

Measles-Mumps-Rubella vaccine for children with egg allergy: Is admission for inpatient vaccination necessary?

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ABSTRACT

Introduction: Children who develop any hypersensitivity reaction to eggs are routinely referred to hospital for Measles-Mumps-Rubella (MMR) vaccination as inpatients to prevent anaphylaxis. We aimed to study the association between hypersensitivity reactions after egg exposure and similar reactions after MMR immunisation; and examine the necessity of hospital admission for vaccination.

Methods: A prospective observational study was conducted in Paediatric Department in Bukit Mertajam Hospital, Penang, between March and December 2014. Children referred from local polyclinics for inpatient MMR vaccination because of a history of egg allergy were recruited. The children were observed in the ward for post vaccination allergic reactions. Concurrently, a group of children without egg allergy was recruited from those admitted for other illnesses but had recent MMR vaccination at polyclinics. Parents of these children were interviewed and asked if they had observed any reactions post vaccination. In both groups, sociodemographics, medical history and family history of atopy were collected.

Results: Eighty-seven subjects were recruited in this study. Fifty-four infants with egg allergy had previous mild allergic reactions after exposure to eggs or egg-related products. They were associated with a family history of egg hypersensitivity, personal history of acute gastroenteritis and upper respiratory tract infections. Two of them developed cutaneous rashes post vaccination during observation, but none developed anaphylactic or anaphylactoid reactions. Two infants among those without egg allergy had post vaccination fever. There was no association between egg allergy and hypersensitivity reactions to MMR vaccine ($p=0.632$).

Conclusions: MMR vaccine can be safely administered to children with mild egg allergy, hence admission for vaccination in the hospital is not warranted. Risk stratification is required to ensure only infants with severe reactions will be admitted for vaccination.

KEY WORDS:

MMR vaccination, hypersensitivity, egg allergy, hospital admission

INTRODUCTION

Since 2002, the two doses of measles-mumps-rubella (MMR) vaccine have been incorporated into the Malaysian National

Expanded Programme of Immunisation. The programme recommends that all children be given their first dose of MMR vaccine at the age of 12 months, and second dose by seven years.¹ This has recently been changed to 9 and 12 months old. The trivalent vaccine is composed of live attenuated viruses, in which measles and mumps are prepared in chick embryo cell cultures and may contain traces of egg antigen.² The National Clinical Practice Guideline on Childhood Immunisation states that children with allergy to eggs can safely receive the MMR vaccine, as the rare and serious allergic reactions after MMR vaccination are believed to be caused by other components of the vaccine.³ However, there are still concerns in the healthcare community over the risk of anaphylactic reaction to the MMR vaccine among these children.³ Thus, it has become common practice for health staff from polyclinics to advise parents to expose their children to eggs or egg-related products prior to MMR immunisation. If any form of hypersensitivity reaction is observed, even without a preceding skin prick test to egg allergen, these children will be referred to local hospitals for MMR vaccine administration as inpatients, anticipating the event of acute anaphylaxis. They will be discharged if they remain well after four to six hours of observation. There are similar practices in Ireland, Denmark and New Zealand.^{4,6} Over the years, many children have been referred to Bukit Mertajam Hospital, one of the district hospitals in mainland of Penang, for this purpose. The objective of this study was to examine the association of egg allergy and risk of allergic reaction to MMR vaccination, and to evaluate if admission for inpatient vaccination is necessary for children with egg allergy.

MATERIALS AND METHODS

In this prospective observational study, we recruited infants who were admitted to paediatric ward in Bukit Mertajam Hospital for MMR vaccination as inpatients between 1st March and 31st December 2014. These infants were referred from various polyclinics located at central region of Seberang Prai, Penang, as they were reported by their guardians to have experienced egg hypersensitivity irrespective of severity. Children who were HIV positive and suspected or confirmed primary immunodeficiency were excluded. Other exclusion criteria include: parents not keen to participate, no legal care provider to give consent and incomplete data collection.

A trained paediatric medical officer took a full history from the parents, focusing on hypersensitivity reaction towards eggs or egg-related products. Sociodemographics, past

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Table I: Sociodemographics, medical and family histories, and allergic reactions towards MMR vaccination of all infants

Characteristics	All subjects (n=87)		Subjects with history of egg hypersensitivity (n=54)		Subjects with history of egg hypersensitivity (n=33)		p-value
	n	%	n	%	n	%	
Demography							
Weight ^a (kg)	8.7	(1.84)	8.9	(2.01)	8.3	(1.47)	0.152 ^b
Gestational age ^a (weeks)	38.4	(1.66)	38.6	(1.83)	38.0	(1.27)	0.156 ^b
Race							
Malay	65	74.7	35	64.8	30	90.9	0.070 ^c
Others	22	25.3	19	35.2	3	9.1	
Gender							
Male	49	56.3	25	46.3	24	72.7	0.016 ^c
Female	38	43.7	29	53.7	9	27.3	
Past history of							
None	36	41.4	18	33.3	18	54.5	0.051 ^c
Bronchial asthma	5	5.7	1	1.9	4	12.1	0.066 ^d
Eczema	5	5.7	4	7.4	1	3.0	0.646 ^d
Allergic rhinitis	0	-	0	-	0	-	-
Allergic conjunctivitis	0	-	0	-	0	-	-
Allergy to other products ^e	9	10.3	8	14.1	1	3.0	0.144 ^d
Bronchiolitis	8	9.2	5	9.3	3	9.1	1.00 ^d
URTI	28	32.2	22	40.7	6	18.2	0.029 ^c
AGE	18	20.7	15	27.8	3	9.1	0.037 ^c
Otitis media	1	1.1	1	1.9	0	-	1.00 ^d
Febrile seizure	1	1.1	0	-	1	3.0	0.379 ^d
Pneumonia	8	9.2	1	1.9	7	21.2	0.004 ^d
Others ^f	11	12.6	10	18.5	1	3.0	0.046 ^d
Family history of							
Egg allergy	11	12.6	10	18.5	1	3.0	0.045 ^d
Atopy	16	18.4	9	16.7	7	21.2	0.595 ^c
Allergy to other products ^e	13	14.9	8	14.8	5	15.2	1.00 ^d
Allergic reactions towards MMR vaccination							
Overall	4	4.6	2	3.7	2	6.1	0.632 ^d
Cutaneous rashes	2	2.3	2	3.7	0	-	0.524 ^d
Post-vaccination fever	2	2.3	0	-	2	6.1	0.141 ^d

Note: ^aPresented as mean (standard deviation); ^bIndependent t-test; ^cPearson's Chi-square test for independence; ^dFisher's Exact test; ^eAllergy to seafood, nuts, penicillin, chicken and lychee; ^fOthers referred to patent ductus arteriosus, gastrointestinal reflux disease, urinary tract infection, hydrocephalus, hemangioma, arm band and haemophilia; URTI denotes upper respiratory infections; AGE denotes acute gastroenteritis.

Table II: Symptoms of egg allergy reported by guardians of children with egg allergy (n=54)

Symptoms	n	%
Cutaneous		
Rash	48	88.9
Itchiness	33	61.0
Swelling / oedema	15	27.8
Respiratory		
(Transient) Shortness of breath	1	1.9
(Mild) Wheezing	2	3.7
Stridor	0	0
Apnoea/respiratory arrest	0	0
Cardiovascular		
Palpitation, syncope or shock	0	0
Gastrointestinal		
Vomiting	2	3.7
Diarrhoea	1	1.9
Abdominal pain	0	0
Abdominal distension	0	0
Neurological		
Seizure	0	0
Symptoms necessitating hospital admission	1	1.9
Symptoms necessitating intensive care unit admission	0	0

medical history and family history of atopy were also collected. The doctor then conducted a clinical examination, after which a trained nurse injected 0.5 ml of the vaccine intramuscularly into the right or left thigh. Priorix® from GlaxoSmithKline Pharma, a lyophilized combination vaccine, was used for the MMR vaccination. The infant was observed in the general paediatric ward for at least four hours, for any hypersensitivity reaction, before being discharged. All relevant information was recorded in the data reporting sheet. If the information collected was incomplete, the principal investigator would follow up via phone calls to the subject's parents.

Concurrently, a separate group of infants was recruited. They were infants admitted to hospital for other illnesses but did not experience any egg allergy after exposure to eggs or egg-related product, and had recently received MMR immunisation in the community setting. History taking was similarly performed. Information on possible allergic reactions post vaccination was gathered by asking the parents to recall any such reactions.

This study was registered with the National Medical Research Register (NMRR-13-1599-17487) and approved by the Malaysian Research Ethics Committee (MREC) of the Ministry of Health, Malaysia. Informed written consent was obtained from the guardians.

Data was collected and analysed using Statistical Package for Social Sciences (SPSS) version 22. The normally distributed continuous variables are presented as mean (standard deviation), while categorical variables are presented as frequency and proportion. Descriptive analyses were performed on demographic characteristics, past medical history, family history and presenting symptoms for egg hypersensitivity. Inferential analyses were performed on these characteristics between infants with and without egg allergy. Statistical significance was set at p-value less than 0.05.

RESULTS

Out of 92 infants admitted as inpatients, 54 were recruited into the study. Another 33 infants were recruited from those who had their immunisation in the community setting. All children were one year of age. The majority were of Malay ethnicity (74.7%) (Table I). More than half of them were males, with an overall gestational age of 38.4 (1.66) weeks. Among infants with a history of egg allergy, more were females and of Malay ethnicity (Table I). There were no differences in terms of personal and family history of atopy between the two groups. More infants with egg hypersensitivity had a past history of upper respiratory infections ($\chi^2=4.8$, $df=1$, $p=0.029$) and acute gastroenteritis ($\chi^2=4.36$, $df=1$, $p=0.037$), but fewer had pneumonia ($\chi^2=9.20$, $df=1$, $p=0.004$), when compared with their counterparts. A higher proportion of these infants had positive family history of egg hypersensitivity ($\chi^2=4.45$, $df=1$, $p=0.046$).

Cutaneous rash (88.9%) was the commonest reaction observed by the guardians when their children were exposed to eggs or egg-related products, followed by itchiness (61%)

and cutaneous swelling or oedema (27.8%) (Table II). A few infants developed transient shortness of breath, mild wheezing and gastrointestinal upset, all of whom resolved spontaneously without seeking treatment. Only one infant was admitted to hospital for two days for conservative management due to cutaneous rash and swelling, and parental concerns. None had reported anaphylactic or anaphylactoid reactions, requiring admission to intensive care unit. However, none of these infants underwent any skin prick or radioallergosorbent (RAST) tests to ascertain their allergic status to eggs.

Among the 54 infants vaccinated as inpatients, two developed cutaneous rashes within two hours post-injection, which spontaneously resolved upon follow up. None developed anaphylactic or anaphylactoid reactions. Two out of the 33 infants without egg allergy experienced post vaccination fever which resolved with conservative management. There was no statistically significant association between history of hypersensitivity to eggs or egg-related products and allergic reactions towards MMR vaccination ($\chi^2=0.26$, $df=1$, $p=0.632$).

DISCUSSION

Egg white protein allergy is one of the common childhood allergies detected early in life, but usually outgrown by age 2 to 3 years.⁷⁻⁹ A local study demonstrated that IgE positivity for children with egg allergy was lower among older children aged 2-10 years compared to those <2 years; this is suggestive of tolerance development.¹⁰ The majority of infants in our study experienced limited skin symptoms (27.8-88.9%) with less systemic reactions involving the respiratory (1.9-3.7%) and gastrointestinal (1.9-3.7%) systems. This is in contrast to a cohort study among 213 children with egg allergy, aged 3-15 months, in the United States where there were equal proportion of limited skin (43.7%) and systemic (43.7%) involvement.⁹ The marginal significance of association between positive family history of egg allergy and children with egg allergy in this study is supported by a population study by Koplin JJ *et al.* This relationship is possibly due to shared environmental and genetic factors.¹¹ More infants with egg allergy had upper respiratory infection and acute gastroenteritis, but less pneumonia, as compared to the infants without egg allergy. This observation warrants further explorations in another study.

Our study showed that there was no association between mild hypersensitivity reaction after exposure to eggs or egg-related products and allergic reaction to MMR vaccination. Another local study reported none of the infants with egg allergy developed reactions towards MMR vaccination as inpatient.¹² There are other evidence supporting safe administration of MMR vaccine to children allergic to eggs, even among those with severe allergic reactions.^{4,13-15} Most of the children who had anaphylactic reactions to MMR vaccine were not allergic to eggs.^{13,16,17} The reaction might be attributable to non-egg protein allergens such as gelatine, which is present in high concentration in the vaccine as a stabiliser.^{18,19} Therefore, in cases of allergic reactions induced by MMR vaccine, sensitisation to gelatine should be explored.¹⁵ In addition, an investigation on an outbreak of hypersensitivity-type

reaction after the national MMR immunisation campaign in Brazil revealed the absence of association with prior egg allergy and other food products including gelatine, but implicated the dextran stabiliser in the MMR vaccine produced by a specific manufacturer.²⁰ MMR vaccine is as safe as any other vaccine and a history of egg allergy should not delay the vaccination schedule, as supported by various international guidelines.^{7,21,22} Only children who had severe allergy leading to cardiorespiratory reactions, and those with coexisting severe, chronic asthma need to be vaccinated in hospital.^{21,22}

Despite the evidence as described above, referral for vaccination in hospital, even for children with mild egg allergy reactions, remains common in our local health care setting. Concerns of litigation, should the anaphylactic reaction occur, might have led to reluctance to vaccinate these children as outpatients. Admission for inpatient vaccination requires additional logistics arrangement which can be a burden to the parents and entire family. In this study, more than half of the children (59.3%) had both their parents working full time. Meanwhile, each child in our study had an average of two siblings, with one-third of them school going. Such admission to the ward usually occurs during weekdays and the accompanying parents need to be absent from work, thus interrupting the family routine. Besides, it can increase parental anxiety unnecessarily and may cause delay or even default in vaccination.^{4,5,23} Admission also predisposes the children to risk of nosocomial infection. This can further decrease the herd immunity and increase risk of unvaccinated children contracting the disease.⁵ Unnecessary admissions also pose an extra burden to the already constrained healthcare system.⁶

This study has its limitations. Children with reported egg allergy did not undergo skin prick testing before MMR vaccination, followed by desensitisation for those with a positive cutaneous test, as suggested by earlier literature.^{14,24} However, some argued it was an invalid screening tool to predict children at risk.²⁵ Data on hypersensitivity reaction towards MMR vaccination in the community was subjected to observation and recall biases from parents. The absence of differences in terms of personal history of atopy between the two groups might be due to the small sample size of our study.

CONCLUSION

We conclude that egg allergy is not associated with allergy towards MMR vaccine. It might be safe to vaccinate children with mild hypersensitivity reaction to eggs or egg-related products. Only children with history of anaphylactic or anaphylactoid reactions warrant referral for vaccination in hospital. We also recommend to cease the practice of advising parents to expose their children to eggs prior to MMR vaccination, due to the lack of association between egg allergy and MMR hypersensitivity reactions.

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