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Agnieszka Kowalczyk, Dominika Tunowska,
Aneta Krogulska, Renata Kuczyńska

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Hypersensitivity to erythritol in a 7-year-old boy

Nadwrażliwość na erytrytol u 7-letniego chłopca

Department of Paediatrics, Allergology and Gastroenterology, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Bydgoszcz, Poland
Correspondence: Agnieszka Kowalczyk, Department of Paediatrics, Allergology and Gastroenterology, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Antoni Jurasz University Hospital No. 1 in Bydgoszcz, Marii Skłodowskiej-Curie 9, 85-094 Bydgoszcz, Poland, Poland, e-mail: a.kowalczyk@cm.umk.pl

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ORCID iDs
1. Agnieszka Kowalczyk https://orcid.org/0000-0003-4915-154X
2. Dominika Tunowska https://orcid.org/0000-0001-9961-7905
3. Aneta Krogulska https://orcid.org/0000-0001-8388-489X
4. Renata Kuczyńska https://orcid.org/0000-0003-3123-3192

Abstract

Hypersensitivity reactions to erythritol are rare, with an incidence of less than 1:1,000,000. In recent years, the widespread use of erythritol has increased significantly, which may result in an increase of the frequency of hypersensitivity reactions. We discuss the clinical features and the diagnostic process in a case of hypersensitivity to erythritol in a 7-year-old boy. The presented patient developed generalised urticaria, vomiting, weakness, and shortness of breath within minutes of eating a homemade cake containing erythritol. A few months later urticaria appeared on the boy's face and trunk 30 minutes after eating a homemade cake containing maltitol. Skin prick tests and intradermal tests with erythritol were performed, yielding negative results. An oral challenge with erythritol, using increasing doses of 250 mg, 500 mg, and 1,000 mg every 30 minutes, was positive. It was recommended to eliminate sweeteners from the diet. It is important to remember about food additives when searching for the causative agents of anaphylactic reactions.

Keywords: children, hypersensitivity reactions, polyols, erythritol

Streszczenie

Reakcje nadwrażliwości na erytrytol należą do rzadkości, a ich częstość szacuje się na mniejszą niż 1:1 000 000. W ostatnich latach coraz szerzej używa się erytrytolu w produktach spożywczych, co może skutkować zwiększeniem częstości występowania reakcji nadwrażliwości. Celem pracy jest omówienie obrazu klinicznego i procesu diagnostycznego nadwrażliwości na erytrytol u 7-letniego chłopca. U prezentowanego pacjenta w ciągu kilku minut od spożycia domowego ciasta zawierającego erytrytol wystąpiły uogólniona pokrzywka, wymioty, osłabienie i duszność. Kilka miesięcy później pokrzywka pojawiła się na twarzy i tułowiu 30 minut po zjedzeniu domowego ciasta zawierającego maltitol. Wykonane punktowe testy skórne i testy śródskórne z erytrytolem dały wynik ujemny. Doustna próba prowokacji erytrytolem we wzrastających dawkach 250 mg, 500 mg, 1000 mg w odstępach 30 minut była dodatnia. Zalecono wyeliminowanie z diety substancji słodzących. W trakcie diagnostyki czynników wywołujących reakcje anafilaktyczne należy pamiętać o dodatkach do żywności.

Słowa kluczowe: dzieci, reakcje nadwrażliwości, poliole, erytrytol

INTRODUCTION

It is difficult to imagine the modern food industry without the use of food additives, including sweeteners. One such example is erythritol (E968), a four-carbon sugar alcohol derived from corn, wheat starch, and certain fruits. It owes its growing popularity to the fact that its sweetness, equal to 70% of that of sucrose, is accompanied by a low caloric content (0.2 kcal/g)[1]. Erythritol can be found in toothpastes, mouthwashes, lotions, and makeup products.

Hypersensitivity reactions to erythritol are rare, with a frequency of less than 1:1,000,000[2]. Hence, only some of the mechanisms involved in the pathogenesis of erythritol hypersensitivity have been identified so far[3]. The dominant one is believed to be the IgE-dependent mechanism, as indicted by positive results of skin prick tests (SPT) and basophil activation tests (BAT)[4,5]. The gold standard in the diagnosis of hypersensitivity to erythritol remains the oral food challenge (OFC) test.

CASE REPORT

A 7-year-old boy, with a history of atopic dermatitis, was admitted to the hospital after an anaphylactic reaction following the consumption of a homemade cake containing erythritol. Allergy tests performed so far had not revealed any allergies to food or airborne allergens, and the child had received periodic treatments with levocetirizine in the form of syrup. At the age of seven, a few minutes after eating a homemade cake, the child developed generalised urticaria, vomiting, weakness, and shortness of breath. Hydrocortisone and rupatadine were administered in the emergency department, resulting in complete resolution of symptoms. However, four months later, hives appeared on the boy's face and trunk 30 minutes after consuming a homemade cake containing maltitol: a derivative of erythritol. The boy was administered rupatadine, resulting in the resolution of skin lesions.

After analysing the ingredients of the cake consumed by the patient, a hypersensitivity reaction to erythritol and maltitol was suspected. However, SPT with 1 mg/mL, 10 mg/mL, 100 mg/mL, 200 mg/mL or 300 mg/mL erythritol solutions, as well as intradermal tests with 0.1 mg/mL or 1 mg/mL erythritol, were negative. An OFC test with erythritol was performed in increasing doses of 250 mg, 500 mg, and 1,000 mg every 30 minutes. A few minutes after the administration of the third portion (1,000 mg, total dose 1,750 mg), generalised urticaria and repetitive cough occurred. The symptoms resolved after the administration of rupatadine and hydrocortisone. The OFC result was therefor considered positive, and the maltitol challenge was abandoned. It was recommended to eliminate sweeteners from the diet. No hypersensitivity reactions were observed during a follow-up period of several months. Previously, the boy had periodically reported abdominal pain, which could be related to the presence of maltitol in the levocetirizine syrup. After the levocetirizine preparation was changed, he stopped reporting any pain.

DISCUSSION

Food hypersensitivity reactions affect approximately 6–8% of the population at developmental age, with non-immune reactions being more common[6]. However, due to a lack of standardised diagnostic methods, it is difficult to set a diagnosis of hypersensitivity to food additives. In the reported case, the adverse reaction could have been caused by many ingredients of the cake, including the sweetener. Allergy testing, including molecular diagnostics, did not reveal any sensitisation to food allergens.

Most publications on erythritol anaphylaxis come from Japan, where the agent has been used longer than in Europe (Tab. 1). While erythritol was approved for use as a safe food additive in the European Union in 2003, it has been used on a large scale in Japan since 1990. Erythritol allergy was first described by Hino et al., who presented the case of a 24-year-old Japanese woman who developed urticaria after drinking a beverage sweetened with erythritol[7].

The difficulties encountered in diagnosing allergies, and the importance of rare allergens, including sweeteners, are highlighted in a case report of an 11-year-old boy with recurrent episodes of anaphylaxis. The boy had episodes of urticaria from the age of seven, after eating various products. Initially, wheat and peanuts, which were found to be sensitisers in asIgE tests, were selected as the potential causative factors. Despite the introduction of an elimination diet, anaphylactic reactions were still observed. At that time, based on the composition of the product, an allergy to erythritol was suspected, and later confirmed in a double-blind, placebo-controlled OFC test[9].

Another study described an oral immunotherapy (OIT) procedure involving increasing doses of erythritol in an 8-year-old girl with a history of anaphylactic reactions to snacks and sweets containing erythritol as a sweetener. The child was confirmed to be allergic to erythritol through SPT and BAT. An OFC test with erythritol was positive. During the OIT with erythritol, the girl was able to achieve a tolerance of 1.8 g of the sweetener (i.e. a typical amount used to sweeten one cup of coffee)[4,13].

A study by Mori et al. presented the case of a 6-year-old boy who suffered three anaphylactic reactions after consuming low-calorie products containing erythritol (chewing gum, jelly drink). SPT with an erythritol solution at a concentration of 300 mg/mL was positive, while the erythritol BAT was negative. Finally, a positive OFC test confirmed the diagnosis of sweetener allergy[5]. In addition, Kim et al. reported the case of anaphylactic reactions (shortness of breath, facial swelling, hypotension) caused by the ingestion of erythritol, contained in peach juice, in a 36-year-old woman. Allergy to erythritol was confirmed through SPT with consumed juices and erythritol[12].

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References by year of publication	Sweetener	Child	Adult	Symptoms	Diagnostic			
					SPT	IDT	BAT	OFC
Hino et al., 2000[7]	Erythritol		24 years old, f	Systemic urticaria	(+)			(+)
Yunginger et al., 2001[3]	Erythritol		28 years old, f	Generalised urticaria	(–)	(+)		(+)
			50 years old, m	Generalised urticaria, hypotension	(+)	(+)		
Kurihara et al., 2013[8]	Erythritol	5 years old, m		Anaphylaxis	(–)	(+)	(+)	(+)
Shirao et al., 2013[9]	Erythritol	11 years old, m		Urticaria, wheezing	(+)		(+)	(+)
Sugiura et al., 2013[4]	Erythritol	8 years old, f		Systemic urticaria, respiratory symptoms, hypotension	(+)		(+)	(+)
Harada et al. 2016[10]	Erythritol		18 years old, f	Systemic urticaria, abdominal pain, respiratory difficulties, loss of consciousness	(–)		(+)	(+)
Trabado et al., 2017[11]	Maltitol		60 years old, m	Dyspnoea, facial flushing, pharyngeal occlusion	(–)		(+)	
Valls and Malo-Cerisuelo, 2021[2]	Erythritol		61 years old, f	Generalised erythema, perioral and lingual oedema, urticaria, respiratory distress, tachycardia, hypotension				
Kim S et al., 2022[12]	Erythritol		36 years old, f	Dyspnoea, facial oedema, urticaria, hypotension	(+)			
Mori et al., 2022[5]	Erythritol	6 years old, m		Eyelid oedema, wheezing, coughing, vomiting, urticaria	(+)		(–)	(+)

BAT – basophil activation test; **f** – female; **IDT** – intradermal test; **m** – male; **OFC** – oral food challenge; **SPT** – skin prick test.

Tab. 1. Hypersensitivity to erythritol and maltitol – summary of published case reports

Currently, only one case report of hypersensitivity to maltitol is known. Trabado et al. described an anaphylactoid reaction in an adult male who developed facial erythema, shortness of breath, and swelling of the throat after contact of the oral mucosa with maltitol candy. Prick-by-prick SPT with maltitol were performed, and no allergy to the sweetener was found. Hypersensitivity was confirmed in BAT tests with maltitol dilutions[11].

CONCLUSIONS

It is important to consider possible food additives, such as erythritol, when searching for the causative agents of anaphylactic reactions to food. This is particularly important in the developmental age population, as erythritol is sometimes used as a sweetener in syrups. Due to the lack of standardised diagnostic methods for hypersensitivity to food additives, the result of an OFC test is decisive.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

Author contribution

Original concept of study; analysis and interpretation of data: AKo, DT, AKr, RK. Collection, recording and/or compilation of data: DT, RK. Writing of manuscript: AKo, DT. Critical review of manuscript: AKo, AKr, RK. Final approval of manuscript: AKr.

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