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Revaccination following suspected vaccine-triggered hypersensitivity reactions: experience of a tertiary care centre

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Abstract
Introduction and objectives: Suspected hypersensitivity reactions (HRs) associated with vaccines are frequently reported, but confirmed cases of vaccine-triggered HRs are rare. Suspected HRs should be distinguished from actual HRs. The aims of this study are to identify the rate of actual vaccine-triggered hypersensitivity in patients who were referred to the paediatric allergy clinic due to a suspected HR and to explore the rate of revaccination in a real clinical setting.
Materials and methods: A retrospective study was performed with a group of preschool children who were evaluated by skin and/or provocation tests (PTs) for the suspected HRs following vaccination.
Results: A total of 26 paediatric patients (61.5% male; median age 9 months) with a previous history of suspected vaccine-triggered HR were included. In this group, 69.2% and 38.5% of the patients had a pre-existing atopic disease and an immediate reaction (emerging <1 hour after vaccine administration), respectively. Skin rash was the most frequent clinical presentation (96.1%). Vaccine-triggered anaphylaxis was reported in six patients (23.1%). Measles-mumps-rubella was the most frequently suspected vaccine causing HRs. The skin test positivity with the suspected vaccine was 4%, whereas PTs revealed no reaction after reimmunisation in 76.9% (20/26) of the study participants tested.
Conclusions: Most incidents of skin rashes after immunisation are not suggestive of actual HRs. The results in the current study showed that the majority of the patients presenting with suspected HRs tolerated revaccination, including those with a previous history of suspected anaphylaxis. Revaccination of these patients is safe with adequate precautions. It is absolutely essential to be equipped for the management of anaphylaxis.

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Introduction

Immunisation in accordance with a regular vaccination schedule throughout childhood is extremely important for the good health of children. Childhood vaccination prevents potential life-threatening infectious diseases and provides immunity. To be on the safe side, children should be screened for contraindications before immunisation and vaccines should be administered with appropriate precautions.[1] Suspected hypersensitivity reactions (HRs) associated with vaccines are the most frequently reported events after local reactions and other systemic symptoms such as fever, irritability and malaise. Although reported HRs associated with vaccines are frequent, confirmed HRs are rare.[2,3] Suspected reactions should be distinguished from actual HRs. Patients with a history to a culprit vaccine or its additives should be subject to special precautions for future vaccine doses.[3] However, overdiagnosis might result in incomplete immunisation coverage. Appropriate diagnosis and management of HRs associated with vaccines is one of the fundamental issues in preventive health services for effective and safe immunisation.

In this study, we aimed to identify the rate of actual vaccine hypersensitivity in patients referred to the paediatric allergy outpatient clinic due to a history of suspected vaccine-related HR. Furthermore, we aimed to explore the rate of appropriate immunisation for subsequent doses in these children in a real-life clinical setting.

Materials and methods

This is a retrospective study including paediatric patients who were referred to the paediatric allergy Department of Health Sciences University, Dr. Sami Ulus Women's and Children's Training and Research Hospital over a nearly 5-year period (from 1 January 2015 to 30 September 2019).

Ethical consideration

The study was conducted according to the declaration of Helsinki and ethical approval was received from Keçiören Training and Research Hospital Ethics Committee with the protocol number of 2012-KAEK- 15/2092.

Participants

The study participants were patients between the ages of 0–18 years who were evaluated at the paediatric allergy department because of a history of suspected HR following immunisation. All the patients underwent diagnostic tests (skin and/or provocation tests (PT)) with the suspected vaccine when applicable. Their demographic and clinical features and the results of diagnostic tests performed for the evaluation of vaccine-triggered HRs were recorded. The patients who had experienced adverse events such as constitutional symptoms (fever and/or malaise), or local injection site reactions following vaccination were excluded from the study. Reactions developing during the first hour following vaccine administration were defined as immediate reaction, while reactions developing more than 1 hour after the vaccination were defined as non-immediate reactions.[4] Anaphylaxis was defined according to the clinical criteria reported in the European Academy of Allergy and Clinical Immunology (EAACI) Anaphylaxis guidelines.[5] The international Brighton Collaboration case definition criteria was used for the classification of anaphylaxis.[6] The Hanifin and Rajka criteria were used for the diagnosis of atopic dermatitis[7] and the diagnosis of asthma was based on Global Initiative for Asthma (GINA) guidelines.[8]

Laboratory findings and skin tests

An epidermal skin prick test (SPT) (full concentration of the vaccine) and intradermal test (IDT; 1/100 dilution of full concentration) with the culprit vaccine were performed as recommended in an EAACI position paper.[3] An SPT or an IDT was considered positive if the induration of the vaccine was at least 3 mm larger than that of saline at 15 and 20 minutes after administration, respectively. Additionally, skin testing to vaccine components was performed as follows. Skin testing to gelatine was performed by prick-to-prick test method. The SPT to latex and food allergens [hen's egg (HE), cow's milk (CM)] were performed using standardised allergens (ALK-Abello, Madrid, Spain) and negative (saline) and positive (histamine 10 mg/ml) controls. A wheal diameter of 3 mm or larger than the negative control was considered positive. The determination of specific IgE to food allergens was performed by Immulite 2000 CLIA (CLIA-I, Siemens, Germany).

Food allergy diagnosis was based on a positive oral food PT in patients with a previous history of suspected food induced allergic reaction.[9]

Vaccine provocation test

After relevant skin tests were performed, the suspected vaccine was administered directly with a single full dose to the patients with a negative skin test and to the patients without a history of anaphylaxis as recommended.[3,10] The suspected vaccine was administered in graded doses (0.5 ml vaccine; 0.05 ml 1/10 dilution and full concentration 0.05 ml, 0.10 ml, 0.15 ml and 0.20 ml) to the patients with a previous history of anaphylaxis as recommended.[3,11,12] The flow chart of diagnostic tests and the protocol used to challenge the patients are shown in detail in Figure 1. The necessity for administering the subsequent dose of the culprit vaccine as a PT to the patient was based on the national vaccination schedule in Turkey recommended by the Immunization Advisory Committee of the Ministry of Health of Turkish Republic.[13]

Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 15 (SPSS Inc., Chicago, USA) was used for statistical analysis of the research data. Categorical variables were presented as frequency and percentage, normally distributed numeric variables were presented as mean ± standard deviation, and non-normally distributed numeric variables were presented as median and interquartile range (IQR).

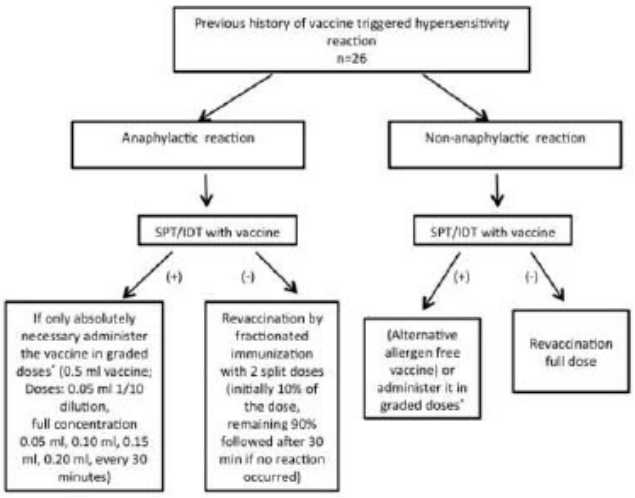

Figure 1 Schematic representation of diagnostic tests.
*Doses were planned to be administered in line with the published guidelines[3,12]

Results

A total of 26 patients with a history of suspected HR to a vaccine were enrolled in the study; 16 of them were male (61.5%), and the median age of the study participants was 9 months [IQR: 4–9 months, minimum–maximum (min–max): 2–86 months]; 18 patients (69.2%) had an allergic disease; 13 patients (50%) were diagnosed with food allergy, and five of them had experienced anaphylactic reactions to CM and/or HE; 12 patients (46.2%) were diagnosed with atopic dermatitis and two patients (7.7%) had asthma. The majority of the participants were infants with a suspected vaccine-triggered HR during the first year of life. Figure 2 shows the culprit vaccines triggering the suspected HRs in our study group.

Skin rash was the most frequent clinical presentation (96.1%) and 19.2% of the patients suffered from itching. Skin symptoms were followed by gastrointestinal system (15.4%), respiratory system (7.7%), cardiovascular system (3.8%) and neurological system (3.8%). The median onset of symptom duration was 3.5 hours (min–max: 5 minutes–24 hours, IQR: 0.5–9 hours). With regard to 26 suspected vaccine-triggered HRs, 38.5% of them were reported within 1 hour of vaccine administration; those were coherent with a possible IgE-mediated allergic reaction. Clinical reactions according to time of onset are shown in Table 1.

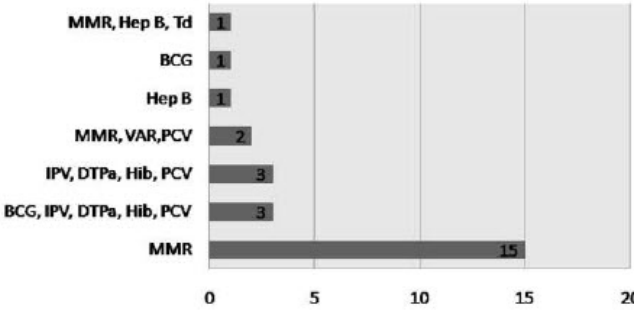

Figure 2 The culprit vaccines in the study group. Hep B: Hepatitis B, Hep A: Hepatitis A, BCG: Bacillus Calmette-Guérin, DTPa: Tetanus-diphtheria-acellular pertussis, Hib: Haemophilus influenza type B, IPV: Inactivated poliovirus, OPV: Oral poliovirus, MMR: Measles-mumps-rubella, PCV13: Pneumococcal conjugate vaccine, Td: Tetanus-diphtheria, VAR: Varicella.

A history of anaphylaxis was reported in six patients (23.1%). The majority of them (84%) were treated with adrenalin injection. None of the patients required hospitalisation after immunisation. Clinical and demographic features of the patients with anaphylaxis following vaccination are given in Table 2. It is important to note that four patients with anaphylaxis in the history had negative STs with the culprit vaccines, but STs were not applicable in two patients. There were no patients with anaphylaxis in the history and ST positivity, so those four patients were revaccinated by fractionated immunisation with two split doses, as designated in Figure 1.

Measles-mumps-rubella (MMR) was the most frequent culprit vaccine causing HRs. In total there were 18 patients (69.2%) who had a history of suspected HR to MMR. Eight from 18 (44.4%) of the reactions were immediate reactions, and six from 18 (22%) of them were presented as anaphylaxis. The characteristic features of the patients who had a history of suspected HR after MMR are shown in Table 3.

SPT to gelatine and latex revealed that only one patient had a positive SPT to latex and to gelatine, but latex allergy and gelatine hypersensitivity were not clinically relevant. SPT and IDT with suspected vaccines were administered to 84.6% of the patients (22/26), and were negative in all but one of the patients. The skin-test positivity rate among 22 tested children with suspected HRs to vaccines was 4%. One patient had a positive skin test with the culprit vaccine as a positive IDT result of 8 mm in diameter with MMR. That patient had experienced an immediate reaction after his first MMR vaccination when he was 9 months old. He developed widespread urticaria and eyelid angioedema in 5 minutes. He was treated with hydroxyzine and methylprednisolone immediately, but recovered completely in 4 hours. When he was 6 months old, he was diagnosed with atopic dermatitis and IgE-mediated CM and HE allergy. He was on an elimination diet. At the time of the adverse reaction with vaccine, the following were the IgE levels to CM: 24 kU/L, casein: 16.9 kU/L, HE: 34 kU/L, total IgE: 234 IU/L. SPTs with gelatine and latex were negative.

Table 1 Clinical reactions according to time of onset in the history.

	Onset of index reaction	
	Immediate (<1 hour)	Non-immediate (>1 hour)
Type of reaction	N	N
Anaphylaxis	4	2
Urticaria-angioedema	8	10
Non-urticarial rash	2	6
Non-cutaneous symptoms	5	3

N indicates the number of patients.

Table 2 Clinical features and diagnostic tests of the patients with anaphylaxis.

Case	Age at admission (months)/ Sex	Allergic disease	Culprit vaccine	Time to symptom onset after vaccination	Symptom/ Brighton classification	Time until test (months)	SPT/ IDT	Provocation test with the culprit vaccine
1	9/M	Urticaria, AE, AD (CM+ HE)	MMR	5 min	Urticaria, AE, cough, vomiting/ Level 2	1	−/−	Negative
2	12/M	Urticaria (HE)	MMR	5th min (vomiting) 5th hour (urticaria)	Urticaria Vomiting/ Level 3	4	−/−	Negative
3	4/M	-	BCG, DTPa, İPV, Hib, PCV	3 hours	Urticaria Decreased level of consciousness/ Level 2	2	−/−	Negative (DTPa, IPV Hib, PCV) NA(BCG)*
4	9/F	-	MMR	4 hours	Urticaria Vomiting/ Level 3	3	−/−	Negative
5	86/M	-	Hep B, MMR, Td	30 min	Vomiting Hypotension Sweating/ Level 2	-	NA*	NA*
6	12/M	Anaphylaxis , AD (CM+HE)	MMR VAR PCV	10 min	Urticaria Wheezing Level 1	-	NA*	NA*

SPT: Skin prick test; IDT: Intradermal test; AD: Atopic dermatitis; AE: Angioedema; CM: Cow's milk; HE: Hen's egg; NA: not applicable; Hep B: Hepatitis B; Hep A: Hepatitis A; BCG: Bacillus Calmette–Guérin; DTPa: Tetanus, diphtheria, acellular pertussis; Hib: Haemophilus influenza type B; IPV: Inactivated poliovirus; OPV: Oral poliovirus; MMR: Measles-mumps-rubella; PCV13: Pneumococcal conjugate; Td: Tetanus, diphtheria; VAR: Varicella; *NA: Not Applicable for children who had not reached the recommended age for future vaccination or no further doses needed.

Before administration of the subsequent dose, to confirm the immunity of MMR the antibody titers (immunoglobulin G levels) to the relevant conditions were checked. Since the SPT with the vaccine was positive and the immune responses to measles-mumps- rubella were sufficient, the second dose of MMR was not administered.

PTs with the culprit vaccines were applicable for 76.9% of the patients (20/26) and no reaction was observed after reimmunisation. The patients who did not need another dose of the culprit vaccine according to the immunisation schedule were not challenged. Considering the parents' preferences and recommendations of the Ministry of Health in Turkey,[13] the diagnostic tests (STs and PT) were not performed for the children who had not reached the recommended age for the future dose of the suspected vaccine. There was no patient who could not be reimmunised with the culprit vaccine according to the immunisation schedule on time due to a previously suspected HR.

Discussion

Suspected HRs to vaccines in children seem to have become a frequent problem associated with public vaccination programmes. Although there are high rates of reported suspected HRs, verified allergic reactions proving real vaccine hypersensitivity are rare.[3] McNeil et al.[14] reported 33 cases of anaphylaxis for 25,173,965 vaccine doses with a rate of 1.31 per million doses in all age groups. Bohlke et al.[15] reported five cases of anaphylaxis for 7,644,049 vaccine doses with a rate of 0.65 per million doses in children. Cheung et al.[16] found an 8% rate of real vaccine allergy in their study group consisting of 73 children who were referred to a tertiary paediatric hospital due to suspected vaccine-triggered HR in a 5-year period. Zafack et al.[2] demonstrated that eight of 135 children experiencing immediate allergic-like events had recurrence of the symptoms on revaccination. In these reports, vaccine hypersensitivity is defined with a positive skin test (IDT) or PT with the culprit vaccine.[16] The patient with positive IDT was not challenged because of the sufficient antibody titers. The rate of vaccine hypersensitivity in our study (excluding four patients who were not challenged or did not undergo skin tests with the suspected vaccine) was 4%, which is lower than the above mentioned reports. However, this difference may be due to the fact that both immediate and non-immediate reactions were included in the current study.

Table 3 The demographic and clinical features of the patients with HRs associated with MMR.

Case	Vaccine	Age at admission (month)/Sex	Allergic disease in the history	Skin test (mm)	spIgE (kU/L)	Time to symptom onset during HR	Symptoms	SPT/IDT vaccine	Provocation Test
	MMR	60/M	Anaphylaxis (CM), U, AE (CM, HE)	CM:10 HE:6	CM:56.2 CAS:36.4 ALA:38 BLG:1.5 HE:3.5	30 minutes	U, AE	−/−	Negative
	MMR	9/F	Anaphylaxis (HE)	CM: 0 HE:6	NA	12 hours	MPE	−/−	Negative
	MMR	9/M	AD, U, AE (CM, HE)	CM:13 HE:6	CM:9.3 CAS:5.5 ALA:0.48 HE:0.77	5 minutes	Anaphylaxis U, AE, cough, vomiting	−/−	Negative
	MMR	12/F	AD	CM: 0 HE: 0	CM:<0.10 HE:<0.10	1 hour	U	−/−	Negative
	MMR	9/F	Anaphylaxis (HE)	CM: 0 HE: 10	CM:<0.10 HE:43	9 hours	U	−/−	Negative
	MMR	13/M	AD, U (CM, HE)	CM: 6 HE: 5	NA	30 minutes	U	−/−	Negative
	MMR	12/M	U (HE)	CM: 0 HE: 0	CM:<0.10 HE:4.09	6 hours	U Vomiting	−/−	Negative
	MMR	12/F	Anaphylaxis (CM), U, AE (CM, HE)	CM:22 HE:13	CM:>100 CAS:>100 BLG: 8.32 HE:15.2	4 hours	U	−/−	Negative
	MMR	12/M	U (HE)	CM: 0 HE: 0	CM:<0.10 HE:<0.18	9 hours	MPE	−/−	Negative
	MMR	12/M	AD, (HE)	CM: 0 HE:6	CM:<0.10 HE:<0.95	13 hours	U	−/−	Negative
	MMR	12/F	Anaphylaxis (HE), U, AE (CM, HE)	CM:8 HE:5	CM:1.69 CAS:0.67 HE:4.5	30 minutes	U	−/−	Negative
	MMR	9/F	-	CM: 0 HE: 0	CM:O.11 CAS:<0.10 HE:0.49	5 hours	U Vomiting	−/−	Negative
	MMR	10/M	U, AE (CM, HE)	CM:13 HE:7	CM:14.9 CAS:9.3 HE:10.6	5 minutes	U, AE	−/+	NA
	MMR	12/M	Asthma, U (HE)	CM:0 HE:0	CM:<0.10 HE:0.76	8 hours	U, AE	−/−	Negative
	MMR	9/M	-	CM:0 HE:0	CM:<0.10 HE:<0.10	3 hours	MPE	−/−	Negative
	MMR VAR PCV	12/M	AD, Anaphylaxis (fish)	CM:0 HE:0	NA	10 minutes	U, Wheezing	NA	NA
	MMR VAR PCV	12/M	AD (HE)	CM:0 HE:4	NA	6 hours	MPE	NA	NA
	MMR Hep B, Td	86/M	-	NA	NA	30 minutes	Vomiting Hypotension Sweating	NA	NA

AD: Atopic dermatitis; AE: Angioedema; CM: Cow's milk; HE: Hen's egg; MPE: Maculopapular eruption; NA: Not Applicable; IDT: Intradermal test; SPT: Skin Prick Test; U: Urticaria; ALA: Alpha-lactalbumin; Cas: Casein; BLG: Beta-lactoglobulin; Hep B: Hepatitis B; Hep A; MMR: Measles-mumps-rubella; PCV; Pneumococcal Conjugate Vaccine; Td: Tetanus, diphtheria; VAR: Varicella.

We did not observe any recurrence of the previous symptoms in any of the reimmunised children. Zafack et al.[2] found that patients with suspected HRs to vaccines could be reimmunised with a rate of 83–97% changing according to the interval to the onset of reaction and type of the vaccine. In the current study, 76.9% of the patients were reimmunised with the suspected vaccine itself without recurrence of the index reaction. The majority of the children with suspected HR were revaccinated safely including patients presenting with suspected anaphylaxis. A low rate of skin test positivity and successful revaccination rate support the safety of the vaccine and the rarity of confirmed allergic reactions.

Suspected HRs after immunisation are frequently observed in infants and adolescents.[4] Our study group mainly consisted of infants. There was no consultation regarding adolescents who fulfil the inclusion criteria within 5 years. According to the National Immunization Schedule of the Ministry of Health of Turkey, hepatitis B (Hep B), hepatitis A (Hep A), bacillus Calmette–Guérin (BCG), tetanus, diphtheria and acellular pertussis (DTPa), haemophilus influenza type B (Hib), inactive polio virus (IPV), oral poliovirus (OPV), MMR, pneumococcal conjugate (PCV13) and varicella (VAR) vaccines are administered free-of-charge to healthy children. The human papilloma virus (HPV) vaccine is not given free-of-charge; thus the rate of immunisation coverage among adolescents is very low in Turkey.[17] The tetanus and diphtheria (Td) vaccine is the only one that is administered to all adolescents at high school. Booster doses for Td mostly cause local swelling at the injection site and systemic reactions are rarely reported.[12] Local reactions were excluded from our study, which would explain the underlying cause for the absence of adolescent patients in the group.

The reports about risk of anaphylaxis after vaccination identified a female predominance after puberty.[14,18] Our study group showed a male predominance both for suspected HRs and suspected anaphylaxis. Changes in sexual hormones have been implicated as a reason for this difference after puberty; however, the underlying mechanism is unknown for pre-puberty.[14]

Pre-existing atopic diseases were noteworthy in our study group. Zafack et al.[2] reported a history of atopy in 24% of patients who consulted for suspected vaccine-associated, allergic-like events, whereas McNeil et al.[14] reported that 85% of the patients with confirmed vaccine-triggered anaphylaxis had pre-existing atopic diseases. The most common atopic diseases in our group were food allergy and atopic dermatitis, while asthma was the most frequent one in McNeil's study.

Vaccine-triggered anaphylaxis is rare and the related fatality rate is extremely low.[12] The rate of anaphylaxis in the history of the patients in the current study seems to be relatively high, but our cohort consists of children presenting with a suspected HR, rather than the general population. Baxter et al.[4] identified that 2.4% of the cases with potential immediate HRs following vaccination were reported as anaphylaxis. Cheung et al.[16] revealed that 16.4% of the patients with a potential IgE- mediated adverse event following vaccination had a history of anaphylaxis. In our study group, four of six patients with a history of anaphylaxis could be reimmunised with the suspected vaccine without recurrence of the index reaction. In this case, a history of anaphylaxis to a vaccine is not a contraindication for reintroduction. Actual vaccine hypersensitivity should be ascertained by allergological evaluation. When a subsequent dose of the culprit vaccine is necessary, reimmunisation with the suspected vaccine by graded desensitisation is a successful method that can be performed even if skin tests for vaccines are positive. However, this approach should not be used where expertise and equipment for managing anaphylaxis is not available.[3]

MMR was the most frequently suspected vaccine causing HRs and also causing anaphylaxis in our study group, a finding that is compatible with the existing literature.[14,19] McNeil et al.[14] defined that the rate of anaphylaxis including all vaccinations at 1.31 per million doses whereas it is 5.14 per million doses when solely including MMR, which causes the highest rates. According to Chilean nationwide reports MMR-triggered anaphylaxis increased from an average of 2.6 to 10 per million doses from 2012 until 2018.[19] Pre-existing atopic disease in the current study was 69% in the whole group of patients; however, it rose to 83% when patients with a suspected HR due to MMR vaccination were considered. In addition, 33% of the patients with a suspected MMR-triggered HR had a history of CM allergy and 67% of them had a history of HE allergy which revealed that. Food allergy with CM and/or HE were apparently noticeable in the patients with suspected HR to MMR in the current study. This result would be due to the fact that the parents of the infants who had a history of food protein induced allergic reaction paid more attention to non-specific rashes observed after immunisation than parents of healthy children. However, Piñones et al.[19] recently reported patients with CM allergy who developed HRs following MMR vaccines containing hydrolysed CM allergens. In their study, the authors emphasised the potential risk of HRs that may occur after the administration of MMR vaccines containing hydrolysed CM allergens in children with severe CM allergy. Since the regular MMR vaccine is propagated in chick embryo cell culture, the individuals who have IgE-mediated egg allergy are suggested to be vaccinated with caution. In Turkey, the regular MMR vaccine does not contain CM allergens, and used to be administered to children at 9 and 12 months of age. For the last 6 months, according to the policy carried out by the Ministry of Health, the sole measles vaccine containing lactalbumin has begun to be administered to infants at 9 months of age instead of MMR. Future studies will show the results of this alteration (i.e., whether there will be an increase in HR reactions after the administration of measles vaccine containing lactalbumin in children with CM allergy) since an association was presented in recent reports.

The low number of participants in our study might be considered a limitation; however, as with other studies investigating drug HRs, this is a descriptive study. The number of patients in this study is sufficient to present the real-life experience and reveal the way for appropriate management of the potential cases with suspected vaccine-triggered HRs.

In conclusion, most instances of skin rashes after immunisation are not suggestive of actual vaccine-triggered HRs. Our results confirmed the rarity of allergic

events after immunisation. There is no need to interrupt or delay immunisation due to allergic-like events related to vaccines. Under appropriate circumstances and with adequate precautions revaccination of the patients presenting with suspected HRs after vaccination is safe. Recognising, treating and being equipped for the management of anaphylaxis is absolutely necessary. Concerns about vaccine-related HRs including anaphylaxis can be handled by education for management of such reactions.

Conflict of interest

All authors declare that they have no conflicts of interest.

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References

1. Ezeanolue E, Harriman K, Hunter P, Kroger A, Pellegrini C. General best practice guidelines for immunization. Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP). Available from: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf [Accessed 04 May 2020].
2. Zafack JG, De Serres G, Rouleau I, Gariépy MC, Gagnon R, Drolet JP, et al. Clinical approach used in medical consultations for allergic-like events following immunization: Case series report in relation to practice guidelines. J Allergy Clin Immunol Pract. 2017;5:718–27.e1. https://doi.org/10.1016/j.jaip.2016.09.048
3. Nilsson L, Brockow K, Alm J, Cardona V, Caubet JC, Gomes E, et al. Vaccination and allergy: EAACI position paper, practical aspects. Pediatr Allergy Immunol. 2017;28:628–40. https://doi.org/10.1111/pai.12762
4. Baxter CM, Clothier HJ, Perrett KP. Potential immediate hypersensitivity reactions following immunization in preschool aged children in Victoria, Australia. Hum Vaccin Immunother. 2018;14:2088–92. https://doi.org/10.1080/21645515.2018.1460293
5. Muraro A, Roberts G, Worm M, Bilò MB, Brockow K, Fernández Rivas M, et al. Anaphylaxis: Guidelines from the European Academy of Allergy and Clinical Immunology. Allergy. 2014;69:1026–45. https://doi.org/10.1111/all.12437
6. Gold MS, Gidudu J, Erlewyn-Lajeunesse M, Law B. Can the Brighton collaboration case definitions be used to improve the quality of Adverse Event Following Immunization (AEFI) reporting? Anaphylaxis as a case study. Vaccine. 2010;28:4487–98. https://doi.org/10.1016/j.vaccine.2010.04.041
7. Hanifin JM. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Suppl). 1980;92:44–7.
8. 2020# GINA report, global strategy for asthma management and prevention. Available from: https://ginasthma.org/ [Accessed 04 May 2020].
9. Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G, Beyer K, Bindslev-Jensen C, et al. EAACI food allergy and anaphylaxis guidelines: Diagnosis and management of food allergy. Allergy. 2014;69:1008–25. https://doi.org/10.1111/all.12405; https://doi.org/10.1111/all.12441; https://doi.org/10.1111/all.12398; https://doi.org/10.1111/all.12429
10. Kelso JM, Li JT, Nicklas RA, Blessing-Moore J, Cox L, Lang DM, et al. Adverse reactions to vaccines. Ann Allergy Asthma Immunol. 2009;103(4 Suppl 2):S1–S14. https://doi.org/10.1016/S1081-1206(10)60350-X
11. Wood R, Setse R, Halsey N. Irritant skin test reactions to common vaccines. J Allergy Clin Immunol. 2007;120:478–81. https://doi.org/10.1016/j.jaci.2007.04.035
12. Kelso JM, Greenhawt MJ, Li JT, Nicklas RA, Bernstein DI, Blessing-Moore J, et al. Adverse reactions to vaccines practice parameter 2012 update. J Allergy Clin Immunol. 2012;130:25–43. https://doi.org/10.1016/j.jaci.2012.04.003
13. Childhood immunization schedule of the Ministry of Health of Turkish Republic. T.C. Sağlık Bakanlığı Çocukluk Dönemi Aşı Takvimi. Available from: https://asi.saglik.gov.tr/asi-takvimi/ [Accessed 04 May 2020].
14. McNeil MM, Weintraub ES, Duffy J, Sukumaran L, Jacobsen SJ, Klein NP, et al. Risk of anaphylaxis after vaccination in children and adults. J Allergy Clin Immunol. 2016;137:868–78. https://doi.org/10.1016/j.jaci.2015.07.048
15. Bohlke K, Davis RL, Marcy SM, Braun MM, DeStefano F, Black SB, et al. Risk of anaphylaxis after vaccination of children and adolescents. Pediatrics. 2003;112:815–20. https://doi.org/10.1542/peds.112.4.815
16. Cheung A, Choo S, Perrett KP. Vaccine allergy? Skin testing and challenge at a Tertiary Pediatric Hospital in Melbourne, Australia. J Allergy Clin Immunol Pract. 2019;7(5):1541–49. https://doi.org/10.1016/j.jaip.2019.01.025
17. Kumru Ş, Yalnızoğlu Ç, Topal S, Altınkaynak S. The relationship between ımmunization status and socio-demographic factors of adolescents. Hemşirelikte Araştırma Geliştirme Dergisi. 2018;20:33–43.
18. Rouleau I, De Serres G, Drolet JP, Skowronski DM, Ouakki M, Toth A, et al. Increased risk of anaphylaxis following administration of 2009 AS03-adjuvanted monovalent pandemic A/H1N1 (H1N1pdm09) vaccine.Vaccine. 2013;31:5989–96. https://doi.org/10.1016/j.vaccine.2013.10.033
19. Piñones M, Landaeta M, Bustos P, Toche P, Morales P, Escobar C, et al. Hypersensitivity reactions to measles-mumps-rubella vaccine in patients with IgE-mediated CM allergy. J Allergy Clin Immunol Pract. 2020;8:349–51. https://doi.org/10.1016/j.jaip.2019.06.040