## Good research paper about rhabdomyolysis4

Technology, Development



There are nearly 5 million cases of epilepsy in the United States every year. The most common and serious form of status epilepticus occurs to people with no prior history of epilepsy. About 5% of adults and 10% to 25% of children will develop this disorder every year. Infants and elderly people are at more great risk of developing Status epilepticus yearly than others1. About 1. 4% of white and 1. 1% of black people will develop this disorder every year compared to 0.6% of Hispanic who will have a lower rate of such incidence. About 1. 23% of women will develop epilepsy every year compared to 1. 1% rate in men.

Status epilepticus is a widespread neurologic emergency, associated with brain activity damage and death occurrence. It is defined as a seizure, which lasts more than 30 minutes whether consciousness is imparted or no. Clinically, this definition has a limited use, as the common seizure is less than 2 minutes; and only 40% of seizures will last 10 to 29 minutes can be allowed to stay without treatment. The rate of pharmacoresistant and deathrise with prolonged seizure interval. Consequently, intense treatment of seizures lasting 5 minutes is highly recommended. Status epilepticus can be seen in many forms that include generalized convulsive status epilepticus and nonoconvulsive status epilepticus2.

As generalized convulsive status, there are systemic variations, progression of motor phenomena, and development of specific EEG findings. An EEG finding shows two differnent, but predictable phases. The first phase beggins during the first 30 minutes of seizure, and the second phase instantantly follows. A prolonged seizure has a potential of destroying neurons. In phase I, every seizure significantly increases plasma epinephrine, norepinephrine,

and steroid concentrations, which can lead to hypertension, tachycardia, and cardiac arrhythmias. In short time, arterial systolic pressure can increase to above 200 mm Hg, and heart rate can increase by 83 beats per minute. Mean arterial pressure does not fall below 60 mm Hg; hence, cerebral perfusion pressure is not compromised. In the incidence of a hypoxic myocardium, seizure-induced increases in sympathetic and parasympathetic stimulation of the heart can cause ventricular arrhythmias. Autonomic neuron stimulation will lead to release of insulin and glucagon. At the same time, circulating catecholamines cause an elevation of hepatic cyclic adenosine monophosphate, which produces glycogenolysis. Although the patient can be hyperglycemic initially, serum glucose begins to fall3. Seizure-induced muscular contractions and hypoxia trigger the release of lactic acid, which can create severe acidosis that maybe accompanied by hypotension and shock. Muscle contractions can be so severe that rhabdomyolysis with secondary hyperkalemia and acute tubular necrosis may occur. The airway can be obstructed, leading the patient to become cyanotic or hypoxic. Moreover, rise in salivation and pulmonary secretions can cause aspiration pneumonia. While transient pleocytosis can develop, it should not be attributed to SE until infectious cause has been removed. Inbetween seizures, the EEG slows and blood pressure normalizes. While metabolic demands are increased, the brain is able to sufficiently compensate that. When seizures last more than 30 minutes (Phase II), the EEG ictal discharge and clonic motor activity become nonstop, and the patient begins to decompensate. Despite raised levels of catecholamines, the patient can become hypotensive. During this period, autoregulation of

cerebral blood flow becomes dependent on mean arterial pressure and begins to fail. There continues to be an excessive consumption of oxygen and glucose; however, compensatory mechanisms are no longer able to meet the needed demands. Throughout Phase II, the serum glucose concentration may be normal - or decreased. Profound hypoglycemia, secondary to hyperinsulinemia, can occur in those with hepatic dysfunction or reduced glycogen stores. Hyperthermia and respiratory deterioration with hypoxia and ventilator failure can develop. Metabolic and biochemical complications, including respiratory and metabolic acidosis, hyperkalemia, hyperkalemia, and azotemia, may develop. Sweating and salivation both increase3.

The symptoms of status epilepticus include impaired consciousness (e. g., lethargy to coma), disorientation, and pain associated with injuries. The injuries include tongue lacerations, shoulder dislocations, back pain, myalgias, headache, and head trauma.

The first signs of status epilepticus include generalized convulsions, incontinence, hypotension and central nervous system insults that cause extensor or flexor posturing. The late signs of status epilepticus include pulmonary edema with respiratory failure, cardiac failure, hypotension, hypertension, disseminated intravascular coagulation and

The ideal drug is given intravenous bolus for the treatment of status epilepticus. This drug prevents or stops seizures by slowing down the central nervous system, which makes abnormal electrical activity less likely to occur. The ideal drug will be administered as a first-order kinetics following a single compartment model. The therapeutic range for this medication is

between 20 - 30 mcg/mL. Plasma concentration of 20 mcg/mL will have the lowest therapeutic effect and plasma concentration of 30 mcg/mL will have the highest therapeutic effect. A plasma concentration (Cp) lower than 20 mcg/mL will not have any therapeutic effect in the body. A plasma concentration higher than 30 mcg/mL would consider toxic for the patient. The initial plasma concentration (Cp0) for the ideal drug is 27 mcg/mL, which is within the therapeutic range and hence provide an immediate therapeutic effect. The volume of distribution (Vd) for patient is 24. 5 L [Vd = 35% of 70kg (average BW) = 24. 5 L]. The fluid portion in an adult makes up approximately 60% of total body weight and is composed of intracellular fluid (35%) and extracellular fluid (25%). Extracellular fluid is made up of plasma (4%) and interstitial fluid (21%). The volume of distribution for this patient is distributed out of extracellular fluid to other parts of body. Initial amount of drug in the body (Xo) calculated to be 662mg [Xo = Vd x Cpo = 24.  $5L \times 27mg/L = 662mg$ ]. A dose of 662 mg to be given once a day will have an affect that last 24 hours. After 24 hours, the plasma concentration of drug (Cp) will be 20 mcg/L. First-order elimination constant can be calculated using Cp = Cpo e-kt. [k=(lnCpt - lnCpo)/t = [ln(20) - ln(27)] / 24 = 0.0125h1]. With the first-order elimination process, although the amount of drug eliminated may change with the amount of drug in the body, the fraction of a drug in the body eliminated over a given time remains constant. Practically, the fraction or percentage of drug being removed is the same with either low or high drug concentration. Half-life of drug can be calculated using half-life = 0.693/k, where k = first-order rate constant. [Half-life = 0.693/0.0125 =55. 44h]. Half-life can be also determined from figure 1. Elimination is 50%

renal (intact) and 50% hepatic which

means elimination is 12. 25L renal (intact) and 12. 25L hepatic. [CLtotal = CIH+ CIR = 12. 25L + 12. 25L = 24. 5L] This drug will be given once a day to provide constant therapeutic effect.

This drug is sterile, nonpyrogenic solution to the case, intended for intravenous administration. It should be contained in either ampul or fliptop vial multiple-dose container. Proper storage of medications ensures optimum efficacy and stability. The ideal drug must be stored at temperature of 20 to 25°C to prevent compromising its stability.

Status epilepticus is a severe condition and it requires immediate treatment. Whereas diagnostic criteria for it may vary, terminating continuous seizure as quickly as possible remains the best solution. Consequently, the ideal drug stands among the best choices for first-line management of status epilepticus problem. It enters the brain swiftly with its Vd of 24. 5L. Moreover, the drug has a first-order constant of 0. 0125h-1 and half-life of 55. 44 hours. The dose for the ideal drug is 662mg, given once a day, with effect lasting 24 hours. It will stay in the body for extended period of time, corresponding to its half-life of 55. 44 hours. All in all, the rapid and broadspectrum effects of the ideal drug provide the best treatment available in the management of status epilepticus.

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- PK book for Volume of distribution and elimination
- CDC for tables