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COVID-19 and epilepsy

OPINIONS

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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.

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