Tidsskriftet Tidsskrift for Den norske legeforening

COVID-19 and epilepsy

OPINIONS

KJELL HEUSER

E-mail: kjell.heuser@ous-hf.no
Kjell Heuser, PhD, senior consultant and researcher in the Department of Neurology, Oslo University Hospital, Rikshospitalet.
The author has completed the ICMJE form and declares no conflicts of interest.

TONI CHRISTOPH BERGER

Toni Christoph Berger, doctor in the Department of Neurology, Oslo University Hospital, Rikshospitalet and a PhD research fellow at the University of Oslo.
The author has completed the ICMJE form and declares no conflicts of interest.

OLIVER HENNING

Oliver Henning, PhD, senior consultant at the National Centre for Epilepsy, Oslo University Hospital.
The author has completed the ICMJE form and declares no conflicts of interest.

SIGRID SVALHEIM

Sigrid Svalheim, PhD, senior consultant in the Department of Neurology, Oslo University Hospital, Rikshospitalet.
The author has completed the ICMJE form and declares no conflicts of interest.

JØRN MANDLA SIBEKO

Jørn Mandla Sibeko, assistant secretary general of the Norwegian Epilepsy Association.
The author has completed the ICMJE form and declares no conflicts of interest.

KARL O. NAKKEN

Karl O. Nakken, retired neurologist. For many years he was medical officer in charge at the National Centre for Epilepsy, Oslo University Hospital.
The author has completed the ICMJE form and declares no conflicts of interest.

ERIK TAUBØLL

Professor Erik Taubøll, senior consultant and head of research in the Department of Neurology, Oslo University Hospital, Rikshospitalet.
The author has completed the ICMJE form and declares no conflicts of interest.

Can COVID-19 cause epilepsy, or increase the tendency to seizures in those with epilepsy? Is it safe for persons with epilepsy to be vaccinated against COVID-19?

The Epilepsy Association's advisory service has noted a marked increase in enquiries since the outbreak of the pandemic. Patients and their families primarily ask for more specific information about COVID-19 and epilepsy. Many have difficulty applying the general information to their particular health and life situation. We conducted a literature search and used a discretionary selection of this literature to provide answers to key questions.

Can COVID-19 give rise to epilepsy?

COVID-19 affects the lungs first and foremost, but it can also affect other organs, including the brain. In cases of cerebral involvement, the effects seen most frequently are altered sense of taste and smell, headache and stroke. The risk of COVID-19 infection causing epilepsy or exacerbating pre-existing epilepsy is very low. Like other neurotropic viral infections, COVID-19 *can* cause epileptic seizures. The infection gives rise to a massive increase in proinflammatory cytokines. This cytokine storm can cause leakage through the blood-brain barrier, enabling the virus to penetrate the brain and bind to angiotensin-converting enzyme 2 (ACE2) receptors. These receptors are found on both neurons and various glial cells. The result is an increase in glutamate and aspartate concentration and reduced gamma aminobutyric acid (GABA) concentration. In addition, a number of ion channels are affected, which may cause increased excitability and hence epileptic seizures (1).

During the first phase of the pandemic, Chinese researchers conducted a retrospective multi-centre study in which 304 hospitalised COVID-19 patients were included, 108 of them with a severe disease course. No cases of new-onset

epilepsy were recorded, including amongst persons with cerebral involvement (2).

A meta-analysis based on 39 studies and 68 362 COVID-19 patients showed that around 21 % had neurological symptoms. Most common were headache (4.6 %) and stroke (4.0 %). Epileptic seizures occurred in 0.7 % (3).

> ***«For many patients with epilepsy the lockdown of society, with a high threshold for visiting hospitals and less contact with health professionals, has been very negative»***

Several case reports have been published describing refractory status epilepticus as part of a COVID-19 infection. Two of them responded to intravenous immunoglobulin therapy and one was associated with anti-NMDA-receptor encephalitis (4–6). In some, the seizures and status epilepticus were linked to the infection itself, while in others they were a consequence of stroke, for instance.

Can epilepsy be exacerbated by COVID-19?

So far there is *no* evidence that COVID-19 infection per se exacerbates the seizure tendency in patients with established epilepsy. However, a number of factors associated with the pandemic may affect seizure frequency indirectly. Three studies found that 8 %, 25 % and 27 % of participants experienced increased seizure frequency during the pandemic. Stress, anxiety, lack of sleep, depression, less physical activity, poorer quality of life and fear of being hospitalised or running out of drugs were given as reasons (7–9).

For many patients with epilepsy the lockdown of society, with a high threshold for visiting hospitals and less contact with health professionals, has been very negative. A retrospective Italian study found that acute admissions of epilepsy patients were almost halved during the pandemic (10).

Telemedicine versus check-ups at outpatient clinics

One aim during the pandemic has been to limit the flow of patients to hospitals. Telemedicine has proved a useful substitute for physical meetings with patients for monitoring epilepsy therapy (11). For example, daily video meetings with the parents of children with protracted stays in ICUs because of status epilepticus have proved very valuable. During these telemedical consultations it is possible, for example, to provide advice on the use of anti-epileptic drugs at home, and to plan further follow-up and treatment. They are not a fully satisfactory substitute for physical meetings between patient and therapist, nonetheless. The Epilepsy Association's advisory services have therefore seen a pronounced increase in enquiries from patients seeking information. Reduced access to health services, but also to special needs teachers and respite measures present a challenge to individuals and families.

Vaccination justifiable

No direct link has been found between the available vaccines and epileptic seizures (12). Some may experience a slight fever from vaccines, which in some individuals may lower the threshold for seizures. Fever associated with COVID-19 infection is nevertheless regarded as far more risky for those with epilepsy.

A possible interaction between anti-epileptic drugs and COVID-19 vaccines is regarded as of very little clinical importance. In the event of an increase in seizures or signs of side effects in the first few days following vaccination, the serum concentration of the drugs should be measured (13).

Conclusion

We believe the risk of a COVID-19 infection giving rise to new-onset epilepsy or an increase in seizures amongst those with pre-existing epilepsy to be very low.

We recommend that persons with epilepsy be vaccinated in the usual way.

LITERATURE

1. Nikbakht F, Mohammadkhanizadeh A, Mohammadi E. How does the COVID-19 cause seizure and epilepsy in patients? The potential mechanisms. Mult Scler Relat Disord 2020; 46: 102535. [PubMed][CrossRef]

2. Lu L, Xiong W, Liu D et al. New onset acute symptomatic seizure and risk factors in coronavirus disease 2019: A retrospective multicenter study. Epilepsia 2020; 61: e49–53. [PubMed][CrossRef]

3. Cagnazzo F, Arquizan C, Derraz I et al. Neurological manifestations of patients infected with the SARS-CoV-2: a systematic review of the literature. J Neurol 2020; 267: 1–10. [PubMed][CrossRef]

4. Dono F, Nucera B, Lanzone J et al. Status epilepticus and COVID-19: A systematic review. Epilepsy Behav 2021; 118: 107887. [PubMed][CrossRef]

5. Manganotti P, Furlanis G, Ajčević M et al. Intravenous immunoglobulin response in new-onset refractory status epilepticus (NORSE) COVID-19 adult patients. J Neurol 2021; 268: 1–5. [PubMed]

6. Monti G, Giovannini G, Marudi A et al. Anti-NMDA receptor encephalitis presenting as new onset refractory status epilepticus in COVID-19. Seizure 2020; 81: 18–20. [PubMed][CrossRef]

7. Zeng C, Meng H, Zhu Y et al. Correlation of seizure increase and COVID-19 outbreak in adult patients with epilepsy: Findings and suggestions from a Nationwide multi-centre survey in China. Seizure 2021; 88: 102–8. [PubMed] [CrossRef]

8. Casassa C, Moss R, Goldenholz DM. Epilepsy during the COVID-19 pandemic lockdown: a US population survey. Epileptic Disord 2021; 23: 257–67. [PubMed][CrossRef]

9. Sanchez-Larsen A, Gonzalez-Villar E, Díaz-Maroto I et al. Influence of the COVID-19 outbreak in people with epilepsy: Analysis of a Spanish population (EPICOVID registry). Epilepsy Behav 2020; 112: 107396. [PubMed] [CrossRef]

10. Cheli M, Dinoto A, Olivo S et al. SARS-CoV-2 pandemic and epilepsy: The impact on emergency department attendances for seizures. Seizure 2020; 82: 23–6. [PubMed][CrossRef]

11. Olivo S, Cheli M, Dinoto A et al. Telemedicine during the SARS-Cov-2 pandemic lockdown: Monitoring stress and quality of sleep in patients with epilepsy. Epilepsy Behav 2021; 118: 107864. [PubMed][CrossRef]

12. Lu L, Xiong W, Mu J et al. The potential neurological effect of the COVID-19 vaccines: A review. Acta Neurol Scand 2021; 144: 3–12. [PubMed] [CrossRef]

13. Kow CS, Hasan SS. Potential interactions between COVID-19 vaccines and antiepileptic drugs. Seizure 2021; 86: 80–1. [PubMed][CrossRef]

Publisert: 28 June 2021. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.21.0429
Received 23.5.2021, first revision submitted 4.6.2021, accepted 7.6.2021.