

Safety of COVID-19 Vaccines and the Effect of COVID-19 Infection in Children with Milk Allergies

Junghyun Kwon^{1*}, Catherine K. Zhu², Pasquale Mule, Msc¹, Bruce Mazer¹, Christine McCusker¹, Liane Beaudette¹, Duncan Lejtenyi, Msc¹, Danbing Ke, PhD¹, Manel Ouamrane, Bsc¹, Moshe Ben-Shoshan, MD, Msc¹

Abstract

This study investigates the safety of COVID-19 vaccines and infection in children with milk allergies. The cohort comprised 50 children with challenge-confirmed milk allergy undergoing oral immunotherapy. Among them, 90% received the first dose, and 88% received the second dose of COVID-19 vaccines (mainly BNT162b2). Results showed that 51.1% had no symptoms after the first dose, and 56.8% had no symptoms after the second dose. Common side effects included injection site reactions, flu-like symptoms, and chest discomfort. None reported allergic reactions or respiratory symptoms. Interestingly, 64% of the children had a history of COVID-19 infection, mostly presenting flu-like symptoms. While the study suggests minimal risk for adverse reactions in children with milk allergies, the limitations, such as a small sample size and specificity to milk allergies, underscore the necessity for broader investigations. This research highlights the ongoing need to refine risk assessments and ensure the safety of COVID-19 vaccination across diverse pediatric populations.

Keywords: Milk allergy; COVID-19; Vaccination; Safety; Children

Introduction

Data are sparse on the risk of allergic reactions associated with COVID-19 infection and COVID-19 vaccination among individuals with food allergies. We aimed to assess the effect of COVID-19 infection and the safety of COVID-19 vaccines among patients with milk allergies.

Milk allergy is an IgE mediated immune system response to milk and is one of the most common food allergies with a global incidence estimated at 2% to 7.5% in the first year of life [1]. Initial reports on COVID vaccine safety raised concern regarding increased risk for allergic reactions in those with a history of anaphylaxis following the Pfizer-BioNTech BNT162b2 (hereafter referred to as BNT162b2) and the Moderna mRNA-1273 (hereafter referred to as mRNA-1273) COVID-19 vaccine [1-2]. The current government guidelines do not involve any restrictions for COVID-19 vaccination for children with milk allergy. However, despite the very low risk, there is a lack of safety data, which may contribute to vaccine hesitancy [2]. We aimed to assess the safety of COVID-19 vaccines in a cohort of children with milk allergy.

Methods

From June 2022 - June 2023, we contacted families with patients aged 4-30 years old from a previously established registry of children with milk allergies recruited for oral immunotherapy from two allergy clinics in Montreal,

Affiliation:

¹Division of Pediatric Allergy and Clinical Immunology, Department of Pediatrics, McGill University Health Centre, QC, Canada

²Faculty of Medicine, McGill University, QC, Canada

*Corresponding Author

Junghyun Kwon, Division of Pediatric Allergy and Clinical Immunology, Department of Pediatrics, McGill University Health Centre, QC, Canada

Citation: Junghyun Kwon, Catherine K. Zhu, Pasquale Mule, Bruce Mazer, Christine McCusker, Liane Beaudette, Duncan Lejtenyi, Danbing Ke, Manel Ouamrane, Moshe Ben-Shoshan. Safety of COVID-19 Vaccines and the Effect of COVID-19 Infection in Children with Milk Allergies. Archives of Clinical and Medical Case Reports. 8 (2024): 210-213.

Received: March 13, 2024

Accepted: March 26, 2024

Published: November 07, 2024

Canada. All children with milk allergies (vaccinated or not) who were reachable by phone and consented to participate in the study were included in the analysis.

Data was collected at study entry with a questionnaire on demographics and comorbidities. Our standardized COVID-19 questionnaire queried on COVID-19 vaccination status and on the post-vaccination development of urticaria/angioedema, respiratory or gastrointestinal symptoms, anaphylaxis (defined as a reaction involving at least two systems and/or hypotension) or any other symptom [4]. An additional questionnaire was given to participants infected with COVID-19 to assess their symptoms.

All data analysis was performed using R version 4.3.1. The demographic data and the association of common post-vaccination symptoms with first and second COVID-19 vaccination visits were analyzed via generalized estimating equation logistic regression using the R package geepack. The statistical difference in children reporting side effects after the first and second doses of vaccination was calculated using the Chi-Square test.

A total of 50 patients with challenge-confirmed milk allergy undergoing oral immunotherapy treatment at the Montreal Children’s Hospital were included in the study. Thirty (60%) were male and their median age was 17 (interquartile range (IQR) = 7.5).

Results

Five children (10.0%) were not vaccinated (Table 1) as they have all previously been infected with COVID-19. One child (2.0%) only received the first dose of the COVID-19 vaccine and not the second dose for unspecified reasons.

Forty-five children (90.0%) received the first dose of the COVID-19 vaccine (Table 1), 42 (93.3%) received BNT162b2 and 3 (6.7%) received mRNA-1273. Following vaccination, 23 (51.1%) did not experience any symptoms, 18 (40.0%) had an injection site reaction (hereafter shown as ISR, i.e., redness, soreness, swelling), three patients (6.7%) reported flu-like symptoms (chills, fatigue, arthralgia, headache, mild fever, myalgia), and 1 patient (2.2%) reported chest discomfort or palpitations (Table 2).

Forty-four children (88.0%) received the second dose of the COVID-19 vaccine (Table 1), 39 (88.6%) received BNT162b2 and 5 (11.4%) received mRNA-1273. Twenty-five (56.8%) did not report any post-vaccination symptoms, 17 patients (38.6%) reported ISR and 2 patients reported flu-like symptoms (4.6%) (Table 2).

For both the first and second doses of COVID-19 vaccines (BNT162b2 and RNA-1273), no patients had been infected by COVID-19 at the time of vaccination. Additionally, no

Table 1: Patient demographics, comorbidities.

	Covid-19 infection	First Dose	Second dose	Unvaccinated children	Difficulty with mask use	Cohort of all milk OIT patients
Population, N(%)	N=32 (64%)	N = 45 (90%)	N = 44 (88%)	N = 5 (10%)	N=6 (12%)	N = 50
Sex: males, N (%)	17 (53.1%)	27 (60%)	27 (61.4%)	3 (60%)	4 (66.7%)	30 (60%)
Age at vaccination (y), (median-IQR)	NA	15.6 (15.0-7)	15.7 (15.5-7)	NA	NA	15.7 (15.0-7)
Asthma, N (%)	19 (59.4%)	29 (64.4%)	29 (64.4%)	2 (40%)	4 (66.7%)	31 (62%)

NA: Not applicable

Table 2: Medication and side effects after COVID-19 infection and first and second doses of COVID-19 vaccine.

		COVID-19 infection (N=32)	First dose (N = 45)	Second dose (N = 44)	P-value
Type of vaccine	BNT162b2 (Pfizer-BioNTech)	NA	42 (93.3%)	39 (88.6%)	NA
	mRNA-1273 (Moderna)	NA	3 (6.67%)	5 (11.4%)	NA
Medication intake on the day, N (%)	Acetaminophen (tylenol)	4 (12.5%) ¹	1 (2.22%) ¹	1 (2.27%) ¹	NA
	Ibuprofen(Advil)	4 (12.5%) ¹	3 (6.67%) ¹	2 (4.55%) ¹	NA
	Ciclesonide	1 (3.13%)	1 (2.22%)	1 (2.27%)	NA
	Albuterol (ventolin)	3 (9.38%)	0 (0%)	0 (0%)	NA
	Montelukast	0 (0%)	1 (2.22%)	1 (2.27%)	NA
	None	21 (65.6%)	40 (88.89%)	40 (90.9%)	NA

Symptoms and Side effects, N (%)			N (%)	N (%)	Onset of symptoms (within ~ days)	N (%)	Onset of symptoms (within ~days)	Chi-square statistic= 0.63 P-value= 0.89 > 0.05
	Allergic reaction							
		Hives/urticaria	0 (0%)	0 (0%)	NA	0 (0%)	NA	
		Flare of current hives	0 (0%)	0 (0%)	NA	0 (0%)	NA	
		Swelling of face/ tongue/ throat	0 (0%)	0 (0%)	NA	0 (0%)	NA	
		Respiratory symptoms	3 (9.38%)	0 (0%)	NA	0 (0%)	NA	
		Chest discomfort or palpitations	0 (0%)	1 (2.22%)	1	0 (0%)	NA	
		Flu-like symptoms (chills, fatigue, arthralgia, headache, mild fever, myalgia)	28 (87.5%)	3 (6.67%)	1	2 (4.55%)	1	
		Severe/high fever (>39°C)	0 (0%)	0 (0%)	NA	0 (0%)	NA	
		Injection site reaction (redness, soreness, swelling)	NA	18 (40%)	1	17 (38.6%)	1	
		No symptoms	1 (3.13%)	23 (51.1%)	NA	25 (56.8%)	NA	

NA: Not applicable

¹One patient took both Acetaminophen and Ibuprofen

patients reported any allergic reactions such as respiratory symptoms after vaccination. Furthermore, there was no statistically significant difference (chi-square statistic= 0.63, P-value = 0.89 > 0.05) when done the Chi-Square test between the proportion of children having reported each type of side effect after the first and second-dose vaccines (Table 2).

A total of 32 patients (64.0%) had been infected by COVID-19. Most infected children (28, 87.5%) reported flu-like symptoms, three (9.4%) reported respiratory symptoms which seemed to be an allergic reaction and one (3.1%) was asymptomatic. At the time of infection, all 32 patients had not been vaccinated (Table 1).

Our results are in line with previous studies in adults suggesting that 99.22% of patients with previous severe allergic diseases (mainly drugs) tolerated mRNA vaccination with no reaction [5]. Another study suggested that the rate of allergic reactions, particularly anaphylactic reactions to the BNT162b2 vaccine, is higher than for other commonly used vaccines, though they can be safely immunized by using an algorithm [4]. Even though there have been incidents like the two employees of the National Health Service (NHS) in England developing severe allergic reactions after being administered the COVID-19 vaccine as they were allergic to the vaccine components, such cases are extremely rare [6].

Conclusion

While our study has provided valuable insights into the safety of COVID-19 vaccination in children with milk allergies, it is important to acknowledge its inherent

limitations. Our research focused primarily on children with milk allergies, and the generalizability of our findings to broader populations requires further investigation through larger-scale studies. Moreover, the low sample size reduces the likelihood of identifying adverse reactions, which are rare complications of COVID-19 vaccination in the general population but may still be more common among milk allergy patients.

Therefore, while our results suggest minimal risk for allergic reactions in children with milk allergies, a comprehensive risk assessment framework that considers various factors, including patient history, vaccine components, and potential cross-reactivity, remains an area for future exploration. As our understanding of COVID-19 vaccination and allergic responses evolves, it is imperative to continue refining our approach to ensure the safety and well-being of all individuals.

Statements and Declarations

Funding Sources: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Conflicts of Interests: The authors have no relevant financial or non-financial conflict of interests to disclose.

Consent to participate: Informed consent was obtained from all individual participants included in the study.

Ethics Committee: This study is approved by the McGill university ethics committee.

References

1. Mousan G, Kamat D. Cow's Milk Protein Allergy. *Clinical pediatrics* 55 (2016): 1054-1063.
2. Alhumaid S, Al Mutair A, Al Alawi Z, et al. Anaphylactic and nonanaphylactic reactions to SARS-CoV-2 vaccines: a systematic review and meta-analysis. *Allergy Asthma Clin Immunol* 109 (2021).
3. Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *The Journal of allergy and clinical immunology* 117 (2006): 391-397.
4. Shavit R, Maoz-Segal R, Iancovici-Kidon M, et al. Prevalence of Allergic Reactions After Pfizer-BioNTech COVID-19 Vaccination Among Adults with High Allergy Risk. *JAMA network open* 4 (2021): e2122255.
5. Rojas-Pérez-Ezquerria P, Crespo Quirós J, Tornero Molina P, et al. Safety of New mRNA Vaccines Against COVID-19 in Severely Allergic Patients. *Journal of investigational allergology & clinical immunology* 31 (2021): 180-181.
6. Klimek L, Novak N, Hamelmann E, et al. Severe allergic reactions after COVID-19 vaccination with the Pfizer/BioNTech vaccine in Great Britain and USA: Position statement of the German Allergy Societies: Medical Association of German Allergologists (AeDA), German Society for Allergology and Clinical Immunology (DGAKI) and Society for Pediatric Allergology and Environmental Medicine (GPA). *Allergo journal international* 30 (2021): 51-55.