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Non-Convulsive Status Epilepticus (NCSE) in ICU



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ABSTRACT

Epilepsy is a neurological disorder characterized by recurrent epileptic seizures. Non-convulsive status epilepticus (NCSE) is defined as a persistent change in mental status as opposed to the previous conditions, lasted at least 30 minutes long, associated with continuous spike wave epileptiform EEG changes. Clinical manifestation of NCSE can present as confusion, personality changes, psychosis, and coma. Indeed NCSE prognosis is dependent on the underlying etiology of persistent EEG changes. Preferred medication is focus on improving its fundamental pathological

changes, such as metabolic disorders, infection, drugs toxicity, and immediate pharmacological treatment. Intravenous benzodiazepine is recommended as the first drug of choice for NCSE and early recognition of treatment response can help to establish the diagnosis. This patient has a good outcome which was influenced with short ictal period from the first episode upon arrival on referred hospital, good initial response and management on emergency department, a conduct and thorough ICU monitoring, as well as the effective treatment response.

Keyword: *Epilepsy, non-convulsive status epilepticus, mental status changes, EEG, benzodiazepines*

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INTRODUCTION

Epilepsy is a brain abnormality characterized by recurrent epileptic seizure (more than one episode). Epilepsy is a brain disorder characterized by the presence of predisposing factors that can trigger epileptic seizures, changes in the neurobiological, cognitive, psychological, and social consequences.¹

Non-convulsive status epilepticus (NCSE) is an altered mental status from previous condition, lasted at least 30 minutes, associated with continued peaks on EEG. Clinical manifestations can vary from confuse state to bizarre behavior disorders and psychosis and coma. NCSE is often undiagnosed, and often also considered as a psychiatric disorder.²

Prognosis of NCSE depends on the underlying disease which cause persistent peak seizure on EEG. Treatment aims mainly to correct the fundamental pathological changes, such as metabolic disorders, infections, drug toxicity and immediately initiate pharmacological treatment. Giving intravenous benzodiazepines is the first option for NCSE and the treatment response may help to confirms the diagnosis. Lorazepam with a dose of 0.05-0.1 mg/g is the best choice from benzodiazepines.^{1,3}

DEFINITION

Epilepsy occurs because the local electrical impulse on brain gray matter that occur at any

time, suddenly, and very quickly which can cause decrease of consciousness, changes on motor or sensory function, intermittent and stereotipic behavioral or emotion.¹ Release of abnormal electrical activity from neurons in the brain occurs because of impaired function of neuronal cells. Disturbance in this function can be found as disturbances in physiological, biochemical, anatomical with both local and general manifestations.

Epilepsy is a brain disorder characterized by recurrent epileptic seizures (more than one episode). International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE) in 2005 redefined the definition of epilepsy which is a brain disorder characterized by the presence of predisposing factors that can trigger epileptic seizures, changes in the neurobiological, cognitive, psychological, and its social consequences. This definition requires at least one previous history of epileptic seizures.⁴

Non-convulsive epileptic seizure is an epileptic seizure that lasts more than 30 minutes marked by a continuous seizure activity or repeated changes electroencephalogram (EEG), which causes a variety of clinical symptoms include impaired consciousness, perception disorders with abnormal behavior.

According to The Epilepsy Research Foundation non-convulsive status epilepticus is series of conditions where was found extending seizure activity

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that causes non-convulsive manifestations. When a child is suspected of having non-convulsive status epilepticus, the EEG should be done immediately. EEG recordings will be easier for the doctor to confirm the diagnosis or exclude the diagnosis of non-convulsive status epilepticus. Ideally, EEG performed before the child received anti-epileptic drugs. EEG is also useful for monitoring treatment response.⁴

Non-convulsive status epilepticus is distinguished with convulsive status epilepticus because no or little discovery of motoric components. The dominant sign of status non-convulsive status epilepticus is altered mental status associated with the changes in EEG.

ETIOLOGY

Epilepsy is a chronic neurological disease characterized by unprovoked recurrent seizure that. The cause is electrical impulse disorder of neural networks that are not well-controlled in some parts or whole parts of the brain. Disruption of brain function that can cause excessive release of electrical charge on the central nervous neuronal cells, could be caused by physiological factors, biochemical, anatomical, or a combination of these factors.^{1,3}

Each diseases or disorders that may interfere brain function or the function of neurons in the brain, can cause seizures or epileptic attack. To define the causative factor can be determined by looking at the age when the first attack occurred. For example, age under 18 years is likely caused by perinatal trauma, febrile seizures, inflammation of the central nervous system, structural, metabolic diseases, toxic circumstances, systemic disease, head trauma diseases, and others.^{1,4}

Seizures can also be caused by a variety of disorders and illnesses of which are birth trauma, head injury, brain inflammation, brain tumors, brain bleeding, circulatory disorders, hypoxia, congenital anomalies of the brain, degenerative disorders of the central nervous system, metabolic disorders, disorder electrolytes, fever, toxic-allergic reactions, drug or chemical poisoning, and heredity.

Various precipitating factors may be involved in the NCSE including metabolic disorders, infections, intoxication, alcohol, pregnancy, drug intoxication, such as amitriptyline, theophylline, cephalosporin, chemotherapeutic drug, withdrawal of anti-epileptic and carbamazepine, very rarely lamotrigine, phenobarbital, and phenytoin.⁴

EPIDEMIOLOGY

According to the Epilepsy Foundation Research, NCSE estimated incidence rate of

6-18/100,000 cases/year. Towne et al, in a prospective study of 236 patients with coma which is not found seizures clinically, reported 8% of the patients met the criteria of NCSE on EEG. De Lorenzo et al acquired the 14% of the patients who review after receiving GCSE. Privitera and Strawburg reported on a prospective study found out on 198 patients with altered level of consciousness in the EEG was found NCSE. NSCE was reported can be found at any age from the very young to very old, both sexes without distinction.⁴

In adults, NCSE estimated happens in quarter of all cases of status epilepticus. Data for NCSE in children is rarely reported due to the lack of consensus on the diagnosis and mainly because of not knowing the symptoms as a disorder or pathologic disorder or misinterpretation as a behavioral problem.

Classification of Epilepsy⁴

A. Partial / Focal Seizure

1. Simple partial seizure (without altered consciousness)
 - a. With motoric symptom
 - b. With sensoric symptom
 - c. With otonomic symptom
2. With psychological manifestation
 - a. Complex partial seizure (with consciousness disturbance)
 - b. Simple partial seizure at the beginning, followed with consciousness disturbance
3. With alteration of consciousness from the beginning of seizure
 - a. Secondary generalized seizure (tonic-clonic, tonic or clonic)
 - b. Simple partial seizure developed to generalized seizure
 - c. Complex partial seizure developed to generalized seizure
 - d. Simple partial seizure developed to complex partial, and then developed to generalized seizure

B. Generalized Seizure (Convulsive or Non-Convulsive)

1. Lena seizure (absence): Lena attack was characterized by short duration, sudden onset and termination, often in frequency, sometimes accompanied by clonic movement on eyes, chin, and lips.
2. Mioclonic seizure: mioclonic seizure is a sudden contraction, rapid, and could be generalized or limited on facial area, torso, one or more extremities, or one muscle group. Can be repeated or single attack.

3. Tonic seizures: rigid muscle contraction, causing the limbs settled in one position. Usually there is deviation of the eyeball and head to one side, can be accompanied by the rotation of the entire torso. The face becomes pale and then red and bluish because unable to breathe. Eyes open or closed, conjunctiva become insensitive, and pupil dilatation.
4. Atonic seizure: Represent as lose of muscle tone. Can occur fragmentally, only head fall forward or the arm drop in hanging position, or generalized so that patient can fall.
5. Clonic seizure: This type of seizure has no tonic component, only clonic seizure will happen, found mainly on children.
6. Tonic-Clonic Seizure: Seizure which is started with tonic seizure, and followed with clonic movement.

PATOPHYSIOLOGY

Neurons have a membrane potential, this occurs because of the difference in ions charge inside and

outside the neuron. Differences in the amount of the charge of these ions cause polarization of the membrane with intraneuron part is more negative. Neuron synapsed with other neurons through axons and dendrites. An excitation input via synapses will cause membrane depolarization which happened in short duration, then inhibition would lead to hyperpolarization of the membrane.

When excitation is quite large and inhibition is small, axon begin stimulated, an action potential is sent along the axon, to stimulate or inhibit other neurons, so epilepsy will happen.

CLINICAL MANIFESTATION

Clinical manifestation of NCSE includes a thorough mental status changes. It can be acknowledge by family or friends, can be found as delirium or coma state. Fluctuation of symptoms can occur at various levels, so can obscure the diagnosis.^{3,5}

Motoric activity is normal in most cases, sometimes found stiffness (clumsiness), apraxia, focal

Table 1 Status Epilepticus Management in ICU¹

Critical care treatment	Timing (minutes post seizure onset)	Goals
Non-invasive airway protection anti gas exchange with head positioning	Immediate (0-2 min)	Maintain airway patency, avoid snoring, administer O ₂
Intubation (if airway/gas exchange compromised or elevated ICP suspected)	Immediate (0-10 min)	Establish secure oxygenation and ventilation
Vital signs: O ₂ saturation, BP, HR	Immediate (0-2 min)	Establish and support baseline vital signs
Vasopressor support of BP if SBP <90 mmHg or MAP <70	Immediate (5-15 min)	Support CPP
Finder stick blood glucose	Immediate (0-2 min)	Diagnose hypoglycemia
Peripheral IV access	Immediate (0-5 min)	Establish medication route
1. Emergent initial AED therapy (i.e. benzodiazepine)		1. Stop seizure
2. Fluid resuscitation		2. Establish euvoemia
3. Nutrient resuscitation (thiamine given before dextrose; dextrose)		3. Reverse thiamine deficiency, treat hypoglycemia
Urgent SE control therapy with AED	Immediate after initial AED given (5-10 min)	Stop seizure
Neurologic exam	Urgent (5-10 min)	Evaluate for mass lesion, acute intracranial process
Triage lab test panel (see Table 2)	Immediate (5 min)	Diagnose life threatening metabolic condition
Refractory SE treatment	Urgent (20-60 min after 2nd AED)	Stop seizures; treatment strategies based on individual patient response and AED concentrations (if applicable)
Urinary catheter	Urgent (0-60 min)	Evaluate systemic circulation
Continuous EEG	Urgent (15-60 min)	Evaluate for NCSE if not waking up after clinically obvious seizures cease
Diagnostic testing (selection depends on clinical presentation)	Urgent (0-60 min)	Evaluate for mass lesions, meningitis, encephalitis

Table 2 Drugs dosing used in refractory status epilepticus in ICU¹

Drug	Initial dose	Continuous infusion dosing recommendations-titrated to EEG	Serious adverse effects	Considerations
Midazolam	0.2 mg/kg; administer at an infusion rate of 2 mg/m in	0.05-2 mg/kg/hr CI Breakthrough SE: 0.1-0.2 mg/kg bolus, increase CI rate by 0.05-0.1 mg/kg/hr every 3-4 h	Respiratory depression Hypotension	Tachyphylaxis occurs after prolonged use Active metabolite, renally eliminated, rapid redistribution (short duration), does NOT contain propylene glycol
Pentobarbital	5-15 mg/kg, may give additional 5-10 mg/kg; administer at an infusion rate ≤50 mg/min	0.5-5 mg/kg/h CI Breakthrough SE: 5 mg/kg bolus, increase CI rate by 0.5-1 mg/kg/h every 12 h	Hypotension, respiratory depression, cardiac depression, paralytic ileus, at high doses - complete loss of neurological function	Requires mechanical ventilation IV contains propylene glycol
Propofol	Start at 20 mcg/kg/min, with 1-2 mg/kg loading dose	30-200 mcg/kg/min CI Use caution when administering high doses (>80 mcg/kg/min) for extended periods of time (i.e., >48 h) Peds: Use caution with doses >65 mcg/kg/min: contraindicated in young children Breakthrough SE: Increase CI rate by 5-10 mcg/kg/min every 5 min or 1 mg/kg bolus phis CI titration	Hypotension (especially with loading dose in critically ill patients), respiratory depression, cardiac failure, rhabdomyolysis, metabolic acidosis, renal failure (PRIS)	Requires mechanical ventilation Must adjust daily caloric intake (1.1 kcal/ml)
Thiopental	2-7 mg/kg, administer at an infusion rate ≤50 mg/min	0.5-5 mg/kg/h CT Breakthrough SE: 1-2 mg/kg bolus, increase CI rate by 0.5-1 mg/kg/h every 12 h	Hypotension, respiratory depression, cardiac depression	Requires mechanical ventilation Metabolized to pentobarbital

CI continuous infusion; EEG electroencephalogram; h hour; IM intramuscular; IV intravenous; IVP intravenous push; min minute; PRIS propofol related infusion syndrome

jerking, twitching of facial muscles (blinking eyes), chewing movement, automatism movement in the form of real motion is very rare, such as flexion, extension of extremity, deviation of the head.⁵

Other symptoms can include mild cognition impairment (attention disorder), difficulty in planning of regular and complex motoric movement (sequentially), minor disorientation or confusion, prolonged confusional state, mood disorders, speech disorders (speech not fluently, aphasia, silent), psychotic symptoms, autonomic disorders (belching, rumbling in the stomach, flatus), sensory disturbances, loss of consciousness, and coma.^{3,4,5}

TREATMENT

Although there are a lot of controversy about when to begin treatment of NCSE, the general principle of treatment for NCSE is as soon as possible to get the etiology and trigger factors and treat as soon as possible the trigger factor of physiologic stress including infections, toxic metabolic disorders, drug interactions or withdrawal and pregnancy.⁴

Administration of intravenous benzodiazepines should be done with EEG monitoring. Diagnostic

confirmation with EEG is required before pharmacological treatment is given. Reportedly, in some cases has a response immediately after administration of intravenous benzodiazepines.¹

Although there is sometimes a tendency of NCSE for recurring and necessary to grant additional anticonvulsants. Benzodiazepines such as diazepam, lorazepam, clonazepam, and midazolam can be given as monotherapy or in combination. The response of the NCSE to benzodiazepines, sometimes slow, or followed by a recurrence of symptoms several hours or days later, the granting of long-acting anti-epileptic may be required. Provision of benzodiazepines should be cautious in patients contained numerous medical problems where hypotension and respiratory depression could occur.^{1,6}

When the diagnosis of NCSE has been confirmed, and seizures have been controlled, long-term medication treatment should be considered. There are a wide range of antiepileptic drugs such as phenitoin, valproic acid, and phenobarbital can be administered intravenously to acute phase and orally for long-term treatment.⁵

Carbamazepine, Phenytoin and a new generation of anti-epileptic (lamotrigine, topiramate,

levetirocetam) can be considered as a long-term treatment. Valproic acid is the drug of choice for epilepsy absence, and clonazepam can also be used. Vigabatrin and Tiagabine is not recommended for allegedly holding role for the occurrence of exacerbations and precipitating factors of NCSE.⁶

Meanwhile in the ICU, the management of status epilepticus include a broad spectrum management ranging from securing the airway to the giving of sedative drugs.

In cases where there is a refractory status epilepticus, some drugs such as midazolam, propofol, pentobarbital and thiopental in accordance with the recommended dose contained in [Table 2](#).

CONCLUSION

According to The Epilepsy Research Foundation, nonconvulsive status epilepticus is a term used to denote a range of conditions in which electrographic seizure activity is prolonged and results in nonconvulsive clinical symptoms. The clinical presentation of patients supports the definition of status epilepticus NCSE which the symptom that appears is elongated period of unconscious patient without repeated seizure during treatment.^{1,3}

Initial treatment performed in the ER and ICU is to maintain patency of the airway and provide oxygen supplementation, application of access intravenous fluids, assessment of vital signs including blood sugar tests, catheter urine, administration of drugs known as benzodiazepines to control seizure activity that occurs in the ER, laboratory tests to exclude other causes of extracranial, and a CT scan to rule out the possibility of intracranial lesions.⁶

In patients with loss of consciousness, enteral and intravenous nutritional therapy and are absolutely

necessary. In these patients, the caloric needs can be fulfilled from enteral feeding, and since the patient regain his consciousness, patient can eat and drink as usual. Paracetamol is given as an analgesic, and may also serve to handle fever, where the fever can also trigger seizures. Omeprazole given for peptic ulcer prophylaxis in hospitalized patients with critical illness

Outcome of patients have either influenced from short duration ranging from first seizure until arrival at the referral hospital, initial treatment in the ER, ICU monitoring conducted in, as well as the course of the disease that is responsive to medication given.

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