerosal

Introduction

The predisposition to acquire a sensitization towards certain contact-allergens was proposed to be heritable. This proposal was based mainly on family and twin studies (reviewed by Menné and Holm 1986). Among