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Keeping people with epilepsy safe during the Covid-19 pandemic

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Abstract

Objectives: To provide information on the impact of the COVID-19 pandemic on people with epilepsy and provide consensus recommendations on how to provide the best possible care for people with epilepsy while avoiding visits to urgent care facilities and hospitalizations during the Novel Coronavirus pandemic.

Methods: The authors developed consensus statements in two sections. The first was "*How should we/clinicians modify our clinical care pathway for people with epilepsy during the COVID-19 pandemic?" The second was "What general advice should we give to people with epilepsy during this crisis?* Authors individually scored statements on a scale of -10 (strongly disagree) to +10 (strongly agree). 5/11 recommendations for physicians and 3/5 recommendations for individuals/families were rated by all authors as 7 or above (strongly agree) on the first round of rating. Subsequently, a tele-conference was held where statements for which there was a lack of strong consensus were revised.

Results: After revision, all consensus recommendations received a score of 7 or above. The recommendations focus on administration of as much care as possible at home to keep people with epilepsy out of health care facilities, where they are likely to encounter COVID-19 (including strategies for rescue therapy), as well as minimization of risk of seizure exacerbation through adherence, and through ensuring a regular supply of medication. We also provide helpful links to additional helpful information for people with epilepsy and health providers

Conclusion: These recommendation may help healthcare professionals provide optimal care to people with epilepsy during the coronavirus pandemic.

Introduction

The coronovairus disease of 2019 (COVID-19) pandemic can affect everyone worldwide and cause additional concerns for those with chronic conditions [1]. An individual's risk of contracting the virus is increased with emergency department visits or hospital admission. People with epilepsy, as well as their families/caregivers and clinicians face further consequences of the pandemic. A coalition of multi-national specialists, representing all continents convened to highlight concerns for people with epilepsy and address safety issues during this period of increased risk and rapid change in access to health care. We seek to provide current information on the possible impact of the COVID-19 pandemic on people with epilepsy, how to keep them safe given disruptions in clinical services and provide them with general advice and guidance to find further information. We also provide two sets of consensus recommendations, one for health care providers and one for people with epilepsy and their families, addressing best practice in our "new reality" of epilepsy care. These recommendations are made in the context of COVID-19 and not for use beyond this pandemic. Further, these recommendations should be considered in the context of local circumstances, regulations and resources.

Methods for consensus statements

The authors collated questions and concerns from the epilepsy community, predominantly through organisations such as Epilepsy Foundation and UK Epilepsy Society. A list of statements addressing common questions, were formulated and provided and the authors asked to individually score them on a scale of -10 (strongly disagree) to +10 (strongly agree). 5/11 recommendations for physicians and 3/5 recommendations for individuals/families were rated by all authors as 7 or above (strongly agree) on the first round of rating. Subsequently, a tele-conference was held where statements for which there was a lack of strong consensus were revised until strong consensus was reached.

1. *Does SARS-COVID-2 directly cause health issues for persons with epilepsy?*
   a. *Does SARS-COVID-2 precipitate or aggravate existing seizures?*

   There is limited evidence that the CNS is a target of the SARS-COVID 2 virus. The virus exploits the angiotensin-converting enzyme 2 (ACE2) receptor to enter cells, and CNS glia and neurons express ACE2 receptors, making them potential targets. Other coronavirus infections may cause variable rates of seizures associated with fever, or seizure exacerbation (CoV-HKU1 infections 50%, HCoV-OC43 14%)[2]. Other coronaviruses are found in the CSF, but the degree to which SARS COVID 2 penetrates the blood brain barrier is unclear[3]. It has been suggested that SARS-COVID 2 virus may penetrate the brainstem, aggravating respiratory impairment[4]. Other neurological manifestations including seizures in severe/end stage disease likely reflect COVID-19 related hypoxia, encephalopathy or encephalitis rather than lowered seizure threshold in susceptibile individuals with pre-existent neurological disease. Recently, there have also been some reports of "neurologic presentations" earlier in disease[5]. Some may include new-onset seizures[6]

b. Are people with epilepsy more predisposed (or vice-versa) to COVID-19 infection?

Limited information from countries with experience of the pandemic (e.g. China, Italy, United States) suggests that individuals with epilepsy are not more likely to be infected by the virus, nor are they more likely to have severe COVID-19 manifestations because they suffer from epilepsy. High risk individuals remain those with diseases restricting mobility, respiratory conditions (including asthma), diabetes mellitus, hypertension, severe heart disease, impaired immune function due to underlying conditions or drug treatment and older age, particularly when associated with frailty[1]. People with epilepsy may also have any of these conditions. Since autoimmune disorders are associated with an increased risk of epilepsy and are often treated with immunosuppressive therapies, this is a concern for some people with epilepsy. Individuals with Tuberous sclerosis Complex (TSC), which is often accompanied by epileptic seizures, may have reduced lung function and may also be treated with immune therapy. For certain epilepsy syndromes such as Dravet syndrome, as well as for other epilepsies where seizures are triggered by fever or illness, there may be a risk of worsening in a person with fever due to COVID-19. To date, case reports of worsening have not come forward, which is reassuring. Children are less likely to suffer severe respiratory illnesses (0.9% 0-14 years[7] in China, 1.5% affected were under 20 years old in Italy[8]).

c. *Are there medications that should be avoided in people with epilepsy?* Information is circulating that certain medications, including nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, should be avoided in the acute phase of infection, although there is no strong evidence to support this recommendation. For people in whom fever control is important (e.g. those with Dravet syndrome), acetaminophen (paracetamol) can be used, followed by ibuprofen as needed[9]. Some medications used to treat individuals with upper respiratory tract infections, such as the decongestant pseudoephedrine or the antihistamine diphenhydramine, may aggravate seizures in people with epilepsy[10].

A number of medications are now being studied as possible treatments for COVID-19 to reduce viral load and/or severity of disease. Possible interactions between epilepsy medications, antivirals and other agents that may be used in the management of COVID-19 may need consideration[11]. Chloroquine and hydroxychloroquine, either alone or with azithromycin[12,13] have been discussed. Although rare instances of seizures have been associated with the use of these agents[14,15], there are no contraindications in people with epilepsy[16]. Risk to benefit ratio must be assessed in each case if these medications are considered useful.

2. *How should we/clinicians modify our clinical care for people with epilepsy during the COVID-19 pandemic?*

The pandemic has led to an extraordinary reduction in health care availability. Further, attendance at medical facilities poses an additional risk of contracting the virus for individuals and their carers/families. What is usually regarded as standard practice in case management must now be reconsidered. Clinicians should formulate approaches to reduce emergency room, clinic and hospital visits to protect people from becoming infected and keep critical resources for those in most urgent need. The pandemic has led to heightened anxiety amongst clinicians and people with epilepsy, let alone the wider community, highlighting a need for guidance and advice.

Below are the consensus guidance statements for professionals caring for people with epilepsy during the COVID-19 pandemic. These recommendations need to be considered in the context of local resources and circumstances.

a. Try to administer as much care as possible at home to reduce risk of exposure. Specifically, try to keep people with epilepsy out of areas where they are likely to encounter COVID-19, such as medical offices, out patient clinics, urgent care facilities and hospitals.

b. Where possible, people with epilepsy should have an emergency care plan. The threshold to provide emergency rescue medication (e.g. benzodiazepines via buccal, nasal or rectal routes, or oral if they can be safely swallowed) may be lowered. Even a well-controlled individual with epilepsy may benefit from having a rescue medication on hand under these unusual circumstances. Individuals with epilepsy and their families/caregivers should have a clear understanding of when and how rescue medications should be used, if they can be repeated, and when emergency room visits are necessary.

c. People with epilepsy and their families/caregivers should be reassured that most tonic-clonic seizures last under 2-3 minutes, and do not require emergency medical services or hospital care. Medical/hospital care may be required if tonic-clonic seizures last more than 5 minutes or occur in clusters with no rescue medication available, or if seizures occur in water (baths, swimming), are followed by unusually prolonged postictal symptoms or abnormal recovery, or cause potentially dangerous injury.

d. A regular supply of antiseizure medication should be ensured as well as access to repeat prescriptions and supplies. The importance of taking medication regularly should be emphasised. Stockpiling of medication should be discouraged.

e. At this time, when regular case review and hospital attendance may be hindered, consider whether changes to treatment could be postponed (e.g. weaning medication, changes to vagal nerve stimulator (VNS) or responsive neurostimulation (RNS) settings, ketogenic diet changes or elective epilepsy surgery). Any initiated withdrawal/wean or down titration of medication should be delayed or reversed unless there are strong reasons for doing otherwise.

f. Key advice on lifestyle issues should be reinforced: the need for regular sleep, consistency in current routines, healthy eating and exercise, avoidance of recreational drugs and alcohol.

g. Telehealth should be utilised where possible, using video ideally, or phone if video is not accessible. Such contact with individuals and caregivers/families can alleviate their anxiety and concerns. Follow-up assessments are all possible by telephone or video link.
h. For new presentations, care can be enhanced through careful history taking and home video where possible.[17] Medical examination and laboratory tests may need to be postponed, unless necessary for short-term management decisions. Many elements of the neurological examination, from gait assessment to neuro-opthalmology, can be done using an ipad or similar device.
i. Most individuals with definite or suspected new onset epilepsy warrant an MRI scan, but during the pandemic, neuroimaging should be postponed unless required to address urgent diagnostic or therapeutic issues. If there is an urgent requirement for imaging, an outpatient facility is preferred and the COVID-19 risk from travel, time in waiting rooms and exposure to health care workers should be weighed against potential benefits.
j. In most cases, diagnostic EEG can be delayed to a later date. Urgent situations including status epilepticus in ICU, concern about electrical status epilepticus of slow sleep, nonconvulsive status, or infantile spasms (although video diagnosis of spasms by an experienced paediatric neurologist might be enough to initiate treatment if the risk of hospital attendance outweighs benefit) may require EEG. In some cases (e.g., infantile spasms), a brief outpatient study can provide critical information with low risk if precautions are used.
k. A system to reduce direct exposure of health care professionals to people with epilepsy is advisable. For example, a clinic or hospital service can have a 'neurologist' of the day or a technician performing all EEGs during a certain period and in a single environment. This will facilitate tracking of contacts, and minimise disruption should individual health professionals become infected. In managing status epilepticus, additional precautions should be undertaken to prevent airborn spread from secretions. Recommendations are evolving rapidly. Those emanating from ACNS and NAEC can be found below.
l. Mental health issues, particularly depression and anxiety, are common in people with epilepsy regardless of age. Anxiety may particularly be heightened among individuals and their families/carers from concerns about the pandemic and their epilepsy, as well as from its economic impact. Direction to resources and possible access to Helplines should be highlighted. Providers can supply critical reassurance to people with epilepsy and their families.

3. *What general advice should we give to people with epilepsy during this crisis?*
    a. At this time of heightened anxiety, reassurance and basic advice about minimising the likelihood of seizure exacerbation is key.
    b. Consider a 'comprehensive care plan', with information about what should happen if families/caregivers are ill or not available.
    c. The importance of adherence and maintaing routines should be emphasized. For example, use of pillboxes, cell phone alarms or phone apps may be helpful, especially if the individual with epilepsy is separated from their usual caregivers/family member, who may be ill and were helping to administer medication.
    d. Instructions should be given to maintain a regular medication supply. People with epilepsy and their families/caregivers should work to prevent medication shortages and ensure that repeat prescriptions are available. Consideration should be given to maintain a 3-month supply, where feasible, and trying to obtain medications outside of the hospital setting (e.g., online pharmacies).
    e. General advice should be given to ensure adequate sleep where possible, engage in routine exercise, healthy eating, and avoidance of alcohol and recreational drugs, where appropriate. For those with stimulus-induced 'reflex' epilepsies (e.g., photosensitive epilepsy), discussion of reducing or eliminating provocative stimuli (e.g., computer games) may be warranted.
    f. Mental health issues, already common among individuals with epilepsy, and families in general, may be exacerbated; reassurance that this is to be expected, with access to telephone advice, may alleviate anxiety.

People with epilepsy may be concerned about whether they are at higher risk of severe COVID-19, and therefore should entertain stricter quarantine. They should be reassured that, in the absence of risk factors, including older age, immobility, co-existent respiratory disease, diabetes mellitus, hypertension, severe heart disease or immunosuppression, people with epilepsy are not at higher risk. It is prudent, however, for them to remain isolated from contacts and symptomatic individuals where possible.

4. *What are the implications for resource poor countries?*

Cases of COVID-19 have been identified in most countries. The numbers of cases reported from many resource-limited countries are low at present, but this may reflect a lack of diagnostic facilties and low ascertainment rate. In some countries, a lockdown has been imposed pre-emptively to contain the spread of infection. Health care systems may be inadequate to deal not only with a massive rise in number of infected cases, but also with the consequences of the lockdown. Telemedicine services might be poorly developed or non-existent. Medication delivery systems are often non-functional and there may be poor disease and treatment literacy in such settings. Maintaining the supply of anti-seizure medication is of great concern. All these pose considerable challenges to epilepsy care providers. Health care professionals are required to make innovative use of available resources to meet these challenges.

The burden of disease overall in resource limited countries is significant and the ripple effect of pandemics, such as COVID-19, can disrupt established or evolving health care structures. For example, the Ebola virus outbreak severely affected the capacity to deliver early child intervention programs, including vaccinations[18]. The result was a wave of inadequately protected children. Similarly, transfer of personnel and resources from obstetric and neonatal services will increase perinatal complications. In Africa, up to a third of epilepsy cases in children may be the result of perinatal insults and a third of adult cases may result from parasitic and other infections. Furthermore, preventive measures will fall away during this pandemic due to lack of resources. Africa has the highest prevalence of HIV infection, significantly increasing the risk of COVID-19 via immunosuppression. Further, the high prevalence of tuberculosis across Africa and Asia adds another layer to the complexity of disease management and risk in these settings. While most of these individuals do not have epilepsy, they are placed at increased risk and we may see a spike in the number of new cases of epilepsy as a result of the sequelae of the pandemic.

5. *Useful information for patients*
   a. The Epilepsy Foundation, TS alliance and the Epilepsy Society UK produced useful information for people with epilepsy, addressing frequently asked questions

https://www.epilepsy.com/article/2020/3/concerns-about-covid-19-coronavirus-and-epilepsy
https://www.tsalliance.org/individuals-families/covid-19/
https://www.epilepsysociety.org.uk/epilepsy-and-coronavirus-covid-19-faqs#.Xnp7d252tcg

6. Useful information for physicians
   a. Link to updating information on best practices for performing clinical neurophysiology testing (eg EEG, ambulatory EEG): https://www.acns.org/practice/covid-19-resources

https://www.acns.org/practice/covid-19-resources NAEC

   b. Link to a library of COVID resources from the American Epilepsy Society:

https://www.aesnet.org/about_aes/position_statements/covid-19/home?_cldee=bmF0aGFsaWUuamV0dGVAbXNzbS5lZHU%3d&recipientid=contact-d4343126d1bee51198a600155da80a47-b9f22fe613064919b1842dd6ea727f96&esid=48c95c52-a26e-ea11-8100-000d3a01cfd3

   c. Resources from the National Association of Epilepsy Centers, including policy updates relevant to epilepsy practices.

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