Journal of the Pediatric Infectious Diseases Society

RESEARCH LETTER

Safety and Acceptance of COVID-19 Vaccination After Multisystem Inflammatory Syndrome in Children (MIS-C) in Spain

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In this cohort of 42 adolescents with a previous multisystem inflammatory syndrome (MIS-C) diagnosis, 32 (76.2%) were vaccinated with COVID-19 vaccines, with a low incidence of relevant adverse events. More importantly, no new MIS-C or myocarditis occurred after a median of 10 weeks (range 5.3-19.7) post-vaccination.

Key words: acceptance; COVID-19; multisystem inflammatory syndrome in children (MIS-C); safety; vaccination.

After the approval of COVID-19 vaccines for children and adolescents, there is a concern about how to act in patients who recovered from multisystem inflammatory syndrome in children (MIS-C). According to the CDC, given the lack of data on safety, vaccination should be considered in patients who achieve clinical recovery, at least 90 days after MIS-C diagnosis, and if they live in an area with a high-risk community level of COVID-19 [1], which is similar to Spanish recommendations [2]. The vaccination of adolescents started in Spain in July 2021, after Cominarty (Pfizer-BioNTech) and Spikevax (Moderna) approval. In this population, COVID-19 vaccination is recommended in Spain, but not mandatory nor required for school attendance.

Here, we present a series of patients ≥12 years previously diagnosed with MIS-C with the aim of assessing the proportion of vaccinated adolescents and the incidence of new MIS-C or myocarditis post-vaccination.

METHODS

We conducted a retrospective, point-prevalence study, selecting patients hospitalized from March 1, 2020, through October 31, 2021, fulfilling WHO criteria for MIS-C [3] and enrolled in the Spanish Epidemiological Study of COVID-19 in Children, a

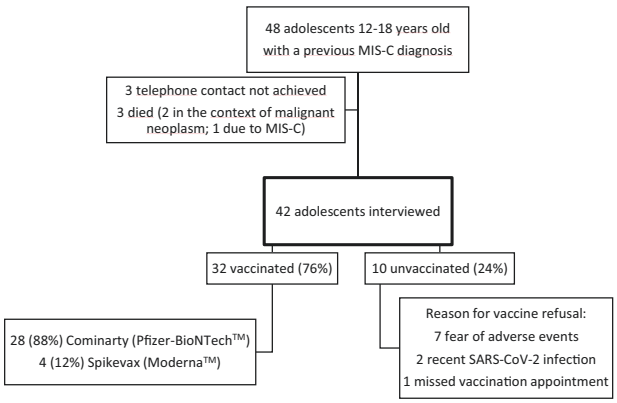

Figure 1. Flow diagram of enrolled MIS-C patients 12-18 years old.

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*A complete list of study group members appears in the Supplementary Appendix.

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Journal of the Pediatric Infectious Diseases Society 2022;XX(XX):1–3

https://doi.org/10.1093/jpids/piac076

cohort study across 92 hospitals in all the regions of Spain [4]. Centers with ≥3 patients with MIS-C diagnosis aged 12-18 years old by October 31, 2021, were contacted. Patients ≥12 years old were selected as COVID-19 vaccines were not approved in Europe for younger population at that moment.

The selected patients and/or their caregivers received a semi-structured telephonic interview (Supplementary Table S1, Supplementary Appendix). The severity of the adverse events (AEs) was evaluated as mild (no interference), moderate (partial limitation), or severe (hospitalization or prevents daily activities). Vaccination and clinical data were also assessed in the electronic charts.

Descriptive statistics were performed and reported in terms of absolute frequencies and percentages, and medians with interquartile range (IQR). The characteristics of vaccinated and unvaccinated patients were compared using Fisher's exact test for categorical variables, and the Kruskal-Wallis test for continuous variables using the Stata version 17, College Station, TX, USA.

This study was approved by the Ethics Committee of the coordinating hospital (Hospital Universitario 12 de Octubre, Madrid, code: 20/101) and by the ethics committees of all other participating centers. Participants were enrolled after consent from parents/guardians and the assent of patients older than 12 years.

RESULTS

A total of 48 adolescents from 8 centers met the inclusion criteria and 42/48 (87.5%) patients were interviewed (Figure 1);

Table 1. Comparison of Patients and MIS-C Episodes According to Vaccination Status and Safety Information After Vaccination

	Total	Vaccinated	Unvaccinated	
	(n = 42)	(n = 32)	(n = 10)	*P*-value
Gender male, n (%)	30 (71.4)	23 (71.9)	7 (70.0)	1.000
Characteristics of MIS-C episode				
Age at MIS-C episode, median (Q1-Q3)	13.1 (12.6-15.1)	13.2 (12.6-15.2)	12.9 (12.7-14.4)	.595
Admission duration (days), median (Q1-Q3)	10.0 (8.0-12.0)	10.5 (8.0-13.0)	9.5 (7.0-11.0)	.288
PICU admission, n (%)	32 (76.2)	24 (75.0)	8 (80.0)	1.000
PICU admission duration (days), median (Q1-Q3)	5.0 (4.0-8.5)	6.0 (4.0-10.0)	4.0 (3.0-5.5)	.082
Oxygen therapy, n (%)	25 (59.5)	22 (68.8)	3 (30.0)	.062
Mechanical ventilation, n (%)	10 (23.8)	9 (28.1)	1 (10.0)	.404
Inotropes, n (%)	26 (61.9)	20 (62.5)	6 (60.0)	1.000
Cardiological complications, n (%)	33 (78.6)	25 (78.1)	8 (80.0)	1.000
Myocarditis/myocardial dysfunction, n (%)	32 (76.2)	24 (75.0)	8 (80.0)	1.000
Coronary abnormalities, n (%)	3 (7.1)	2 (6.2)	1 (10.0)	1.000
Coronary aneurysm, n (%)	0	0	0	.
Information related to COVID-19 vaccination				
Hesitancy about vaccination, n (%)	8 (19.0)	6 (18.8)	2 (20.0)	1.000
Sought medical advice before vaccination, n (%)	7 (16.7)	6 (18.8)	1 (10.0)	1.000
Time between MIS-C and vaccination (weeks), median (Q1-Q3)	–	42.0 (27.4-68.1)	–	–
Time between vaccination and survey (weeks), median [range]	–	10.0 [5.3-19.7]	–	–
Patients reporting adverse events after vaccination, n (%)	–	22 (68.8)	–	–
Number of patients reporting, n (%)				
One adverse event	–	17 (53.1)	–	–
Two adverse events	–	2 (6.3)	–	–
Three adverse events	–	3 (9.4)	–	–
Type of adverse event, n (%)				
Local reaction in injection site	–	14 (43.8)	–	–
Fatigue	–	11 (34.4)	–	–
Fever	–	4 (12.5)	–	–
Headache	–	1 (3.1)	–	–
Severity of adverse events, n (%)				
Mild	–	26 (86.7)	–	–
Moderate	–	4 (13.3)	–	–
Severe	–	0	–	–
Duration of the adverse events (days), median (Q1-Q3)	–	1 (1-2)	–	–
Sought medical assistance for side effects, n (%)	–	1 (3.1)	–	–

Abbreviations: MIS-C, multisystem inflammatory syndrome in children; PICU, pediatric intensive care unit; Q1, first quartile; Q3, third quartile.

Information about vaccination in the total population is not included because it is the same as for the vaccinated population.

all clinically recovered, including cardiac function. At MIS-C diagnosis, their median age was 13.1 years old (IQR: 12.6-15.1). In all the cases, MIS-C occurred before vaccination was offered. Finally, 32/42 (76.2%) patients had received a COVID-19 vaccine. The median time between MIS-C diagnosis and vaccination was 42 weeks (IQR: 27-68) and the telephonic interview took place after a median of 10.0 weeks (range 5.3-19.7) post-vaccination.

After vaccination, 22/32 (68.8%) patients reported 30 different AEs. The most common reported AE was a local reaction in the injection site (14/32 patients, 43.8%) followed by fatigue (11/32 patients, 34.4%). Their intensity was reported as mild in 26 of the 30 reported events (86.7%) and moderate in 4/30 (3.3%). One patient sought medical assistance due to a mild local reaction in the injection site. No severe AE was described (Table 1). No new MIS-C or myocarditis or pericarditis episodes were reported after vaccination.

The main reason for refusal of vaccination was fear of AEs (7/10, 70%), followed by recent SARS-CoV-2 infection (2/10, 20%) and missed vaccination appointment (1/10, 10%). The severity of the previous MIS-C episode does not seem to be associated with a higher vaccine refusal (Table 1).

DISCUSSION

We present a series of 32 adolescents with a previous MIS-C episode that received a COVID-19 vaccine. The characteristics and frequency (68.8%) of the reported AEs were similar to the local (63.4%) and systemic reactions (48.9%) reported in a passive vaccine survey that enrolled approximately 129 000 adolescents aged 12-17 years in the United States [5].

The previous MIS-C diagnosis leads to hypothesize that they could be at a high risk of myocarditis or new MIS-C after COVID-19 vaccination. Although the small number of children included in this series is a limitation, our study suggests a low risk of AEs in children with MIS-C after vaccination. No cases of myocarditis or new MIS-C cases were observed in this series during a median of 10 weeks after vaccination.

We believe that the results of this study are reassuring and may help to decide for patients with previous MIS-C who are considering COVID-19 vaccination. Further studies with a larger number of participants may confirm these results.

Supplementary Data

Supplementary materials are available at the *Journal of the Pediatric Infectious Diseases Society* online.

Notes

Financial support. This work was supported by the Instituto de Salud Carlos III (Ministry of Economy, Industry and Competitiveness) and cofounded by the European Regional Development Fund and by the Servicio Madrileño de Salud-Fundación para la Investigación Biomédica del Hospital 12 de Octubre [Project PI20/00095]. C. G. is supported by the Spanish Ministry of Science and Innovation—Instituto de Salud Carlos III and Fondos Europeos de Desarrollo Regional [Contrato Río Hortega CM19/00015]. D. A. A. is supported by the Spanish Society of Paediatrics (Asociación Española de Pediatría) [COVID-19 EPICO-AEP 2020].

Potential conflicts of interest. The authors have no conflicts of interest relevant to this article to disclose. All authors have submitted the ICMJE Form for Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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