Synopsis of Original Research Paper

Epitope analysis of gelatin allergy and development of low-allergic gelatin

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Anaphylactic reactions to measles, mumps and rubella vaccines and the combined measles-mumps-rubella (MMR) vaccines have been suggested to be caused by allergy containing bovine gelatin in the vaccines as a stabilizer. Since gelatin can be derived from collagen molecules present in all multicellular animals, it has long been believed to be nonimmunogenic and thought to be weakly allergic in human. Therefore, gelatin has been widely used as a stabilizer in vaccines. The present study was designed to investigate the reactivity of IgE in bovine gelatin-sensitive children to gelatins from various animals by enzyme linked immunosorbent assay (ELISA). The IgE in the children reacted to mammalian gelatins including kangaroo and mouse gelatins, to which they had little or no exposure as a food or a vaccine stabilizer. Most of the children who displayed sensitivity may be due primarily to the antigenic cross-reactivity between mammalian gelatins.

Gelatin, obtained from bone and skin, consists mainly of denatured type I collagen, which is composed of two α1 and one α2 chains. Furthermore, the study was designed to elucidate the IgE reactivity to α1 and α2 chains of bovine type I collagen in gelatin-sensitive children. Purified α1 and α2 chains of bovine type I collagen were obtained by separation of column chromatography. All serum samples which were reacted with bovine type I collagen showed positive reaction to α 2 chain. In our previous study, we reported that homology (98%) between α1 chains of human and bovine type I collagen is higher than homology (93%) between α2 chains of them. These homology data might suggest that the α2 chain has higher allergenicity than the α1 chain. To analyze IgE-binding sites of α2 chain, recombinant proteins covering 100 kDa collagenous domain of α2 chain were expressed by pRSET vector. One of five recombinant proteins located in central portion of collagenous domain showed strong reactivity for patients sera. To further determine epitope, several small recombinant proteins covering the central collagenous domain were prepared. The 4 kDa recombinant protein spanning from ^{461}Pro to ^{500}Glu was shown cross-reactivity to patients sera but the protein from ^{431}Ala to ^{475}Gly was not shown. Taken together these data, a major epitope in the α2 chain of bovine type I collagen was suggested to locate in 25 amino acid residues with ^{475}Gly to ^{500}Glu.

In the future, our analyzed data of IgE-binding epitope in the α2 chain of bovine type I collagen may become tool for developing a gelatin which has no or low allergenicity to humans.