






Unexpected Early-Type Hypersensitivity Reactions Induced by Rectal Enema in Two Pediatric Cases and Review of the Literature

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ABSTRACT

Rectal drug formulations (RDFs) are used for local and systemic treatments. In addition to their therapeutic use, they are also be used in the diagnostic evaluations of lower and upper gastrointestinal system diseases. RDFs can lead to the development of early-type hypersensitivity reactions, even anaphylaxis. On the other hand, early-type hypersensitivity reactions following rectal enema administration are extremely rare in children. Here, two pediatric cases are presented where one developed urticaria and angioedema, and the other experienced anaphylaxis, immediately after rectal enema administration for the treatment of constipation. In this case report, through a literature review with two pediatric cases, we believe that we draw attention to the potential early-type hypersensitivity reactions that may develop with rectal enemas, which are frequently used in daily practice.

Keywords: Anaphylaxis, early-type hypersensitivity reactions, methylparaben, pediatric, rectal enema

INTRODUCTION

Rectal drug formulations (RDFs) are used for local treatment in conditions such as constipation, hemorrhoids, anal fissures, and for systemic treatment in cases of pain, fever, nausea/vomiting, seizures, etc. RDFs can also be used in the diagnostic evaluations of lower and upper gastrointestinal system diseases, apart from treatment. These can be found in solid dosage forms such as suppositories, as well as in liquid/semi-liquid dosage forms such as enemas and foams. The use of rectal enemas (REs) as a laxative in the treatment of constipation is one of the most common forms of utilizing RDFs (1).

The development of early-type hypersensitivity reactions following RE administration is extremely rare in children (2-4). The objective of this case report is to pro-

vide a comprehensive literature review, accompanied by two pediatric cases. One case involves the development of urticaria and angioedema, while the other experienced anaphylaxis, both following the administration of RE for constipation treatment.

CASE 1

A twelve-year-old male patient presented to the emergency department with complaints of constipation and abdominal pain, one month after undergoing appendectomy. There were no symptoms of fever, nausea or vomiting, and the physical examination revealed no signs of acute abdomen. Fifteen minutes after the administration of RE (E.S. Enema®), the patient developed urticaria in the bilateral upper extremities and genital area, along with angioedema in the periorbital region.

No accompanying symptoms and/or clinical signs suggestive of anaphylaxis were identified. Within one hour after treatment with diphenhydramine and methylprednisolone, the urticaria completely resolved and the angioedema diminished. No other medication was given to the patient before or during the enema administration. It was the first time that the patient had received enema treatment. There was no known history of atopic disease in the patient or his family. Six weeks after the reaction with urticaria/angioedema diagnosis following RE, the prick to prick test (PtoP) performed with E.S. Enema® was negative. The enema contained sodium dihydrogen phosphate and disodium hydrogen phosphate as active ingredients, and methylparaben sodium, deionized water, and liquid paraffin as excipients. It did not contain latex; however, a skin prick test (SPT) with latex was still performed, and it was found to be negative. Despite a history of mild reaction and negative PtoP and SPT, a provocation test could not be performed due to the unavailability of consent from the patient’s family.

CASE 2

A five-year-old male patient presented to the emergency department with complaints of constipation and abdominal pain. Twenty minutes after the administration of RE (E.S. Enema®), generalized urticaria developed, and the patient experienced several episodes of vomiting. The examination of other systems was normal, and there was no desaturation or hypotension. No other medication was given to the patient before or during the enema administration. Intramuscular adrenaline was administered for the diagnosis of moderately severe anaphylaxis following

RE, and the patient’s symptoms completely subsided within minutes. It was learned that he had received the first RE treatment (B.T. Enema®) one year ago for constipation, and it was administered without any problems. There was no known history of atopic disease in the patient or his family. Six weeks after anaphylaxis, skin tests performed with enema and latex were evaluated as negative.

DISCUSSION

In this case report, two pediatric cases developing early-type drug hypersensitivity after RE administration are presented. Apart from our cases, early-type hypersensitivity with RE has been reported in only three pediatric cases so far (Table I). Similar to the second case, all three cases presented with the development of anaphylaxis (2-4).

Early-type hypersensitivity associated with RE was first described with the use of barium enema, which is employed in the diagnosis of gastrointestinal system diseases (5-7). Subsequently reported case reports have also demonstrated that these reactions can present in a wide spectrum ranging from mild reactions such as urticaria and angioedema to severe anaphylaxis (8-11). In fact, Feczko et al. reported a case of fatal anaphylaxis following barium enema in an adult patient (8). Hypersensitivity reactions associated with barium enema have been attributed to the excipients in the enema, primarily methylparaben and carboxymethylcellulose, as barium sulfate itself is considered inert (5,11). Differently, in a case report by Tarlo et al., it was suggested that carrageenan, present in the barium enema, was the responsible allergen in an adult patient who developed anaphylaxis. This was confirmed by skin prick

Table I: Review of the pediatric cases who developed early-type hypersensitivity reactions after rectal enema reported by previous studies.

	Kimata et al. (2)	Raulin-Gaignard et al. (3)	Arroabarren et al. (4)
Age (months)	10	108	72
Sex	Female	Unspecified	Male
Atopic comorbidities	Asthma	Allergic rhinitis	None
Primary disease	Constipation	Constipation	Unspecified
Clinical symptoms and signs of the reaction	Facial flushing, periorbital edema, wheezing, dyspnea, loss of consciousness	Generalized erythema, loss of consciousness, hypotension	Abdominal pain, diarrhea, generalized urticaria, facial edema, delayed capillary refill
Culprit agent	Latex	Methylparaben	Honey
SPT	Positive	NA	Positive
Specific IgE	Positive	NA	Positive

SPT: Skin prick test, NA: Not applicable

and specific IgE tests (12). Additionally, Thien reported a case of an adult patient who developed anaphylaxis following the use of homemade chamomile tea as a RE (13).

In addition to the excipients in the enema content, there are reported cases of early-type hypersensitivity associated with latex-containing enema tubes in adults, as well as a case of anaphylaxis reported in a pediatric patient (2,14-16). This pediatric case is also a patient who received an RE for constipation, and in vivo and in vitro tests confirmed that the responsible allergen was latex (2). We also checked whether the enema tube contained latex or not to identify the responsible allergen in both of our cases. Although the package insert stated that it did not contain latex, we still performed a SPT with latex on both of our patients.

Apart from this reported pediatric case of anaphylaxis with a RE containing latex in the application device, methylparaben and honey were held responsible in the other two reported pediatric cases where anaphylaxis developed with RE (Table I). In the first case, no diagnostic test was performed for methylparaben, while in the second case, SPTs with honey and *compositae* pollens and specific IgE testing were found to be positive (3,4). The active ingredients (sodium dihydrogen phosphate and disodium hydrogen phosphate) of the enema used in both of our cases are inert in nature. Therefore, we thought that the responsible allergen in our patients could primarily be methylparaben, which is used as an excipient.

Nowadays, methylparabens are widely used as preservatives in the cosmetic, food, and pharmaceutical industries. Therefore, it is believed that sensitization to methylparaben can occur through various pathways (17,18). In our second case, RE had been previously administered, while in our first case, urticaria and angioedema developed upon the initial exposure. Therefore, we suspected that the sensitization of this patient to methylparaben was due to exposure to different products containing methylparaben, apart from the enema. We wanted to perform skin testing with methylparaben itself and conduct specific IgE testing for methylparaben in our patients. However, we were unable to perform these tests as we could not obtain consent from the families of the patients. Additionally, we could not assess whether the reactions that occurred were related to the other excipient, paraffin, in the enema content. Patients were invited to the clinic for testing with paraffin, but they did not return for further evaluation.

In conclusion, it should be kept in mind that not only drugs administered orally or parenterally but also RDFs can lead to the development of urticaria, angioedema, and even anaphylaxis. Considering the widespread use of REs in the daily practice of constipation treatment, caution should be exercised regarding the potential occurrence of hypersensitivity reactions associated with RE administration. In case of a reaction occurring with an enema, the excipients in the enema content should especially be carefully reviewed. The use of latex in the enema tube should be investigated, and accordingly, appropriate tests should be planned for the patients.

Funding

The authors declare that they have not been financially supported.

Conflict of Interest

The authors declare that they have no conflict of interest.

Authorship Contributions

Concept: **Gizem Koken, Hacer Ilbilge Ertoy Karagol**, Design: **Gizem Koken, Hacer Ilbilge Ertoy Karagol**, Data collection or processing: **Gizem Koken, Sinem Polat Terece**, Analysis or interpretation: **Gizem Koken, Sinem Polat Terece, Hacer Ilbilge Ertoy Karagol**, Literature Search: **Gizem Koken, Hacer Ilbilge Ertoy Karagol**, Writing: **Gizem Koken, Hacer Ilbilge Ertoy Karagol**, Approval: **Gizem Koken, Sinem Polat Terece, Hacer Ilbilge Ertoy Karagol, Oksan Derinoz Guleryuz, Arzu Bakirtas**.

Acknowledgements

The authors are very grateful to the patients and their parents for granting permission for publication of this case report.

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