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Don't Just Stand There: Do Something! The Case for Peri-Ictal Intervention

Hypoxemia Following Generalized Convulsive Seizures: Risk Factors and Effect of Oxygen Therapy

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Objective: To analyze the factors that determine the occurrence or severity of postictal hypoxemia in the immediate aftermath of a generalized convulsive seizure (GCS). Methods: We reviewed the video-electroencephalogram (EEG) recordings of 1006 patients with drug-resistant focal epilepsy included in the REPO2MSE study to identify those with $\geq$1 GCS and pulse oximetry (SpO_2) measurement. Factors determining recovery of SpO_2 $\geq$90% were investigated using Cox proportional hazards models. Association between SpO_2 nadir and person- or seizure-specific variables was analyzed after correction for individual effects and the varying number of seizures. Results: A total of 107 GCS in 73 patients were analyzed. A transient hypoxemia was observed in 92 (86%) GCS. Rate of GCS with SpO_2 <70% dropped from 40% to 21% when oxygen was administered early ($P = .046$). Early recovery of SpO_2 $\geq$90% was associated with early administration of oxygen ($P = .004$), absence of postictal generalized EEG suppression (PGES; $P = .014$), and extratemporal lobe epilepsy ($P = .001$). Lack of early administration of O_2 ($P = .003$), occurrence of PGES ($P = .018$), and occurrence of ictal hypoxemia during the focal phase ($P = .022$) were associated with lower SpO_2 nadir. Conclusion: Postictal hypoxemia was observed in the immediate aftermath of nearly all GCS, but administration of oxygen had a strong preventive effect. Severity of postictal hypoxemia was greater in temporal lobe epilepsy and when hypoxemia was already observed before the onset of secondary GCS.

Commentary

Sudden unexpected death in epilepsy (SUDEP) is the leading cause of premature death in patients with epilepsy, affecting both children and adults, with an average incidence of 4 per 1000 patient-years with higher rates for those with intractable epilepsy, generalized convulsive seizures (GCS), and failed epilepsy surgery. Other causes of death include status epilepticus, suicide, drowning, and physical injuries due to falls or motor vehicle accidents.[1] The cumulative mortality rate over 40 years is as much as 12% in patients with chronic, poorly controlled epilepsy of childhood onset.[2] A high frequency of generalized tonic–clonic seizures, polytherapy, and long duration of epilepsy have been identified as leading risk factors for SUDEP.[3]

A study of mortality in epilepsy monitoring units identified postictal alteration of cardiorespiratory function following a generalized tonic clonic seizure as the likely mechanism in SUDEP, prompting better surveillance of patients in the EMU especially after medication withdrawal. Postictal generalized electroencephalogram (EEG) suppression (PGES) at seizure termination has been identified as a biomarker for brain stem dysfunction.[4] Postictal generalized EEG suppression is often associated with profound hypotonia and immobility, which may lead to suffocation if the patient ends up in a prone position. In patients with GCSs, hypercapnia was noted in all patients with desaturation below 85%, suggesting that ictal oxygen desaturation is due to alveolar hypoventilation.[5] This may explain oxygen desaturation occurring prior to or in the absence of secondary generalization, especially those with temporal lobe onset seizures and with contralateral seizure spread.

Ictal apnea is more often central than obstructive and more common with temporal lobe onset.[6,7] In a patient with orbitofrontal seizure onset, apnea occurred only when the seizures spread to the amygdala; electrical stimulation of the amygdala also resulted in apnea.[8] These reports highlight the influence of limbic structures on brain stem nuclei involved in the control of respiration. Patients taking a serotonin reuptake inhibitor like fluoxetine had less frequent hypoxemia during GCS than those not taking it (6% vs 20%).[9] Endogenous opioids are released during focal and generalized seizures, prompting some to suggest a potential role for opioid receptor antagonists such as naloxone and naltrexone for treating seizure-related hypoxemia.[10]

Rheims and investigators from several centers prospectively examined the effect of oxygen administration during GCS using pulse oximetry measurements. The rate of severe

desaturations <70% dropped from 40% to 21% when oxygen was administered early, defined as during or within 5 seconds of seizure end ($P = .046$). Lack of early oxygen administration, PGES, and hypoxemia prior to generalization were associated with a lower SpO_2 nadir (70% without O_2 vs 79% receiving O_2). On the other hand, earlier recovery of SpO_2 >90% occurred with early administration of oxygen, lack of PGES ($P = .046$), and extratemporal lobe epilepsy ($P = .001$). It should be noted that oxygen treatment was not randomized. Although oxygen shortened the duration of hypoxemia at 30 and 60 seconds after seizure end, by 120 seconds there was no difference between the groups. Not discussed was the obvious fact that patients receiving oxygen would also have received other nursing interventions, namely, lateral positioning, airway suction, and so on. The importance of early nursing intervention was shown in 2 studies, where it was associated with shorter duration of hypoxemia and PGES.[11,12] In the study by Wu et al, peri-ictal interventions occurred in 122 of 150 GCS; oxygen was administered in 29 of 122 GCS. No difference in the length of the PGES was seen in those receiving oxygen versus those who did not. The tonic phase was longer in patients with PGES.[12,13] Oxygen administration appeared to shorten the duration of hypoxemia but not the duration of postictal immobility. When we examined the effect of oxygen administration to patients having 2 or more GCS seizures and receiving oxygen in one seizure but not another, oxygen administration resulted in no difference in duration of desaturation or the oxygen nadir; however, postictal recovery was faster in those receiving oxygen, as expected. This speaks to limited air-exchange during the ictus due to tonic contraction of the respiratory muscles, central apnea/hypoventilation, or both.

Additional studies would be helpful to examine the differential effects of proper patient positioning during GCS, ensuring a patent airway by suctioning and/or neck repositioning and of course oxygen administration. It is worth noting that even nonconvulsive seizures can be associated with oxygen desaturation and hypoventilation, especially those of temporal lobe origin. Instead of reflexively ordering home oxygen, a suction machine and education regarding proper intervention during GCS may serve the patient better. Wearable devices to alert the caregiver of GCS occurring sleep are also becoming available now.

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