

Anaphylaxis to gelatin-containing rectal suppositories

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Background: Some children—though the number is few—have been sensitized with gelatin.

Objective: To investigate the relationship between the presence of antigelatin IgE and anaphylaxis to gelatin-containing rectal suppository, we measured antigelatin IgE in the sera of the children with anaphylaxis.

Methods: Ten children showed systemic allergic reactions, including anaphylaxis, to a chloral hydrate rectal suppository containing gelatin (231 mg/dose) that had been used as a sedative. These children's clinical histories and serum samples were submitted from physicians to the National Institute of Infectious Diseases during a 2-year period from 1996 to 1997. **Results:** Of the 10 children, 5 showed apparent anaphylaxis, including hypotension and/or cyanosis, along with urticaria or wheezing; 2 showed both urticaria and wheezing without hypotension or cyanosis; the other 3 showed only urticaria. All of the children had antigelatin IgE (mean value $\pm$ SD, 7.9 ± 8.4 Ua/mL). As a control, samples from 250 randomly selected children had no antigelatin IgE. These findings suggest that the 10 children's systemic allergic reactions to this suppository were caused by the gelatin component.

Conclusion: Gelatin-containing suppositories must be used with the same caution as gelatin-containing vaccines and other medications. (*J Allergy Clin Immunol* 2001;108:1033-4.)

Key words: Anaphylaxis, gelatin, IgE, suppository

Kelso et al¹ reported that a child with anaphylaxis to a gelatin-containing measles-mumps-rubella vaccine had antigelatin IgE. In Japan, most children experiencing systemic immediate-type reactions, including anaphylaxis, to gelatin-containing measles, mumps, rubella, and varicella vaccines have been reported to have antigelatin IgE.² Gelatin can cause food allergy,³ and we recently found that anaphylaxis to erythropoietin (EPO) products can be caused by gelatin in the products.⁴ It is thus clear that the gelatin included in vaccines, medicine, and food can induce anaphylaxis.

Abbreviation used
EPO: Erythropoietin

In Japan, children are frequently given rectal suppositories as sedatives to facilitate diagnostic procedures such as magnetic resonance imaging and computed tomography. Hasegawa et al⁵ reported the case of a child who experienced anaphylaxis to a gelatin-containing rectal suppository used as a sedative (chloral hydrate).

In the present study, serum samples from children who showed systemic allergic reactions to gelatin-containing rectal suppositories were sent from physicians to the National Institute of Infectious Diseases for measurement of antigelatin IgE during a 2-year period (1996 and 1997).

METHODS

Subjects

Physicians submitted serum samples from children who had allergic reactions to gelatin-containing rectal suppositories to the National Institute of Infectious Diseases. These sera and data were collected during a 2-year period, from January 1996 to December 1997.

As a control, serum samples from 250 children (125 male, 125 female) ranging in age from 1 to 5 years who were randomly selected without regard to vaccine or allergy history were supplied by the World Health Organization Serum Reference Bank, National Institute of Infectious Diseases.

Gelatin-containing rectal suppositories

Rectal suppositories (Escre, SS Pharmaceutical Co, Ltd, Tokyo, Japan)⁶ that are used as sedatives (chloral hydrate, 250 or 500 mg) contain bovine gelatin (231 mg/dose).

Measurement of gelatin-specific IgE antibody

The CAP system (Pharmacia, Uppsala, Sweden) was used to determine the concentration (Ua/mL) of IgE to bovine gelatin.²

RESULTS

Table I shows data from 10 children who had systemic immediate-type reactions to gelatin-containing rectal suppositories. Five of these children (nos. 1-5) showed severe anaphylaxis to this suppository. Of these 5 children, 4 (nos. 1-4) showed anaphylactic shock (eg, cyanosis, hypotension) and 1 (no. 5) had severe airway obstruction and cyanosis. All 5 of these children received the necessary treatments for anaphylaxis and recovered completely. Each of them had antigelatin IgE (mean value $\pm$ SD, 13.6 ± 8.8 Ua/mL).

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TABLE I. Clinical and laboratory findings for children with systemic allergic reactions

Child no.	Age	Sex	Allergic reaction	Time of onset (min)	Antigelatin IgE (Ua/mL)*
1	1 y 11 m	F	Urticaria, angioedema, cyanosis, hypotension	20	26.1
2	1 y 8 m	F	Urticaria, cyanosis, hypotension	20	18.9
3	3 y	F	Urticaria, angioedema, cyanosis, hypotension	30	9.7
4	3 y	F	Urticaria, angioedema, hypotension	60	9.0
5	5 y	M	Cyanosis, wheezing, airway obstruction	20	4.3
6	1 y 7 m	F	Urticaria, wheezing	15	4.2
7	3 y 3 m	F	Urticaria, wheezing	75	1.3
8	1 y 11 m	F	Urticaria	30	3.5
9	2 y	M	Urticaria	40	1.3
10	3 y 1 m	F	Urticaria	30	0.79

F, Female; M, male.

* Positive values > 0.35 U/mL.

Two other children (nos. 6 and 7) showed both a cutaneous reaction (urticaria) and a respiratory reaction (wheezing) without the cardiovascular reactions; the symptoms were relatively mild. These 2 children had antigelatin IgE (mean value $\pm$ SD, 2.8 ± 2.1 Ua/mL).

Three other children (nos. 8-10) showed only systemic urticaria. They also had antigelatin IgE (mean value $\pm$ SD, 1.9 ± 1.4 Ua/mL).

None of the 250 control children had antigelatin IgE (data not shown).

DISCUSSION

In Japan, it is rare for people to have a gelatin allergy or to have antigelatin IgE.^{4,7} In 1996, the numbers of cases (per million doses) of severe anaphylaxis to gelatin-containing measles, rubella, mumps, and varicella vaccines were only 8.13, 7.80, 8.33, and 18.8, respectively.⁷ As a control, 276 children who showed no reaction to gelatin-containing vaccines had no antigelatin IgE.⁷ Furthermore, approximately 100,000 Japanese patients undergoing dialysis received gelatin-containing EPO products from 1995 to 1996; of these, only 1 patient was reported to have anaphylaxis to this EPO product and had antigelatin IgE.⁴

In this study, we found that all of the children who showed systemic allergic reactions to the suppository had antigelatin IgE. These findings suggest that such reactions in these children were caused by the gelatin contained in the suppository.

It has been reported that children might show delayed side effects after sedation (mainly after chloral hydrate administration)⁸; however, anaphylaxis to chloral hydrate was not reported. In another study, patients had shown local or systemic allergic reactions to a lysozyme-containing suppository⁹; these patients showed a vigorous T-cell response to lysozyme, so it was suggested that the reactions might be induced by lysozyme.

The numbers of these rectal suppositories sold in Japan in 1996 and 1997 were 508,640 and 765,340, respectively (personal communication from SS Pharmaceutical Co, Ltd), but there is no information available on the number of actual doses of this suppository that were given. The systemic allergic reactions shown by 5 of the children in

our study (nos. 1 to 5) were apparent anaphylaxis. We estimated that the minimum incidence of severe anaphylaxis to this rectal suppository was 3.9 cases per million doses in 1996 and 1997.

One of the children in this investigation had shown systemic urticaria to gelatin-containing measles vaccine 20 minutes after vaccination; this had occurred 6 months before anaphylaxis to the suppository. No information on vaccine histories or adverse reactions to vaccines was available for the other 9 children in this study.

The suppositories used in this study have been used in Japan and contain a large amount of gelatin (231 mg/dose). We think that children with gelatin allergies were administered gelatin-containing suppositories, from which the gelatin was absorbed from the rectum into the bloodstream, causing the systemic reactions. Gelatin-containing suppositories should be used with the same caution as gelatin-containing vaccines.

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