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The practice of COVID-19 vaccination in patients bleeding disorders

Memiş Hilmi ATAY*, Engin KELKİTLİ

Department of Hematology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Türkiye

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Abstract

Subcutaneous injections are recommended instead of intramuscular for patients with bleeding disorders to avoid bleeding complications. This study aimed to determine whether the intramuscular administration of COVID-19 vaccines would increase bleeding-associated complications in patients with bleeding disorders followed in our clinic. We collected the data of 47 patients with bleeding disorders older than 18 years followed at the hematology outpatient clinic and screened between March 15, 2020, and December 31, 2021. We obtained the data from the hospital's electronic information system, including age, gender, type of bleeding disorder, factor levels, and whether they received prophylaxis. We interviewed the participants about the type of vaccine they received and the duration of compression they applied to the injection site, whether they received factor replacement before and after the injection, and whether there were any complications following the injection. We included in the study thirty-nine male patients vaccinated against COVID-19. The mean age of the patients was 39.05 (18–73 years). Factor VIII deficiency constituted 79.4%, XI 10.3%, and other bleeding disorders 10.3 % of the cases. The patients with bleeding disorders had a mean factor level of 2.02 (0–9). Twenty-nine (74.4%) patients were on regular factor prophylaxis for their bleeding disorder. In terms of the compression duration to the injection site following injection, 6 (15.4%) patients had applied compression for 10 min, 4 (10.3%) for 5–10 min, and 29 (73.4%) for less than 5 min. Two (5.1%) patients developed ecchymosis after the first vaccine dose on the injection arm. The results of this study demonstrate that the rate of bleeding complications remains low in patients with bleeding disorders if they receive intramuscular vaccination after necessary precautions.

Keywords: COVID-19, vaccination, bleeding disorders, bleeding complication

1. Introduction

Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Turkey began on January 13, 2021, after the coronavirus disease 2019 (COVID-19)-inactivated vaccine CoronaVac (Sinovac, Beijing, China) was approved for use (1, 2). The widespread release of this vaccine and others from different manufacturers worldwide has resulted in the administration of more than 10.5 billion doses (3). So far, 61.4% of the population in Turkey has been fully vaccinated, and 5.86% are partially vaccinated (1). Subcutaneous injections are recommended instead of intramuscular for patients with bleeding disorders to avoid bleeding complications (4). However, the subcutaneous administration of vaccines elicits lower seroconversion than intramuscular administration, leading to a faster decline of the antibody response (5, 6). This study aimed to determine whether the intramuscular administration of COVID-19 vaccines would increase bleeding-associated complications in patients with bleeding disorders followed in our clinic.

2. Materials and Methods

We collected the data of 47 patients with bleeding disorders older than 18 years followed at the hematology outpatient clinic of the Ondokuz Mayıs University (OMU), Turkey, and screened between March 15, 2020, and December 31, 2021. We included in the study 39 patients vaccinated against COVID-19 and excluded Eight patients as they were unvaccinated. We obtained the data from the hospital's electronic information system, including age, gender, type of bleeding disorder, factor levels, and whether they received prophylaxis. We interviewed the participants about the type of vaccine they received, and the duration they applied compression to the injection site, whether they received factor replacement before and after the injection and whether there were any complications following the injection, they had visited the outpatient clinic, or communicated via phone using

*Correspondence: draatay@gmail.com

their registered phone numbers in the electronic information system of the hospital. The Local Ethics Committee accepted the study with OMU KAEK 2022/67 reference number.

2.1. Statistical Analysis

After being encoded, we transferred the study data to a computer and analyzed them with SPSS software (Version 20 for Windows, SPSS Inc, Chicago, IL, USA). We expressed continuous variables by median (min.-max.) and frequency data by percentage (%) in data evaluation and used The Chi-square test to assess the correlation between bleeding and other parameters. We considered P <0.05 statistically significant.

3. Results

Table 1 shows the characteristics of 39 adult bleeding disorders patients. All the participants were male with a mean age of 39.05 (18–73 years) and a mean factor level of 2.0 (0–9). Thirty-one had hemophilia A (79.5 %), four had hemophilia B (10.3 %), and four had other bleeding disorders (10.3%). Based on their factor levels, 19 (61.2%) of the patients with factor VIII level disorder were classified as severe (<1%), 8 (25.8 %) as moderate (1%–5%), and 4(13%) as mild (>5%); while 1 (25%) of the patients with factor IX level disorder were classified as severe, 2 (50%) as moderate, and 1 (25%) as mild. Two of the patients with Von Willebrand disease were classified as Type 1.

Table 1. Clinical characteristics of patients with a bleeding disorder after COVID-19 vaccine and vaccine doses

	N (%)
Bleeding Disorder Type	
- Hemophilia A	31 (79.5 %)
- Hemophilia B	4 (10.3 %)
- Von Willebrand's disease	2 (5.1 %)
- Factor 13 deficiency	1 (2.6 %)
- Afibrinogenemia	1 (2.6%)
Hemophilia A severity	
- <1%	19 (61.2%)
- 1-5 %	8 (25.2%)
- > 5%	4 (13%)
Hemophilia B severity	
- <1%	1 (25%)
- 1-5 %	1 (25 %)
- >5 %	2 (50%)
Factor prophylaxis	
	29 (74.4)
Vaccine doses	
- 1st vaccination	39 (100%)
- 2nd vaccination	37 (95%)
- 3rd vaccination	23 (59%)
- 4th vaccination	7 (18%)

A total of 106 doses of the COVID-19 vaccine had been administered, with 29 (74%) of the patients receiving the Pfizer–BioNTech vaccine, two patients (5%) the Sinovac vaccine, and eight patients (21%) both vaccines. Out of the 39 patients, 95% had been fully vaccinated (two doses), 59% had received the first booster dose, and 18% the second.

Twenty-nine (74.4%) patients were on regular factor prophylaxis for their bleeding disorder. Only the patient with factor XIII deficiency was on regular two units of fresh frozen plasma per month, while seventeen (43.6%) patients received pre-vaccination counseling from a hematologist. In terms of the compression period following injection, six (15.4%), four (10.3%), and 29 (73.4%) patients had applied compression to the injection site for 10 min, 5–10 min, and for less than 5 min, respectively. 16 (41%) patients received prophylactic factor replacement before injection; three (7.7%) required post-vaccination factor prophylaxis. None of the patients had injection site uncontrollable bleeding. Only two (5.1%) developed ecchymosis on the injection arm after vaccination; the complication developed following the first vaccine dose. Both received prophylaxis and factor replacement before subsequent vaccine doses.

Eight patients were unvaccinated; two had chosen not to be vaccinated, four were not vaccinated due to the potential side effects of their disease, and two remained unvaccinated because they were afraid.

4. Discussion

This study examined the experiences of patients with bleeding disorders after receiving COVID-19 vaccination. We found a low rate of bleeding-related complications associated with the intramuscular administration of COVID-19 vaccines in patients with bleeding disorders.

The World Federation of Hemophilia has provided several recommendations for the vaccination of patients with bleeding disorders, such as the subcutaneous administration of the vaccine to prevent bleeding, using the smallest gauge needle (25–27 gauge), and applying a cold compress to the injection site for 5 minutes before and pressure 10 minutes after vaccination respectively (7). Following the global introduction of COVID-19 vaccination programs, hematology experts announced that patients with hemophilia with a factor level above 10% (factor VIII or IX) do not require hemostatic treatment before the vaccination to minimize vaccine-related hemorrhage. They also recommended that patients with factor levels below 10% or other rare bleeding disorders consult follow-up centers to discuss the required hemostatic precautions before the vaccination (8,9).

A study regarding other intramuscular vaccines in pediatric patients found a bleeding rate of <1% at the injection site (10); however, it provided no information concerning whether the patients had applied compress for 10 min following the vaccination to the injection site. In our patients, the post-vaccination bleeding rate (5.1%) at the injection site was higher than the general population (2.4%) (11). The high bleeding rates observed in our patients could result from most not applying compression to the injection site for 10 min after the vaccination. However, our study's bleeding rate was lower than the research conducted with adult patients with bleeding disorders vaccinated against COVID-19 (8%) (12). This difference might stem from the fact that many of our patients had received regular factor replacement.

Overall, 17% of the patients screened during the study were unvaccinated. The percentage of unvaccinated individuals for COVID-19 among the patients we followed up with was twice as high as that of the unvaccinated individuals within the general population of Turkey. Kocher F et al. found a higher proportion of bleeding disorders in patients vaccinated against COVID-19 compared to the general population (13). The most common reasons why our patients did not get vaccinated could be the side effects of the vaccines and misinformation on social media (14). Patients with bleeding disorders have high bleeding stress factors. Hence, the high proportion of unvaccinated individuals among our patients may be attributed to their fear of increased bleeding or vaccine-related complications.

The limitations of this study included not being able to directly observe whether the patients developed bleeding complications following each dose of vaccination, the retrospective evaluation of the data, and the small number of patients due to the inclusion of a single center.

Hence, the results of this study demonstrate that the rate of bleeding complications remains low in patients with bleeding disorders if they receive intramuscular vaccination after necessary precautions. Post-vaccination bleeding complications could be prevented if patients seek counseling from specific bleeding disorders specialists. The strength of this study is that it could serve as guidance for specialists and patients with bleeding disorders interested in the intramuscular administration of COVID-19 vaccines. Larger-scale, randomized, and prospective studies examining patients with bleeding disorders are required.

Conflict of interest

We declare no financial or other relationships leading to a conflict of interest. All authors read and approved the manuscript.

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Authors' contributions

Concept: M.H.A, E.K., Design: M.H.A, Data Collection or Processing: M.H.A, Analysis or Interpretation: M.H.A, Literature Search: M.H.A., E.K, Writing: M.H.A., E.K.

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