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BRIEF COMMUNICATION

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Measles, mumps and rubella vaccine 12 months after hematopoietic stem cell transplantation

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ABSTRACT

The measles, mumps and rubella (MMR) vaccine is usually recommended from 24 months after a hematopoietic stem cell transplant (HSCT). Some authors have demonstrated that the MMR vaccination can be safe from 12 months post-HSCT in non-immunosuppressed patients, as recommended by the Brazilian National Immunization Program/Ministry of Health, since 2006. The objectives of this study were to evaluate when patients received MMR vaccine after an HSCT in our care service and if there were reports of any side effects. We retrospectively reviewed the records of HSCT recipients who received at least one MMR dose in our care service, a quaternary teaching hospital in Sao Paulo city, Brazil, from 2017 to 2021. We identified 82 patients: 75.6% (90.1% in the autologous group and 45.1% in the allogeneic group) were vaccinated before 23 months post-transplantation. None reported side effects following the vaccination. Our data support that the MMR vaccination is safe from 12 to 23 months after HSCT.

KEYWORDS: Measles-mumps-rubella vaccine. MMR vaccine. Hematopoietic stem cell transplantation. Measles. Transplantation.

INTRODUCTION

Measles is a highly contagious infection usually seen in children. Severe forms can occur, particularly in immunocompromised individuals, such as solid organ transplant or hematopoietic stem cell transplant (HSCT) recipients[1].

The Advisory Committee on Immunization Practice (ACIP), the American Society for Transplantation and Cellular Therapy and the 2017 European Conference on Infections in Leukaemia (ECIL 7)[2,3] recommend the measles, mumps and rubella vaccine (MMR) 24 months after an HSCT, provided that the patient is not immunosuppressed or has graft-vs-host disease (GVHD)[4]. In the event of a measles outbreak, ECIL 7 recommends that the MMR vaccination should be considered 12 months after transplantation in patients with low-grade immunosuppression[3].

In Brazil, since 2006, the National Immunization Program/Ministry of Health recommends the MMR vaccination from one year after HSCT, provided that the patient is not immunosuppressed or has GVHD. This recommendation was based on Brazilian studies conducted during a measles outbreak in late 1990s[5,6].

The Centro de Referencias para Imunobiologicos Especiais (CRIE) is part of the Brazilian public health system (Sistema Unico de Saude [SUS]). CRIE' purposes are to recommend and administer vaccinations for individuals with chronic conditions and to investigate, follow and report to the Events Supposedly Attributable to

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Vaccination or Immunization (ESAVI). The CRIE linked to the Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (HC-FMUSP) is responsible for vaccinating patients who underwent an HSCT at HC-FMUSP and any other public or private transplantation centers. We conducted a retrospective study to assess the time after HSCT when patients received the MMR vaccine in our service and whether there was any reported ESAVI.

MATERIALS AND METHODS

We retrospectively searched at the CRIE Immunization Information System for HSCT recipients who received at least one dose of MMR at CRIE-HC, from 2017 to 2021. Afterwards, we reviewed the medical records of patients who underwent an HSCT at HC-FMUSP to collect data about the transplant. For those who underwent HSCT in other hospitals, there was no access to clinical data and therefore were excluded.

In Brazil, ESAVI reporting to health authorities has been mandatory since 2005, as part of a national passive surveillance system of vaccine safety initiated in 1992. Any healthcare worker can report ESAVI to this system. In Sao Paulo State (SP), the ESAVI Surveillance System is managed by the Epidemiological Surveillance Center (Centro de Vigilancia Epidemiologica/CVE) of the Sao Paulo State Health Department. We checked whether the HSCT recipients included in our study had an event registered at the SP ESAVI Surveillance System database.

This retrospective report was approved by the Research Ethics Committee of our institution (CAPPesq Nº 5.647.163/2022).

RESULTS

We identified 552 HSCT recipients who received at least one dose of MMR at CRIE-HC. Among these, 470 were excluded because they underwent HSCT in another hospital or the data were not available. Thus, 82 patients (51 in the autologous group and 31 in the allogeneic group) who underwent an HSCT at HC-FMUSP and received the MMR vaccine at CRIE-HC from 2017 to 2021 were included. In this period, a total of 397 bone marrow transplantations were performed in our care service (255 in the autologous group and 142 in the allogeneic group). Therefore, our population represents 20.6% (20% in the autologous group and 21.8% in the allogeneic group) of all transplants.

Among the 82 patients who were included, 75.6% (90.1% in the autologous group and 45.1% in the allogeneic group) were vaccinated before 23 months post-transplantation. The median time of the MMR vaccination was 13.8 months after an HSCT (interquartile range: 12.5–22.3). Their characteristics are shown in Table 1. Notably, only a small proportion of them completed the 2-dose schedule: 28% (25.4% in the autologous group and 29% in the allogeneic group).

Table 1 - Characteristics of hematopoietic stem cell transplant (HSCT) recipients who received the MMR vaccine at CRIE-HC-FMUSP, Sao Paulo, Brazil, 2017–2021.

	Total	Autologous	Allogeneic
N (%)	82	51 (62.1)	31 (37.8)
Age in years, median (IQR)	48 (32–56)	51 (45–60)	32 (16–48)
Male, N (%)	47 (57.3)	26 (50.9)	21 (67.7)
Baseline disease, N (%)			
Multiple myeloma	38 (46.3)	38 (74.5)	0
Hodgkin's lymphoma	8 (9.75)	7 (13.7)	1 (3.2)
Non-Hodgkin's lymphoma	7 (8.5)	5 (9.8)	2 (6.4)
Acute myeloblastic leukemia	10 (12.1)	0	10 (32.2)
Acute lymphoblastic leukemia	5 (6.0)	0	5 (16.1)
Chronic myeloblastic leukemia	2 (2.4)	0	2 (6.4)
Bone marrow aplasia	5 (6.0)	0	5 (16.1)
Myelofibrosis	3 (3.6)	0	3 (9.6)
Others	4 (4.8)	1 (1.9)	3 (9.6)
Month of 1st MMR dose post-HSCT, median (IQR)	13.8 (12.5–22.3)	13.1 (12.4–14.9)	24.5 (13.3–34.8)
Vaccination before 23 months of HSCT, N (%)	62 (75.6)	46 (90.1)	14 (45.1)
2nd MMR dose, N (%)	23 (28.0)	13 (25.4)	9 (29.0)

IQR = interquartile range

During the study period, no severe side effects following the MMR vaccination in the HSCT patients were reported to CRIE-HC. None of the patients included in this study were registered in the SP ESAVI Surveillance System database, which received 6,758 reports of side effects following the MMR vaccine in the general population, during the study period.

DISCUSSION

This is the first description of the time of the MMR vaccination after HSCT in our country since the Brazilian National Immunization Program/Ministry of Health recommendation from 2006. We found that a high proportion of patients (75.6%) received the first MMR vaccine before 23 months after transplantation. This proportion was higher in the autologous group than in the allogeneic group (90.1% vs. 45.1%). The late initiation of vaccination in the allogeneic patients can be partially explained by the fact that only they can develop GVHD (a contraindication for administration of live attenuated vaccines). Vaccination was safe, since no severe side effects were reported to the state surveillance system. Unfortunately, the full vaccination coverage with two MMR doses was low (28%). Since this was a retrospective observational study, we did not have data regarding immunogenicity of the MMR vaccine in this population.

During the study period (2017–2021), 40,403 cases of measles were confirmed in Brazil, with 42 deaths[7]. We did not have access to information if any cases of measles occurred in the patients in our study.

Measles can be severe in immunocompromised patients. Ge *et al.*[8] described 23 children with hematological malignancies and post-HSCT, among whom 56.5% (n = 13) had measles complications, including pneumonitis and acute liver failure, and 21.7% (n = 5) died. In a Brazilian case series of eight allogeneic HSCT recipients with measles, one recipient had interstitial pneumonitis and the other seven only had mild symptoms[6].

In 1997, after a controlled period , measles reemerged in the Americas. Brazil had a large outbreak of 53,335 cases and 61 deaths, mainly among unvaccinated young adults. Sao Paulo State (SP), in Southeastern Brazil, was the epicenter of this outbreak, with over 42,000 reported cases (79% of all cases)[9]. From SP, the measles cases spread to other Brazilian states[10-12]. The genomic characterization classified the circulating measles virus as the wild-type genotype D6[13].

During this epidemic, Machado *et al.*[6] conducted a seroepidemiological survey among HSCT recipients in SP, using Enzyme Immunoassay (EIA). They assessed 156 HSCT patients; 34 of them had received the MMR vaccine after the HSCT and 122 were unvaccinated (76 were within two years after HSCT; 8 were immunosuppressed; and 38 had not complied with the vaccination schedule). Among 32 patients who had received the MMR vaccination after the HSCT, a significant loss of measles immunity after the 3rd year of vaccination was seen: 27.3% of those who had been vaccinated within 3 years were susceptible to measles (IgG ≤ 100 mIU/mL), in contrast with 70% of those vaccinated ≥ 3 years previously. Among the 122 unvaccinated HSCT patients, 33.6% were susceptible to measles. Measles immunity decreased after a year of HSCT: 8.5% of those within the first year after HSCT were susceptible to measles, in contrast with 49.3% of those with more than one year after HSCT[6]. Next, Machado *et al.*[5] administered early MMR vaccination (from 9 to 18 months [median of 12 months] after HSCT) to 61 patients; 52.9% of them were immunosuppressed and 17.6% were susceptible to measles at vaccination. Only mild side effects, such as myalgia and low-grade fever, were noted. Among 17 patients with pre-vaccination IgG levels < 200 mUI/mL, 82.3% seroconverted or had a four-fold increase in antibody titers. The authors concluded that early measles vaccination is safe. Despite this, the global recommendation of the administration of the MMR vaccine remains to be 24 months after HSCT.

Recently, Desjardins *et al.*[14] conducted a retrospective review of patients who received the MMR vaccine within two years after HSCT. They reported 129 patients vaccinated from 300 to 729 days after HSCT (median, 718 days) and 39 (30%) vaccinated before 23 months post-HSCT. Only seven patients had mild side effects (one of them had a maculopapular rash related to the rubella vaccine strain). The authors concluded that MMR vaccine is well tolerated when given 300–729 days post-HSCT.

CONCLUSION

The strategy of administering the MMR vaccine a year after HSCT, provided that the patient is not immunosuppressed, is a widespread practice in Brazil, since 2006. Our data show a greater proportion of patients being vaccinated before 24 months post-transplantation when compared to the study of Desjardins *et al.*[14] None of our patients had side effects reported to CRIE-HC or to the ESAVI Surveillance System. A limitation of our investigation is that it was based on passive reporting, however, it is unlikely that any of our patients had any unreported serious side effects. The Brazilian ESAVI Surveillance System's sensitivity is variable, but higher in states with better socioeconomic indicators and

health services organizations, such as Sao Paulo State. Furthermore, the study has been successful in identifying more reactogenic vaccines or batches and rare or not previously described ESAVI[15]. Our study, together with Desjardins *et al.*[14], reinforces the safety of this practice, as previously described by Machado *et al*.[5]

AUTHORS' CONTRIBUTIONS

BAR, EGH and HRH collected and analyzed data; MHL, VGR, SFC and AMCS actively participated in the manuscript preparation.

CONFLICT OF INTERESTS

All authors report no conflict of interests relevant to this article.

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