RESEARCH ARTICLE

IV LIDOCAINE: A SECOND LINE DRUG THERAPY FOR PEDIATRIC CONVULSIVE STATUS EPILEPTICUS?

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Abstract:

Objective

Refractory convulsive Status Epilepticus (SE) which does not respond to first line drugs (benzodiazepines, phenytoin and phenobarbital) heralds an emergency condition in pediatric neurology which can cause irreparable brain damage. There is no consensus on the choice of drug treatment for refractory generalized convulsive status epilepticus in children. Lidocaine is a valuable forgotten antiepileptic agent with favorable properties which include prompt responses, less alteration of consciousness, and fewer adverse effects such as respiratory depression.

Materials & Methods

In a retrospective study conducted to investigate clinical efficacy and safety of intravenous lidocaine in treating refractory generalized convulsive SE of children, the medical records of 13 patients admitted to the Shaheed Sadoughi Hospital of Yazd between 2003 and 2005 and treated with intravenous lidocaine, were reviewed.

Results

13 patients, 7 girls and 6 boys (average age 3 years, SD = 2.7years) were treated with lidocaine. Neurodevelopmental delay was seen in 38.5 %, and in 46.2% of them EEG and neuroimaging abnormalities were observed. Seizures ceased in eight patients (61/5 %), without any undesirable side effects. Two patients had to be intubated because of non-responsiveness to lidocaine, and other treatments were begun .Mean duration of ICU stay was 4.77 days, SD = 3days.

Conclusion

It is recommended that lidocaine be used as a second-line, anticonvulsive drug in the treatment of status epilepticus, especially when faced with unavailability of appropriate respiratory care and intubation equipment.

Key words: Status Epilepticus, Refractory Status Epilepticus, Generalized Convulsive Status Epilepticus, Intravenous Lidocaine.

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Introduction

Status epilepticus (SE), defined as a seizure that persists for a duration long enough, or is repeated frequently enough, to produce a fixed and enduring epileptic condition lasting 30 minutes or longer, is a common neurologic medical emergency(1), of which generalized convulsive SE is the most common and dangerous type. SE occurs more frequently in young children and elderly adults, although patients of all ages may experience prolonged seizures (2). It is estimated

that this life-threatening condition occurs in 1.3% to 16% of all epileptic children and in some patients presents as the initial seizure.(3) Correct management strategy involves prompt control of seizures and treatment of the underlying etiology.

The morbidity and mortality of status epilepticus are significant and directly dependent upon availability of prompt and appropriate medical therapy; the sequelae and neurocognitive deficits are particularly pronounced and potentially fatal in children when the condition progresses beyond 30 to 60 minutes. Refractory status epilepticus is defined as seizures that are ongoing, despite the use of two first-line drugs, usually a benzodiazepine plus either phenytoin or phenobarbital, or seizures that continue for more than 60-90 minutes in spite of adequate treatment(4,5,6). All these patients must be managed in a pediatric ICU, with aggressive monitoring of their hemodynamic and respiratory status. There is no consensus on the choice of drug treatment for refractory generalized convulsive status epilepticus in children. If cessation of seizures cannot be achieved, other therapeutic strategies may have to be used such as induction of barbituric coma with thiopental, general anesthesia using propofol(7), diazepam drip(8,9), buccal, nasal or continuous infusion of midazolam(10,11,12) and intravenous valproate(13,14) .

Use of these modalities, however, may be associated with respiratory depression needing mechanical ventilation and hypotension requiring vasopressor support and invasive hemodynamic monitoring.

Lidocaine has many pharmacologic attributes such as antiarrhythmic, local anesthetic and antiepileptic properties; 1 - 2 mg/kg intravenously, once or twice, and if necessary, followed by continuous infusion at 2 - 4 mg/kg/hour is one of the second-line drugs in treatment of SE(15). The properties of this drug effective in SE treatment include prompt responses, less alteration of consciousness, and fewer adverse effects such as less respiratory depression(16). The basic mechanisms of lidocaine as an antiepileptic are thought to be analogous to its local anesthetic action; it has a specific membrane sealing or stabilizing effect on the CNS that restricts the movement of sodium and potassium across the membrane, thereby decreasing membrane excitability(17). Pascual et al suggested that lidocaine may be used as a first–line drug, as a diazepam substitute, in patients in whom respiratory or consciousness depression is undesirable and in those with no response to intravenous diazepam. The absence of response to lidocaine indicates SE is resistant to treatment and has poor prognosis(18). Aggarwal et al document lidocaine as a valuable drug, forgotten in the emergency department(19). Evidence of lidocaine efficacy has been demonstrated in many clinical studies, most of which were case reports or were performed on a limited number of patients(less than 10).

The purpose of this retrospective study was to investigate the clinical efficacy and safety of intravenous lidocaine in controlling refractory generalized convulsive SE in children admitted to the Shaheed Sadoughi Hospital of Yazd .

Materials and Methods

In a retrospective study, medical records of all generalized convulsive status epilepticus of children treated with intravenous lidocaine between 2003 and 2005 in Yazd Shaheed Sadoughi Hospital reviewed.

Inclusion criteria: No history of liver or kidney dysfunction- past or current-, no hypotension, cardiac arrhythmia or block and electrolyte abnormality; a first time occurrence of status epilepticus; BUN, Cr, sodium, potassium, total calcium, and glucose values within normal limits to exclude electrolyte abnormalities and hypoglycemia as causes of seizures; admission to the ICU for aggressive cardiac monitoring

Lidocaine was used as a second–line drug, because of lack of seizure-response to benzodiazepines plus either phenytoin or Phenobarbital.

Lidocaine treatment protocol:

Initial dose of 1 mg/Kg was given intravenously at a rate of 25 mg/min. If no response occurred or seizures recurred, a second bolus dose of 1 mg/Kg was infused. If seizures did not stop within 15 minutes following the second dose, continuous lidocaine infusion of 1 mg/Kg/h was used and increased for 1 mg/Kg/h every 15 minutes until control of seizures or maximum dose of 5 mg/Kg/h. If the drug was effective in control of seizures, the same dose would be repeated for 12 hours and then decreased 0.5 mg/kg/hour until cessation of seizures, when the treatment would be considered

effective. ECG, blood pressure, and oxygen saturation were continuously monitored to detect any cardiovascular complications. Serum lidocaine concentration was not measured. Lidocaine was not administered to patients with known or suspected cardiac diseases. If seizures did not cease with maximum dose of drug infusion drip, it was regarded as being ineffective and unsuccessful, and hence was discontinued, and a benzodiazepines or pentobarbital drip was introduced. Data were gathered from the medical records of the pediatric ICU. All information on variables such as age, sex, neuroimaging and EEG findings, concomitant fever, neurodevelopmental delay, adverse effects (hypotension, arrhythmia, respiratory depression needing intubation and mechanical ventilation, acidosis, hypothermia, hypoxia), seizure control and length of stay in the ICU were carefully recorded. The data were analyzed using SPSS 13 statistical software. P values< 0.05 were considered statistically significant. Written informed consent was obtained from subject's parents.

Results

In this retrospective study conducted to determine the efficacy and safety of intravenous lidocaine in treating seizures caused by refractory generalized convulsive status epilepticus, the ages of children ranged from one month to 9 years(mean age 3 years and SD=2.7 years). Clinical and Para clinical characteristics of patients are presented in Table 1.

In eight of 13 patients(61/5 %), lidocaine was effective in controlling seizure; in three patients, seizures stopped with the initial dose of 1 mg/Kg and in another three with second bolus dose of 1 mg/Kg; in one this was with infusion of 1 mg/Kg/h and in another with 2 mg/Kg/h .

Etiology of SE and response to treatment of patients are showed in Table 2. No undesirable side effects (paraclinical or clinical) were observed in patients. Two patients had to be intubated because of non-responsiveness to lidocaine; they were treated with other drugs. Duration of stay in the ICU ranged between 1 to 11 days (mean 4.77, SD=3.03).

Table 1: Clinical and Para clinical characteristics of patients

Parameters		Number	Percent
Gender	Girl	7	54
	Boy	6	46
Neurodevelopmental delay		5	38.5
Abnormal EEG		6	46
neuroimaging abnormalities		6	46

Table 2: SE Etiology and treatment response to IV lidocaine

Etiology / Response	Symptomatic epilepsy	Idiopathic epilepsy	encephalitis	hypoxic-ischemic encephalopathy .	Total
Yes	3	1	2	2	8
No	3	0	1	1	5
total	6	1	3	3	13

SE:Status Epilepticus

Discussion

The purpose of this retrospective study was to investigate intravenous lidocaine efficacy and safety in refractory convulsive SE of children. According to the results of the study the drug was effective in 61.5 % of patients. Other similar studies have shown a response rate ranging from 35.8 to 100% (15,16,20,21,22). One possible explanation for this discrepancy is the small number of our patients. Further studies need to be carried to confirm the efficacy of intravenous lidocaine in treating refractory status epilepticus.

The results of this study indicate that intubation and mechanical ventilation were not needed in lidocaine use, which is in agreement with recommendations of other studies that recommend use of lidocaine in the management of SE of patients in whom respiratory depression is undesirable (18) or management of respiratory depression is not possible. Considering the fact that no alteration of consciousness and respiration occurred, the lidocaine treatment was cost-effective since cessation of seizures without side effects shortened the duration of ICU stay. Our results which show no occurrence of undesirable effects are in agreement with those of other studies(16,20,23,24).

Walker and Slovis recommended lidocaine before barbiturate coma in SE treatment, which agrees with observations of the current study(25).

The initial bolus doses of lidocaine were effective in six of eight patients in whom SE was controlled, indicating that lidocaine is a rapid acting anticonvulsant, useful in the short term management of SE.

One limitation of this study was lack of video-EEG monitoring and hence our inability to identify/recognize electrographic seizures cessation.

We conclude that lidocaine, based on its prompt effectiveness and low risk of side effects, can be used as a second-line, anti-convulsive drug in status epilepticus, especially for patients with chronic respiratory disease or in those having severe disability and respiratory impairement .

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