Seizures in Patients with Epilepsy Receiving COVID-19 Vaccination: A Retrospective Review in A Level 4 Epilepsy Center

Mohankumar Kurukumbi, Laura Madarasz, Yun Fang, Karlie Smith, Rohan Karanth, and Anne Giles

ABSTRACT

Objective: To identify the incidence of seizures within 48 hours of COVID-19 vaccination in PWE

Methods: This is a retrospective cross-sectional observational study performed at two Northern Virginia neurology clinics. PWE that had been vaccinated against COVID-19 were surveyed to report occurrence of a seizure within 48 hours of COVID-19 vaccination and the presence of additional triggers surrounding the seizure.

Results: Of the 189 patients included in the analysis, 13 (7%) reported a seizure within 48 hours of vaccination. Of the 13 participants with reported seizures, 10 identified possible triggers present at the time of their seizure. Additionally, patients with intractable epilepsy were found to have a non-statistically significant (p = 0.16) increased risk of seizure (odds ratio = 2.2) within 48 hours of vaccination.

Conclusion: The results show a low incidence of seizure within 48 hours of receiving a COVID-19 vaccination in this cohort of PWE. Those that reported seizures had additional provoking factors present that may have triggered the seizure. For patients with intractable epilepsy it appears they may have some increased risk of breakthrough seizures within 48 hours of vaccination. It is recommended that clinicians counsel their epilepsy patients, especially those with an intractable diagnosis, to mitigate potential seizure triggers prior to vaccine administration. Further research is recommended to observe for long term effects if present and to control for provoking seizure factors/triggers.

Keywords: COVID-19 vaccination, patients with epilepsy, seizures.

I. INTRODUCTION

The COVID-19 Pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has greatly affected society since its onset in March 2020. Areas changed include public health, social systems, living conditions, and many other aspects of individuals’ daily lives. Thus, the development of safe and effective vaccinations against SARS-CoV-2, including the Pfizer-BioNTech mRNA vaccine (BNT162b2), Moderna mRNA vaccine (mRNA-1273), and Johnson and Johnson/Janssen vaccine (JNJ-78436735), have signaled a long-awaited turning point in the pandemic. In order to capitalize on the benefits of the vaccine it is imperative that as many individuals as possible get vaccinated including members of at-risk groups.

Epilepsy is a common neurological disease characterized by affected individuals being more predisposed to recurrent seizures. Comorbidities are common in people with epilepsy (PWE) and include conditions such as hypertension or diabetes [1]. These comorbidities put this population at a potentially increased risk of a worse outcomes with COVID-19 infection. Additionally, studies done in PWE and COVID-19 have shown an association with fatality during hospitalization and epilepsy [2]. Therefore, it is important that PWE receive vaccination for COVID-19 for individual protection as well as contribution to overall public health.

Unfortunately, vaccine rollout has faced its own struggles limiting the number of vaccinated individuals. The challenges facing vaccine rollout include issues related to development, deployment, and hesitancy. Hesitancy over vaccine safety has proven to be quite the barrier [3]. Surveys done in PWE have shown concern over the long-term side effects of the COVID-19 vaccines as well as concern for how vaccination could affect their epilepsy [4]. Thorough reviews of existing literature in the general population have sought to address these concerns and have shown low risks of neurologic adverse event following vaccination [5]. However, these reviews did not focus on whether patients had an underlying diagnosis of epilepsy. There are some existing studies evaluating the safety of COVID-19 vaccination in PWE that show the vaccines are well tolerated and have low incidence.
of worsening epilepsy. These studies though are limited though by their small sample size [6], [7].

This study aims to build upon existing studies in examining the safety of COVID-19 vaccination in PWE by evaluating the incidence of seizure within 48 hours of vaccine administration in a larger PWE population. By examining this in a larger PWE population this study will provide further evidence showing COVID-19 vaccination does not increase the incidence of seizures experienced by PWE. This will give providers an important resource to assure patients of vaccine safety and encourage vaccine uptake in this population.

II. METHODS

A. Study Design and Participants

This is a retrospective cross-sectional observational study performed at two Northern Virginia neurology clinics. Participants were surveyed at clinic visits that occurred from February 2021-September 2021. Inclusion criteria for the study included all patients aged 18 years or older of all genders and races/ethnicities with a diagnosis of epilepsy who had an appointment at one of the participating clinics from February 2021 to September 2021. At clinic visits participants were asked to fill out a survey that asked them about their COVID-19 vaccination status, whether they experienced a seizure within 48 hours of vaccination, and further questions to characterize the seizure. A 48-hour time frame was chosen as most vaccine side effects have been shown to occur within 48 hours of vaccination [8].

Participants with an unconfirmed epilepsy diagnosis, those that declined participating in the survey, and those that responded they had not received one of the COVID-19 vaccinations were excluded from the study. The primary focus of this study was to determine the incidence of seizures in PWE after a COVID-19 vaccination. Demographic information on patients and whether the patient had a diagnosis of intractable epilepsy were collected via chart review on EPIC.

Instrument

The survey was written in English and included the following sections:

- Demographics
- Vaccination status and Vaccine Received (Pfizer-BioNTech mRNA vaccine (BNT162b2), Moderna mRNA vaccine (mRNA-1273), or Johnson and Johnson/Janssen vaccine (JNJ–78436735)
- Occurrence of seizure within 48 hours of vaccine administration
- Dose of vaccine that seizure occurred

If participants reported a seizure, they were further asked to characterize the seizure by answering the following:

- Type of Seizure: A free response question asking them to describe the type of seizure that occurred, duration of the seizure, and characterize post-ictal event
- Intractable Seizure status defined as on 2 or more antiepileptic drugs continuing to have seizures or on 2 antiepileptic drugs and a Vagal Nerve Stimulator or on more than 2 antiepileptic drugs
- Seizure triggers: A multiple choice question asking if the seizure had other triggers including missed medication, ingestion of intake of alcohol, lack of sleep, physical exhaustion, emotional stress
- Emergency Department Visit: A yes/no question asking whether they needed to go to an emergency department because of the seizure
- Treatment plan changes: A multiple choice question asking did the seizure cause changes to their treatment plan including medication changes, dose adjustment, or additional testing
- Comparison to prior seizures: A multiple choice question asking if the seizure they experienced was their baseline seizure or a new type of seizure

An example of the administered survey is shown below in Fig. 1.

![Survey administered to participants.](image-url)

B. Outcome

The primary outcome evaluated in this study was the incidence of seizures within 48 hours of a COVID-19 vaccination to evaluate safety of the vaccines in PWE. Secondary data points collected were information characterizing the participant’s epilepsy and the seizure experienced, and demographic characteristics of the participants.

C. Data Storage and Analysis

Data were managed and analyzed using the SAS statistical software platform. All data were deidentified prior to analysis and deleted permanently after the study concluded.

D. Standard Protocol Approvals, Registrations, and Patient Consents

A waiver of informed consent and a waiver of HIPPA authorization was requested for this study and was approved by WCG IRB. Informed consent and HIPPA authorization were waived due to the minimal risks this study posed to participants.
III. RESULTS

A total of 222 participants participated in the survey included in the study for analysis. 33 participants who answered the questionnaire were unvaccinated and were excluded from the study. Of the 189 remaining participants who were included in the analysis, 128 received the Pfizer-BioNTech mRNA Vaccine, 46 received the Moderna mRNA vaccine, and 15 received the Johnson and Johnson vaccine. Of those who were included in the analysis, 128 received the Pfizer vaccine, and 15 received the Johnson and Johnson vaccine. Demographic characteristics of this cohort are shown below in Table 1 and Fig. 2.

### Table 1: Participant Demographic Characteristics

<table>
<thead>
<tr>
<th>Gender</th>
<th>Overall (n = 189)</th>
<th>No Occurrence of Seizure (n = 176)</th>
<th>Occurrence of Seizure (n = 13)</th>
<th>Odds Ratio (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45.2 ±17.8</td>
<td>45.6 ± 18.1</td>
<td>40.6 ± 13.8</td>
<td>1.0 (0.95-1.02)</td>
</tr>
<tr>
<td>Gender</td>
<td>92 (48.7%)</td>
<td>85 (48.3%)</td>
<td>7 (53.8%)</td>
<td>1.2 (0.90-3.9)</td>
</tr>
<tr>
<td>Race</td>
<td>81 (42.9%)</td>
<td>76 (43.2%)</td>
<td>5 (38.5%)</td>
<td>1.2 (0.40-3.9)</td>
</tr>
<tr>
<td>White</td>
<td>108 (57.1%)</td>
<td>100 (56.8%)</td>
<td>8 (61.5%)</td>
<td>2.2 (0.71-6.9)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>110 (62.5%)</td>
<td>110 (62.5%)</td>
<td>7 (53.8%)</td>
<td>4.2%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>45 (24.0%)</td>
<td>45 (25.2%)</td>
<td>3 (23.1%)</td>
<td>1.0 (0.90-3.9)</td>
</tr>
<tr>
<td>Other</td>
<td>11 (5.8%)</td>
<td>11 (6.1%)</td>
<td>7 (53.8%)</td>
<td>4.2%</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>11 (6.3%)</td>
<td>11 (6.1%)</td>
<td>7 (53.8%)</td>
<td>4.2%</td>
</tr>
<tr>
<td>Asian</td>
<td>108 (57.1%)</td>
<td>108 (59.7%)</td>
<td>7 (53.8%)</td>
<td>4.2%</td>
</tr>
</tbody>
</table>

Fig. 2. Racial/ethnic makeup of cohort.

A. Seizure Incidence within 48 hours of Vaccination

Of the 189 vaccinated, 13 (7%) reported a seizure within 48 hours of vaccine administration. Fig. 3 below shows the breakdown by the vaccine administered. Of those who received the Pfizer-BioNTech mRNA vaccine, 10 reported seizures, and of those who received the Moderna mRNA vaccine, 3 participants reported seizures.

B. Intractable Status and Seizures

Of the 13 participants who reported a seizure within 48 hours of vaccine administration, 7 (46%) of these participants had an underlying diagnosis of intractable epilepsy as defined by the limits used in this study described above. A comparison of seizure incidence between intractable and non-intractable members of the cohort, as shown in Fig. 4, shows those with an intractable status have a non-statistically significant increased risk ($p = 0.1618$) of seizures after vaccination with the odds ratio being 2.2.

C. Additional Triggers for Seizure

Of the 13 participants who reported a seizure within 48 hours of vaccine administration, 7 (54%) reported another trigger coinciding with the seizure. These triggers included missing medications, fever, lack of sleep, stress, and physical exhaustion. Fig. 5 shows the breakdown of these triggers.

D. Emergency Department Visits and Treatment plan Change Following Seizure

Of the 13 patients who reported a seizure, 1 reported going to the emergency department for their seizure and having their epilepsy treatment plan changed.

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**Fig. 3. Case counts of seizure within 48 hours of vaccine administration separated by the vaccine administered.**

**Fig. 4. Occurrence of seizures based on intractable epilepsy status.**

**Fig. 5. Potential additional triggers of participant's seizure.**

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IV. DISCUSSION

The results from this study show low incidence, 7%, of seizures within 48 hours of COVID-19 vaccine administration. The slightly higher frequency of seizures amongst the Pfizer-BioNTech mRNA vaccine group is likely due to the larger number of individuals receiving that vaccination and less likely due to an underlying risk associated with that specific vaccination.

Of the 13 participants reporting seizures following vaccination, further investigation revealed there may be other provocative factors that could explain the participants’ breakthrough seizures. 7 of the 13 participants reporting seizures had a diagnosis of intractable epilepsy. These patients had an increased risk of seizures within 48 hours, but this result was not statistically significant (OR 2.2, p=0.1618). Patients with intractable epilepsy have seizures that are resistant to most treatment and in some studies have been shown to have higher rates of seizure relapse following remission [9]. Thus it is within reason that these patients may have a slight increased risk of seizure following vaccine administration. Given this finding of a slight increased risk for patients with intractable epilepsy, clinicians should counsel their patients with intractable epilepsy appropriately when advising them to receive a COVID-19 vaccination. This would include reminding them to avoid potential seizure triggers such as missing medications, lack of sleep, ingesting alcohol, etc. prior to vaccine administration. Further observation in patients with intractable epilepsy is recommended to continue to explore the relationship between breakthrough seizures, intractable epilepsy, and COVID-19 vaccination.

This study also identified additional potential seizure triggers, aside from vaccine administration, that were present in participants reporting seizures. Out of the 13 participants reporting seizures, 7 indicated other possible triggers for the seizure. These triggers included missed medication or lack of sleep. Only 6 out of 178 (3%) participants who provided information on seizure occurrence had breakthrough seizures with no identified provoking factors. This low incidence is reassuring for overall vaccine safety and this finding of possible confounding triggers provides clinics treating PWE with potential mitigation strategies for reducing seizures with vaccination.

The results of this study are further strengthened in that it confirms prior results seen in German and Kuwait cohorts that also showed low incidence of seizures and worsening epilepsy following COVID-19 vaccination [6], [7]. This study also has a larger sample size than the two prior studies showing the prior observations made are seen in a larger population. However, it should be noted this sample size of around 200 participants is still small in comparison to the estimated 50 million people worldwide diagnosed with epilepsy [10]. The demographic makeup of this study’s participants is also fairly representative of the county demographics where the study took place, indicating the study was able to capture a sample representative of the local area [11]. A limitation of this study is the retrospective design and the self-reported nature of the data making the results subjective. This could be mitigated in future studies through controlled trials.

Overall this study shows a low incidence of seizures in PWE within 48 hours of COVID-19 vaccination and the majority of occurred seizures had another associated possible provocation. Given the findings identified in this study of patient’s intractable epilepsy diagnosis contributing as well as possible confounding triggers, future studies that control for confounding triggers in patients with a diagnosis of intractable epilepsy are recommended to further explore the vaccine safety profile in this population. In the meantime, it would be reasonable for clinics treating PWE to coordinate with their patients to mitigate potential triggers prior to them receiving a COVID-19 vaccination. Additionally, given the subjective nature of the data reported and the relatively small sample size in comparison to the general PWE population, larger controlled prospective studies are recommended to further evaluate the safety profile of the COVID-19 vaccines in this population overall. Nonetheless, this study as well as the existing data so far is reassuring that the COVID-19 vaccines are safe, well tolerated, and effective in this population.

V. ACKNOWLEDGEMENTS

The authors thank the staff of the two participating clinics for helping in the care of these patients and the numerous healthcare workers helping to vaccinate our population during this pandemic.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

REFERENCES


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