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Retrospective study on the safety of COVID-19 vaccination in myasthenia gravis

Alejandra Urra Pincheira MD[1,2] ⓘ | Sara Alnajjar MD[1,2] | Hans Katzberg MD[1,2] |
Carolina Barnett MD, PhD[1,2] ⓘ | Lubna Daniyal MD[1,2] | Ritesh Rohan MD[1] |
Vera Bril MD[1,2] ⓘ

[1]Ellen & Martin Prosserman Centre for Neuromuscular Diseases, Toronto General Hospital, University Health Network, Toronto, Ontario, Canada

[2]University of Toronto, Toronto, Ontario, Canada

Correspondence
Vera Bril, 5EC-309, TGH, 200 Elizabeth St, Toronto, Ontario, Canada, M5G 2C4.
Email: vera.bril@utoronto.ca

Abstract

Introduction/Aim: Given the lack of information on safety of coronavirus disease 2019 (COVID-19) vaccination in myasthenia gravis (MG) patients, we aimed to review our experience after surveying patients, as part of routine clinical practice, to ensure that advice on safety is accurate.

Methods: We performed a retrospective chart review of MG patients from the Prosserman Family Neuromuscular Clinic at the Toronto General Hospital who received two injections of any COVID-19 vaccine from February to August 2021. Demographic data were abstracted from the patient medical records. We assessed changes in the severity of MG using the virtual Myasthenia Gravis Impairment Index (vMGII), the simple single question (SSQ), and Patient Acceptable Symptom State (PASS). We also assessed adverse effects after vaccination.

Results: We included 200 patients with a mean age of 64.3 ± 13.9 y, 51.5% were men, and 82% had generalized MG. The vMGII, SSQ, and PASS scores remained stable after each vaccine dose, and at last follow-up. Of the patients, 60% reported an adverse reaction after the first injection, and 56% after the second. The most common adverse reactions reported were local pain at the injection site, fatigue, headache, and fever.

Discussion: COVID-19 vaccinations were well tolerated in MG patients and were not associated with worsening severity of their MG. The prevalence of vaccine-related adverse reactions was the same as in the general population.

KEYWORDS
COVID, myasthenia gravis, relapse, safety, vaccination

1 | INTRODUCTION

The most common cause of myasthenia gravis (MG) exacerbations are infections.[1–3] The coronavirus disease 2019 (COVID-19) pandemic has raised concerns about the care of individuals with MG as COVID-19 has the potential to trigger MG relapse including crisis; additionally the immunosuppressive treatments for MG are a risk factor for severe COVID-19 infection.[4–8]

Vaccines to prevent COVID-19 infection became available at the end of 2020. In Canada, the current vaccines are BNT162b2 (Pfizer-BioNTech COVID-19 vaccine), mRNA-1273 (Moderna COVID-19 vaccine), and ChAdOx1 nCoV-19/AZD1222 (University of Oxford, AstraZeneca, and the Serum Institute of India ChAdOx1 nCoV-19/AZD1222).[9] Side effects for all the vaccines are common, and include local and systemic reactions.[9]

Concerns about the safety of COVID-19 vaccines in special populations such as individuals with MG are prevalent.[10–14] In particular, there is a theoretical concern of potential flare-ups of MG symptoms after vaccinations, although high-quality studies in influenza vaccines have shown these are overall safe.[15,16] There is no information available regarding the safety of the COVID-19 vaccines in MG patients including the risk of vaccine-associated disease exacerbations. Our aim was to assess the safety of COVID-19 vaccination in MG patients.

2 | METHODS

We conducted a retrospective chart review of adult MG patients evaluated by phone from February to August 2021 at the Prosserman Family Neuromuscular Clinic of the Toronto General Hospital. Patients were included in this study if they had received two injections of any of the available COVID-19 vaccines in that time frame. We included patients who received both doses of the same vaccine or mixed doses. We excluded patients with congenital MG, those lacking both vaccinations, and patients who did not complete telephone assessments. The study was approved by the Research Ethics Board of the University Health Network.

The diagnosis of MG was made based on the clinical presentation, repetitive nerve stimulation, and single fiber electromyography results with or without the presence of specific antibodies (acetylcholine receptor, muscle-specific kinase, low density lipoprotein receptor-related protein-4).

Data abstracted from the patient medical records included: age, gender, generalized or pure ocular classification, thymoma status, type of positive antibody, treatment prior to the first injection of the COVID-19 vaccine including the use of acetylcholinesterase inhibitors, immunomodulatory therapies such as plasma exchange and immune globulin (IVIG or SCIG), chronic immunosuppressive therapies (IST) and thymectomy.Our clinical practice was modified after vaccinations became available so that MG patients were assessed routinely prior to the first injection, and about 2 wk after each injection to assess potential worsening of their MG status. Data arising from any further follow-up assessments were also noted. All patient visits were virtual by phone. In all routine MG clinic assessments in our center, the virtual Myasthenia Gravis Impairment Index (vMGII), single simple question (SSQ), and Patient Acceptable Symptom State (PASS) are done.

As the primary outcome, we assessed any changes in the severity of MG using the vMGII, the SSQ, and the PASS. The MGII is a novel measure of MG severity with demonstrated feasibility, reliability, and construct validity.[17] It has 22 patient-reported and six examination

TABLE 1 Demographic variables of MG patients

Number of patients	200
Age in years	64.3 ± 13.9
Males/females	103 (51.5)/97 (48.5)
Generalized MG	164 (82)
Ocular MG	36 (18)
Antibody positive (AChR + MuSK)	107 (53.5)
Generalized antibody positive	99/164 (60)
Ocular antibody positive	8/36 (22)
Thymectomy	95 (47.5)
Thymoma	36 (18)
Thymic hyperplasia	24 (12)
Normal	35 (17.5)
Treatment	
On treatment	188 (94)
No treatment	12 (6)
Only pyridostigmine	73 (36.5)
IVIG/SCIG/PLEX	56 (28.0)
One immunosuppressant agent	91 (45.5)
Two immunosuppressant agents	30 (15.0)
Three immunosuppressant agents	7 (3.5)

Note: Values presented as means ± standard deviations or number (per cent).

items. When the questionnaire section is obtained during a telephone consultation, foregoing the physical examination item scores, we use the adapted version of the MGII; the virtual MGII (vMGII), which has an excellent correlation with patient disease status.[18] The SSQ asks the patient the question: "what percentage of normal do you feel regarding your MG? In this score 100% is normal, and this question reflects the patient's perception of their overall disease status.[19] The PASS is a holistic evaluation of the patient's satisfaction with their overall disease burden and identifies health scores that are associated with patients who "feel well" rather than just "better" after treatment.[20]

As a secondary outcome, we assessed the safety of COVID-19 vaccination in patients with MG by assessing all the local and systemic adverse effects reported to us after each injection.

Analysis was performed using SPSS version 20 software (IBM, Armonk, New York). Demographic data are reported as means and standard deviations for continuous variables or percentages for discrete variables. One-way analysis of variance (ANOVA) was used to evaluate differences in MG outcome measures. All p values of < 0.05 were considered significant.

3 | RESULTS

We identified 220 MG patients. We excluded two patients with congenital MG, five lacking both vaccinations, and 13 patients who did not complete telephone assessments. One of those patients developed Bell's palsy after the first dose of vaccine and refused to have

TABLE 2 Comparison of MG disease status before and after COVID vaccination

	Before 1st dose		After 1st dose[a]		After 2nd dose[a]	
	No.	%	No.	%	No.	%
PASS						
Yes	172	86	179	89.5	176	88
No	28	14	21	10.5	24	12
SSQ						
Mean ± SD	81.07 ± 18.67		82.61 ± 15.92		82.30 ± 17.15	
vMGII						
Mean ± SD	8.38 ± 11.28		7.26 ± 8.22		7.05 ± 7.87	

[a]Assessment done about 2 wk after each vaccination.

the second dose. Two patients developed hives and rash after the first dose of COVID-19 vaccine BNT162b2 without a previous history of anaphylaxis and were advised not to receive the second injection of the COVID-19 vaccine; they were not included in the study. A total of 200 patients with MG satisfied the selection criteria. Detailed demographic parameters are summarized in Table 1.

In our 200 patients, 73.5% received BNT162b2, 12% received mRNA-1273, and 6% ChAdOx1 nCoV-19/AZD1222 vaccine. Seventeen patients received mixed vaccines (BNT162b2 + mRNA-1273, BNT162b2 + ChAdOx1 nCoV-19/AZD1222).

The vMGII, SSQ, and PASS remained stable after the first and second vaccinations, and at the last follow-up as presented in Table 2, $p > 0.05$ for all comparisons. Almost 90% of patients were PASS yes at the end of the study with a mean SSQ value of 82% and mean MGII of 7, indicating a well-controlled population. The SSQ declined by 10% in 11 patients after the vaccinations, and improved by 10% in nine patients, without any clear pattern. At last follow-up, 12 patients were worse and 14 better by 10% on the SSQ. The MGII did not show a meaningful change in patients who worsened or improved on the SSQ. No patient had an emergency room visit or hospital admission.

After the first and second injection, 60% and 56% of individuals, respectively, reported adverse reactions, injection site pain being the most common.

4 | DISCUSSION

We found that COVID-19 vaccination was safe and well tolerated in a cohort of MG patients and not associated with worsening severity of their MG.

MG patients may be at greater risk from severe COVID-19 infection due to use of immunosuppression and are also at risk of MG exacerbation, including respiratory failure, if infected with this respiratory virus.[3] There are several reports of COVID-19 infection in MG patients with variability in disease outcomes, which probably reflects small cohorts, selection bias, and that more severe cases are more likely to be reported[2,6,8,21–23] Despite this variability, the general recommendation for MG patients is to be vaccinated to reduce the possibility of disease exacerbation and poor health outcomes.

In our patients, the demographics are similar to those reported in the literature other than an older age, which may have been related to the local vaccine roll-out giving preference to older individuals.[2] Also, the seropositivity rate was low in those with generalized disease, and this might be due to several factors: variation in sensitivity of testing methods over the years, lack of data in those assessed many years ago prior to widespread availability of serological testing, and lack of testing for newer antibodies.

We found that two injections of the COVID-19 vaccine did not cause deterioration of MG, based on the stable vMGII, SSQ, and PASS. This observation can be reassuring to both MG patients and providers as evidence of the safety of vaccination. It has been described in the literature that individuals with a prior history of COVID-19 infection may be more likely to experience local and systemic adverse effects from vaccination.[24] In our cohort, we had a single patient with a mild COVID-19 infection 5 mo before the vaccination, who reported only mild injection site pain and did not worsen on any of the MG measurements. Our cohort included a 34-y-old pregnant woman who received COVID-19 vaccinations at 13 and 22 wk of pregnancy. She reported local pain at the site of injection and fatigue without worsening of MG symptoms.

The most common adverse reaction was injection site pain followed by fatigue, with similar prevalence as reported in the literature.[9]

The weaknesses of our study are that it was a retrospective study including mainly well-controlled patients. The results may not be generalizable to patients with newly diagnosed MG who are not yet controlled or those with refractory MG, although about 10% of our patients felt that their MG was not well controlled.

5 | CONCLUSIONS

This study provides evidence that a two-dose regimen of any of the available COVID-19 vaccines is safe without worsening MG status, and with adverse reactions similar to those in the general population. We recommend strongly that MG patients receive the COVID-19 vaccine, as COVID-19 infection has a greater likelihood of worsening MG than the vaccination.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ORCID

Alejandra Urra Pincheira https://orcid.org/0000-0003-3931-1407
Carolina Barnett https://orcid.org/0000-0001-5546-0221
Vera Bril https://orcid.org/0000-0002-5805-4883

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