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Topical Review

Current Status of Continuous Electroencephalographic Monitoring in Critically Ill Children

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ABSTRACT

The utilization of continuous electroencephalographic monitoring in critical care units has increased significantly, and several consensus statements and guidelines have been published. The use of critical care electroencephalographic monitoring has become a standard of care in many centers in the United States and other countries. The most common indication is to detect electrographic seizures and status epilepticus. Other indications include monitoring treatment efficacy in patients with electrographic seizures and status epilepticus, evaluating the degree of disturbance of function in patients with encephalopathy, monitoring brain function in patients treated with sedation and neuromuscular blocking agents, and event characterization. The urgent initiation of critical care electroencephalographic monitoring is recommended in certain clinical populations, but varies among institutions. The consensus among neurologists is to start treatment after identifying electrographic seizures or electrographic status epilepticus with or without clinical signs. However, the optimal treatment of nonconvulsive and electrographic-only seizures remains controversial. Critical care electroencephalographic monitoring has significant impact on clinical management, but there is lack of clear evidence that treatment guided by critical care electroencephalographic monitoring leads to improvement of clinical and neurodevelopmental outcome. There are substantial discrepancies among institutions on personnel and technical support used for critical care electroencephalographic monitoring. The optimal critical care electroencephalographic monitoring team should include electroencephalographers with experience in critical care electroencephalographic monitoring interpretation and appropriately trained technologists certified in electroencephalography by the American Board of Registration of Electroencephalographic and Evoked Potential Technologists specializing in critical care electroencephalographic monitoring or long-term monitoring.

Introduction

Disorders of the brain and nervous system, such as central nervous system infections, cerebral ischemia, traumatic injury, and clinical and subclinical epileptic seizures are common in children who are admitted to pediatric intensive care units (PICUs).[1] Electroencephalography (EEG) is an objective noninvasive measure of brain function. Continuous EEG monitoring (cEEG) is a valuable tool to observe the evolution of brain dysfunction and identify clinically significant changes. Historically, EEG monitoring has been used for a wide range purposes, and particularly for evaluation and management of seizures and status epilepticus. The advantage of EEG as an extension of the clinical examination is that it can be used in sedated patients and provides quantitative data for following functional changes over time. There has been increasing use of continuous EEG for patients in the intensive care unit (ICU) in recent years.[2,3] A survey of 61 large pediatric hospitals in the United States and Canada showed that the median number of patients who had critical care EEG monitoring (CCEEG) increased 30% from 2010 to 2011.[4]

CCEEG is recorded for longer periods than standard EEG and is often requested as an urgent or emergency study in critically ill patients. There are no randomized trials evaluating the impact of CCEEG on patient outcomes. Challenges in investigations of CCEEG

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are significant owing to substantial variability in the indications for the procedure, the inconsistent integration into clinical pathways for specific patient populations, and barriers to CCEEG access. The majority of institutions do not have CCEEG clinical pathways.[2] CCEEG can only be ordered by neurology in more than 50% of the institutions. Some institutions require a short EEG before CCEEG. Remote EEG reviewing and in-house EEG technologists are not available in some hospitals. There are often no standard EEG review protocols by epileptologists or EEG screening by EEG technologists. There is also a lack of standard communication tools among clinical neurophysiology, neurology, and critical care teams regarding how to communicate the EEG results.[2]

Several guidelines and consensus statements have been published in the recent years (Table 1). These recommendations are created by expert consensus based on experience and literature review. The recommendations are supported by weak or poor quality evidence. An early consensus on the use of EEG in the ICU was published in 2009 to assess the depth of coma and EEG reactivity and variability in the ICU.[5] A guideline of EEG utilization in patients with status epilepticus in 2012 recommended CCEEG in patients with status epilepticus to guide treatment due to concern of ongoing non-convulsive seizures and status epilepticus.[6] A consensus statement by a multidisciplinary group published in 2013 on the use of EEG monitoring included broad indications for seizure detection in patients with status epilepticus, refractory status epilepticus, and comatose patients in the ICU; detection of ischemia in comatose patients with subarachnoid hemorrhage; and prognostication of coma after cardiac arrest.[7] A statement from the Neurocritical Care Society and the European Society of Intensive Care Medicine was published in 2014, and CCEEG was recommended in patients with persistent altered consciousness, comatose patients with cardiac arrest, and those with subarachnoid hemorrhage.[8] The American Clinical Neurophysiology Society (ACNS) first published a guideline on cEEG in critically ill neonates in 2011.[9] The most recent consensus statement on continuous EEG in critically ill adults and children, published in 2015 by the CCEEG task force of ACNS, included comprehensive consensus-based recommendations of CCEEG for the diagnosis and treatment of seizures, status epilepticus, event characterization, identification of cerebral ischemia, assessment of degree of encephalopathy, and monitoring of cerebral suppressive therapy.[10]

Clinical indications

The common indications for CCEEG in PICU are summarized in Table 2. The most common clinical indication for CCEEG is to detect electrographic seizures.

Electrographic seizures are defined as abnormal, paroxysmal, rhythmic electrographic pattern that evolves in frequency, amplitude, or morphology with a clear onset and offset lasting for at least 10 seconds or shorter if associated with clinical signs.[11] The seizures are classified as electroclinical seizures (clinically evident seizures) and EEG-only seizures (subclinical seizures). Electrographic seizures lasting more than 30 minutes or recurrent seizures lasting over 30 minutes without return of normal consciousness in

TABLE 1.
Summary of Published Guidelines and Consensus Statements on EEG Monitoring

Neurophysiology (2009) 39, 71–83. Consensus on the use of neurophysiological tests in the intensive care unit (ICU): Electroencephalogram (EEG), evoked potentials (EP), and electroneuromyography (ENMG).
Indications:
Assessment of the depth of coma; EEG reactivity and variability in ICU

Neurocrit Care (2012) 17:3–23. Guidelines for the evaluation and management of status epilepticus.
Indications for continuous EEG: For patients with suspected SE:
- Recent clinical seizure or SE without return to baseline >10 minutes
- Coma including postcardiac arrest
- Epileptiform activity or periodic discharges on initial 30-min EEG
- Intracranial hemorrhage including TBI, SAH, intracranial hypertension
- Suspected nonconvulsive seizures in patients with altered mental status

Intensive Care Med (2013) 39:1337–1351. Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM.
Indications:
- Seizure detection in patients with refractory SE
- Seizure detection in patients with SE that does not return to functional baseline within 60 minutes after administration of seizure medication
- Seizure detection in comatose patients in the ICU (TBI, SAH, ICH, coma after cardiac arrest, encephalitis, and septic and metabolic encephalopathy) with unexplained and persistent altered consciousness
- Ischemia detection in comatose patients with SAH when neurological examination is unreliable
- Assisting prognostication of coma after cardiac arrest

Neurocrit Care (2014) 21:S1–S26. Consensus summary statement of the international multidisciplinary consensus conference on multimodality monitoring in neurocritical care
- Patients with acute brain injury and unexplained and persistent altered consciousness
- Patients with convulsive SE that do not return to functional baseline within 60 min after seizure
- Patients with refractory SE
- Comatose patients after cardiac arrest during therapeutic hypothermia and within 24 hour of rewarming to exclude nonconvulsive seizures
- Comatose patients in the ICU without an acute primary brain condition and with unexplained impairment of mental status or unexplained neurological deficits to exclude nonconvulsive seizures
- Comatose patients with SAH to detect delayed cerebral ischemia

J Clin Neurophysiol 2015; 32: 87–95. Consensus statement on continuous EEG in critically ill adults and children, Part I: Indications
- Diagnosis of nonconvulsive seizures, nonconvulsive SE, and other paroxysmal events
- Assessment of efficacy of therapy for seizures and SE
- Identification of cerebral ischemia
- Assessment of severity of encephalopathy and prognostication
- Monitoring of sedation and high-dose suppressive therapy

Abbreviations:
EEG = Electroencephalography
ICH = Intracerebral hemorrhage
SAH = Subarachnoid haemorrhage
SE = Status epilepticus
TBI = Traumatic brain injury

between, or recurrent nonconvulsive seizures more than 50% of a given hour, are defined as electrographic status epilepticus.[12-15]

Electrographic seizures and electrographic status epilepticus are common in critically ill children and often have no associated clinical signs or have only subtle manifestations. Multiple observational studies have shown that electrographic seizures occur in 7% to 47% in critically ill children in PICUs or emergency department undergoing cEEG.[3,16-25] Electrographic status epilepticus identified on CCEEG ranged from 1% to 23% of patients.[3,18,23,25-27] The majority (70% to 80%) of electrographic seizures in PICU have no clinical signs or only subtle clinical signs that are unlikely to be detected without CCEEG.[3,26-30] These studies also showed that all children with status epilepticus experienced subclinical seizures and one-third of these children only had subclinical seizures.[3,18,26-28] These studies suggested that seizures and status epilepticus in critically ill children cannot be accurately diagnosed or effectively managed without the use of CCEEG.

The high-risk factors associated with seizures and status epilepticus are summarized in Table 3. Electrographic seizures and status epilepticus are common in critically ill children with persistent altered mental status with diverse diagnoses and wide range of etiologies, such as altered mental status after convulsive seizures or status epilepticus, traumatic brain injury, hypoxic-ischemic encephalopathy after cardiac arrest or birth asphyxia, intracranial hemorrhage, acute ischemic stroke, metabolic encephalopathy, and encephalopathy with unclear etiology.[3,31,32] Critically ill children who may require neuromuscular blocking medications and are at high risk for brain injury such as patients on extracorporeal membrane oxygenation should also be considered for CCEEG.[33] The identified risk factors included younger age, history of epilepsy, abnormal development, clinical seizures and clinical status epilepticus before CCEEG, structural brain injury, and acute neuroimaging abnormalities.[3,24,26,29,30] Some EEG features such as generalized periodic discharges, lateralized periodic discharges, interictal epileptiform discharges, lateralized rhythmic delta activity, and absence of reactivity were associated with electrographic seizures and status epilepticus.[18,34-36]

CCEEG is also indicated to guide the treatment for critically ill children with electrographic seizures and status epilepticus because the majority of electrographic seizures do not have reliable clinical signs.

Event characterization is another common indication for CCEEG. Critically ill children may have various episodic abnormal movement or autonomic changes concerning for seizures. Exclusion of seizure will prevent initiation or escalation of antiseizure medications. Episodic events that may benefit from CCEEG included motor movement (e.g., subtle myoclonic movements, nystagmus, gaze deviation, eyelid fluttering, and tonic posturing) and periodic autonomic changes (e.g., tachycardia, apnea).[10]

CCEEG is also suggested by the ACNS guideline in conjunction with clinical examination to monitor brain function in patients receiving sedation, to assess the severity of encephalopathy, and for prognostication.[10] The use of EEG for prognostication lacks rigorous studies that take into account the many factors influencing EEG. Most publications were conducted in adult populations. Several EEG patterns were identified to predict unfavorable outcomes in certain patient populations. In comatose adult survivors after cardiopulmonary resuscitation, EEG findings associated with poor outcome included generalized suppression to $\leq$20 μV, burst suppression with generalized epileptiform discharges, and generalized periodic complexes on a flat background.[37] EEG pattern of status epilepticus, nonreactive EEG, burst suppression, or generalized suppression predicted high mortality.[38] In children with therapeutic hypothermia after cardiac arrest, unreactive EEG, lack of cerebral activity, burst suppression, or any degree of discontinuity were associated with severe disability, vegetative state, or death.[39]

Timing, duration, and end point

The indications to initiate CCEEG vary among centers based on available resources. The timing of CCEEG initiation depends on available institutional resources. The ACNS consensus statement recommended initiating CCEEG as soon as possible in critically ill children with high risk for developing seizures.[10] About 50% of critically ill children with CCEEG had the first electrographic seizures during the initial hour of EEG monitoring.[26-30] Short 30- to 60-minute EEG will not be able to capture the majority of electrographic seizures. The first 24 hours of EEG captured 87% of seizures in critically ill children.[26] Recording for 24 to 48 hours captures about 90% of nonconvulsive seizures.[25] Most institutions perform CCCEG for one to two days if no seizures occur on EEG.[40] Longer monitoring may be indicated in certain patients such as those in

TABLE 2.
Common Indications for CCEEG

Acute encephalopathy with neurological disorders
Traumatic brain injury
Hypoxic-ischemic brain injury
Clinical seizures or status epilepticus
CNS infection
Brain tumor
Stroke
Acute encephalopathy with systemic disorders
Cardiac arrest
Immunotherapy for hematological or oncological disorders (CAR-T)
Toxic/metabolic
Postcardiac transplant/cardiac surgery
Sepsis
Unknown cause
Assessment of treatment efficacy in patients with electrographic seizure and status epilepticus
Event characterization
Apnea
Abnormal movements
Autonomic changes
Monitoring patient treated with sedation and neuromuscular blocking agents

Abbreviations:
CAR-T = Chimeric antigen receptor T-cell therapies
CCEEG = Critical care EEG monitoring
CNS = Central nervous system

TABLE 3.
Common Risk Factors Associated With Electrographic Seizures in Critically Ill Children

Clinical Features	EEG Features
Persistent encephalopathy (e.g., after clinical seizures, sepsis, unknown etiology)	Generalized periodic discharges
Younger age	Lateralized periodic discharges, LRDA
Clinical seizures and status epilepticus with encephalopathy	Interictal epileptiform discharges
History of epilepsy or brain malformation	Absence of reactivity on EEG
Acute brain structural injury (e.g., HIE, TBI, stroke, CNS infection/inflammation, tumor)	
Clinical seizures/status before CCEEG	

Abbreviations:
CCEEG = Critical care EEG monitoring
CNS = Central nervous system
EEG = Electroencephalography
HIE = Hypoxic-ischemic encephalopathy
LRDA = Lateralized rhythmic delta activity
TBI = Traumatic brain injury

coma or those with certain EEG features on early recordings. If seizures are identified, it is recommended to continue EEG monitoring until the patient is at least 24-hour seizure free and off continuous infusions of antiseizure medications for 24 hours.[10]

Treatment of clinical and electrographic seizures

There has been a long-standing controversy as to whether seizures are just biomarkers of brain injury or seizures independently lead to brain injury. Some studies have shown an association between electrographic seizures and unfavorable neurodevelopmental outcome in critically ill children. Electrographic seizures in comatose children were associated with unfavorable outcome in survivors.[41] Electrographic seizure burden ($\geq$12 minutes in an hour) was independently associated with worse short-term neurological outcome in critical ill children.[28] Electrographic status epilepticus was associated with increased mortality and neurological morbidity.[3,15,42] Even though it is unknown if early identification and treatment of electrographic seizures improve outcome, the current standard of care is to use anticonvulsants when seizures are identified due to concerns of additional injury secondary to ongoing electrographic seizures. Although there is no optimal management regimen, the most commonly used medications include benzodiazepines such as lorazepam as first-line agents, and phenytoin/fosphenytoin, phenobarbital, and levetiracetam as second-line drugs.[40] Common continuous infusion agents to induce pharmacologic coma for refractory status epilepticus include midazolam and pentobarbital.[40]

Impact of CCEEG on clinical management and practice

Studies have shown that use of CCEEG has significant impact on patient management in both adult and pediatric critically ill patient populations. A few reports showed that CCEEG led to change in treatment in approximately 50% patients, including initiating, escalating, or discontinuing seizure medications, or obtaining urgent neuroimaging, which leads to changes in clinical care.[43,44] The impact may be higher in certain patients, with a change in clinical management reported in as many as 90% adults with traumatic brain injury.[45] Even though CCEEG is an expensive, labor-intensive procedure, it has been shown that CCEEG is cost effective and reduces length of hospital stay in certain patient populations.[43,46]

However, studies have not investigated whether the management changes brought about by CCEEG improve neurodevelopmental outcome. One retrospective cross-sectional study in mechanically ventilated adults using Nationwide Inpatient Sample evaluating inpatient mortality, hospital discharges, and length of stay by comparing patients with cEEG and only routine EEG suggests that cEEG is favorably associated with inpatient survival.[47] One prospective study on adult patients in the ICU evaluated the outcomes in patients with and without cEEG in ICU including Glasgow Coma Scale at Discharge and disposition of discharges, Glasgow Outcomes Scale, and modified Rankin Scale.[48] Performing CCEEG did not improve discharge outcome; however, patients admitted due to seizures were excluded from this study.

Value of review of initial epoch of EEG

Limited studies have shown that findings in the initial 30 to 60 minutes of EEG have high predictive value for seizure detection in patients with altered mental status of various causes.[46,49,50] Absence of epileptiform discharges has a high predictive value for lack of seizure detection with subsequent CCEEG. Epileptiform discharges were detected in a majority of patients in the initial 30 to 120 minutes of EEG monitoring, and subsequent CCEEG increased the yield of identifying epileptic seizures by about 20%. These studies only involved very limited patient populations, and further studies are needed. Importantly, there are no published data in pediatric critically ill patient populations.

Quantitative EEG

Large volumes of EEG data are acquired with cEEG. It is time consuming to review the raw EEG data and may result in delay in seizure recognition and treatment. Quantitative EEG (QEEG) transforms raw EEG using several analytic methods to view the data in different time domains, color-coded graphic displays, and channel reduction. QEEG provides a rapid view of the temporal evolution of seizure burden, background changes, and real-time summary of EEG data over several minutes to hours. Current QEEG software can analyze amplitude, frequency, symmetry, rhythmicity, seizure and spike detection, and continuity including a measure of a burst suppression index. QEEG has been used in seizure identification in the ICU with sensitivity of over 80%.[51] Sensitivity is reduced if the seizures are of low amplitude, focal, and of short duration. There is high false-positivity if there are abundant artifacts such as movement, electrical artifacts, and periodic discharges, or burst suppression background. In the pediatric population, the sensitivity is over 60% and seizures lasting longer than two minutes have a higher detection rate.[52] There is significant variability in the sensitivity and false-positive rates in QEEG analysis for seizures. Designs and development of optimal QEEG analytic methods tailored to specific populations to increase accuracy will be needed for routine utilization of QEEG at bedside by staff not trained in clinical neurophysiology. QEEG shows promise for its use as a biomarker of disease and the ability to monitor

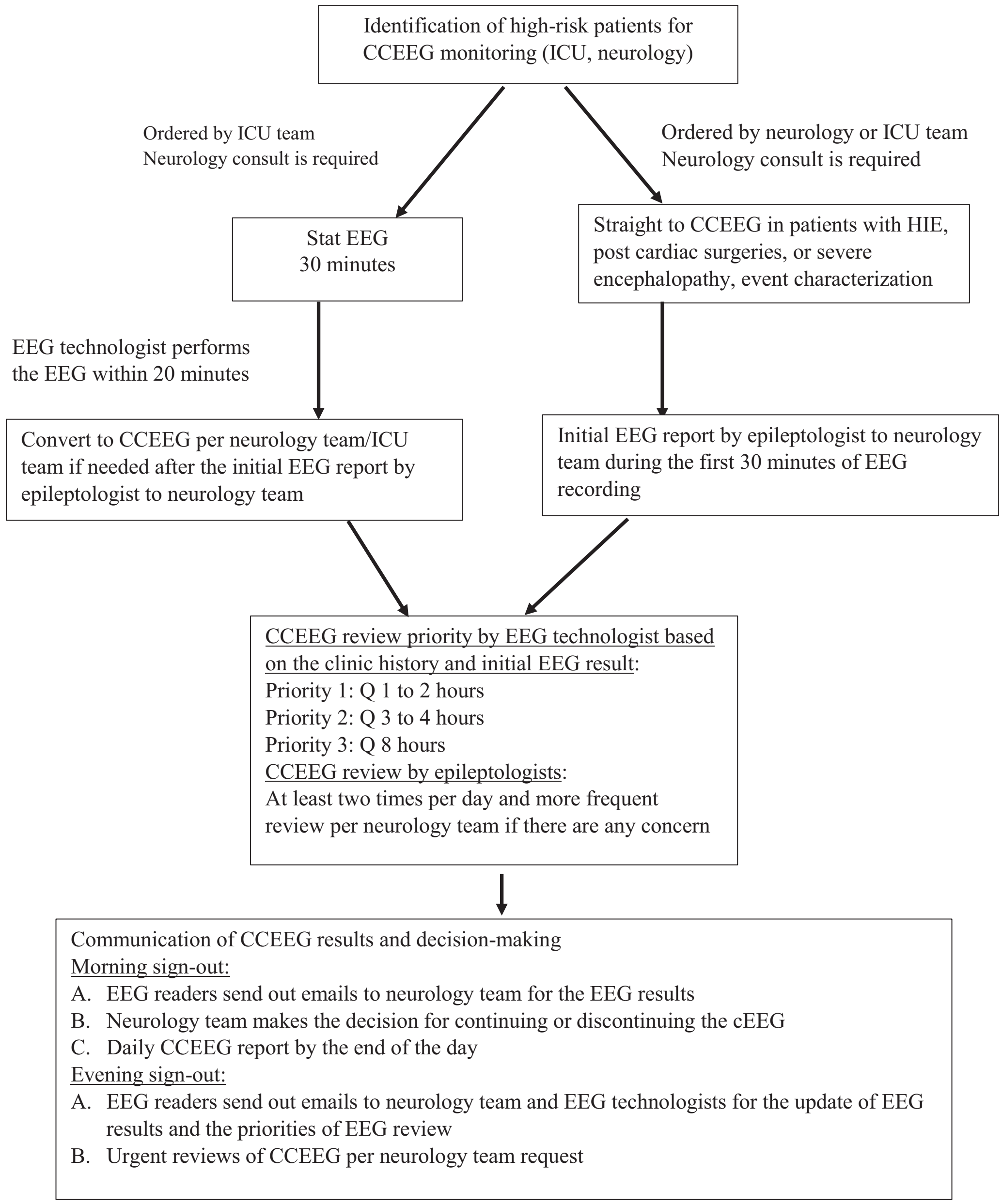

FIGURE. CCEEG pathway at the Seattle Children's Hospital. CCEEG, critical care EEG monitoring; EEG, electroencephalography; HIE, hypoxic-ischemic encephalopathy; ICU, intensive care unit.

treatment interventions. QEEG may also detect gradual temporal EEG changes or subtle asymmetries that may be missed by electroencephalographers on review of raw EEG data.

Technical issues and consideration

The ACNS has published specific recommendations for personnel and technical requirements for CCEEG, even though there are large discrepancies among hospitals with variable resources.[4,53,54] The optimal CCEEG team should include electroencephalographers with experience in CCEEG interpretation and appropriate trained technologists certified in EEG by American Board of Registration of Electroencephalographic and Evoked Potential Technologists specializing in cEEG or long-term monitoring. CCEEG acquisition systems should meet minimum technical acquisition requirements, have the capacity to perform simultaneous video monitoring with the EEG, and have the ability to remotely access the EEG data. These systems require information technology support.[55]

There is great variability in the current practice of CCEEG and review. The challenges include limitations of personnel such as EEG technologists, EEG equipment, and neurophysiologists. The use of EEG technologists in screening EEG and the frequency of EEG review by neurophysiologists are highly variable among institutions. Communication is challenging among ICU staff, ICU nurses, and the neurology and neurophysiology teams. ACNS CCEEG guidelines recommend that the cEEG should be reviewed by both neurodiagnostic technologists and electroencephalographers at least twice a day.

CCEEG at Seattle Children's Hospital

We have established an ICU EEG monitoring program and developed CCEEG protocols and procedures based on ACNS guidelines (Fig).[10,53] The initial policy and protocol included recording a 30-minute stat EEG before converting to CCEEG study. We then integrated the use of CCEEG into an extensive existing infrastructure of ICU clinical pathways and guidelines of care at Seattle Children's Hospital. The process involved an interdisciplinary approach to incorporation of this neurodiagnostic procedure into ICU care with involvement of nursing, pharmacy, intensivists, electroneurodiagnostic technologists, and neurology and clinical neurophysiology providers. Nursing education for CCEEG was conducted in the ICUs before starting the CCEEG program. Ongoing bedside teaching is implemented by the EEG technologists with ICU nurses when the EEG electrodes are applied to a patient in the ICU. Our EEG technologists are ASET (American Society of Electroneurodiagnostic Technologists, Inc) certified, and some are certified in long-term EEG monitoring by American Board of Registration of Electroencephalographic and Evoked Potential Technologists. We provide neurodiagnostic services to the pediatric, cardiac, and neonatal ICUs. Stat EEG and CCEEG are available seven days per week with technical support 24/7. Dedicated EEG technologists review EEG periodically every one to three hours. A stat EEG is read at the time of the EEG recording by a clinical neurophysiologist. CCEEGs are reviewed every one to two hours by EEG technologists when the patient is in status epilepticus or has frequent seizures, every four to six hours for patients who have high risk for seizures but in whom no seizures have been detected, and every eight hours for event characterization. QEEG (Persyst v13, Prescott, AZ, USA) is used for spike and seizure detection and trending of CCEEG data. The most common indication for CCEEG was acute encephalopathy. The number of monitoring days ranged from one to 52 with average days of 2.5. The CCEEG was discontinued after being seizure free for 12 to 24 hours in the majority of the patients. Clinical management of seizures and neurological disorders was made based on both clinical and EEG findings.

One of the major challenges has been communication among the multiple staff and clinical teams involved and maintaining collaborative clinical care involving ICU, neuro-critical care team, EEG technologists, ICU nurses, and neurophysiologists, and this continues to be a challenge even with a CCEEG communication protocol. EEG interpretations are regularly communicated from electroencephalographers to the neurology service residents and attending physicians. Neurology service residents or attending physicians communicate the CCEEG results and further treatment recommendations to the ICU teams. Formal CCEEG reports are generated and entered into the medical record every 24 hours. The quality of EEG interpretation is excellent in our current CCEEG clinical pathway, but we continue to have the challenge of the timely coverage of these neurodiagnostic studies, because clinical neurophysiologists are the first-line EEG readers for all stat and CCEEGs. Neurology residents and neurophysiology fellows are not regularly involved in reviewing ICU EEGs. The increasing CCEEG volume and demand has also created a higher workload for our electroencephalographers. Possible solutions include modifying future pathways and guidelines to involve neurology residents, neurophysiology fellows, and general neurologists on service in preliminary EEG interpretation; integration of CCEEG into a neurocritical care service; and education of intensivists and ICU staff to interpret trends such as amplitude-integrated EEG and trends provided by QEEG.

Conclusion

Substantial evidence justifies the use of CCEEG in critically ill children for a wide range of indications. Even though ACNS has made recommendations regarding CCEEG in children, there is tremendous variability among institutions regarding access to CCEEG, timing or duration of EEG monitoring, frequency of EEG review, and first-line personnel to review CCEEGs. Successful CCEEG requires extensive infrastructure and an interdisciplinary effort involving ICU staff (intensive care physicians and ICU nurses), neurophysiologists, EEG technologists, and neurology service team (attending physicians and residents). There are important questions to be answered especially if CCEEG utilization and treatment of seizures will improve long-term neurological outcome.

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