Guideline of status epilepticus management 2017

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Professor of Neurology

Guideline

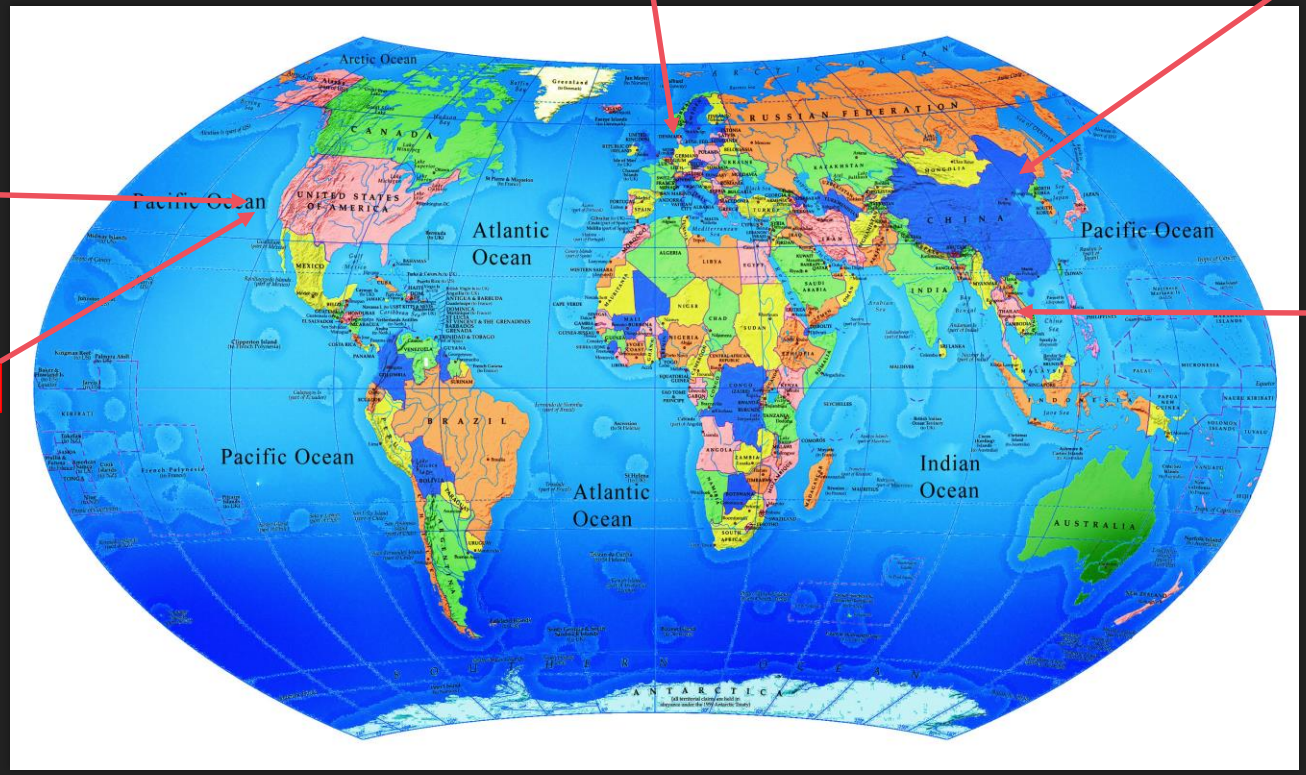
1966 to Jan 2005

European Foundation Neurology Society 2010

Hong Kong Epilepsy Society Society 2017

Published through Aug 2011

American Neurocritical care Society and American epilepsy society 2012



Thailand Epilepsy Society Society 2015

American epilepsy society 2016

Jan 1940-sep 2014

Guideline of status epilepticus

- Initial treatment: pre-hospital; hospital
- Second step treatment
- Refractory status epilepticus
- Super-refractory status epilepticus

Guideline

Type of antiepileptic drugs and alternatives therapy

Initial or emergent or early status epilepticus

- Lorazepam [1, 2, 3, 4]
- Midazolam [2 , 3, 4]
- Diazepam [1 (+PHT) , 2, 3 (±PHT), 4]
- Phenytoin/fosphenytoin [1 (+DZP), 2, 4 (+DZP)]
- Phenobarbital [2, 3, 4]
- Valproate [1?, 2]
- Levetiracetam [2]

Pre-hospital
VS
Hospital

[1]European Foundation Neurology Society 2010

[2]American Neurocritical care Society and American epilepsy society 2012

[3]American epilepsy society 2016

[4]Hong Kong Epilepsy Society Society 2017

Initial or emergent or early status epilepticus

AEDs	European Foundation Neurology Society 2010	American Neurocritical care Society and American epilepsy society 2012	Hong Kong Epilepsy Society Society 2017
Lorazepam	0.1 mg/kg (4 mg)	0.1 mg/kg (4 mg)	0.1 mg/kg (4 mg)
Diazepam	5 mg	0.15 mg/kg (10mg)	0.15-0.2 mg/kg (10mg)
Diazepam + Phenytoin	5 mg + 18mg/kg	-	-
Phenytoin	-	20 mg/kg add 5-10 mg/kg (10 min after loading)	-
Phenobarbital	-	= PHT	-
Valproate	-	20-40 mg/kg add 20 mg/kg 3-6 mg/kg/min	
Midazolam		0.2 mg/kg max. 10 mg	10 mg IM; 5-10 buccal

Urgent, established Status epilepticus

- Valproate [2, 3, 4,]
- Phenytoin/fosphenytoin [2, 4 (no document fosphenytoin)]
- Midazolam [2]
- Phenobarbital [2, 4]
- Levetiracetam [2, 3?,4]

[3]American epilepsy society 2016

[4]Hong Kong Epilepsy Society Society 2017

[2]American Neurocritical care Society and American epilepsy society 2012

Urgent or establish status epilepticus

AEDs	American Neurocritical care Society and American epilepsy society 2012	Hong Kong Epilepsy Society Society 2017
Phenytoin	20 mg/kg add 5-10 mg/kg (10 min after loading) (up to 50 mg/min)	15-20 mg/kg (up to 50 mg/min)
fosphenytoin	20 mg/kg add 5 mg/kg (10 min after loading) (up to 150 mg/min)	
Phenobarbital	= PHT (50-100 mg/min)	15 mg/kg (max rate 100 mg/min)
Valproate	20-40 mg/kg add 20 mg/kg 3-6 mg/kg/min	40 mg/kg,max 3,000 mg (infusion > 5-10 min) -
Midazolam	0.2 mg/kg max. 10 mg	-
Levetiracetam	1-3 g IV (2-5 mg/kg/min)	60 mg/kg, max 4,500 mg/dose (infusion >10 min)

Refractory Status epilepticus

- Midazolam [1, 2, 4]
- Propofol [1, 2, 4]
- Pentobarbital/thiopental [1, 2, 4]
- Lacosamide [2]
- Topiramate [2]

[1]European Foundation Neurology Society 2010

[2]American Neurocritical care Society and American epilepsy society 2012

[4]Hong Kong Epilepsy Society Society 2017

Initial or emergent or early status epilepticus

AEDs	European Foundation Neurology Society 2010	American Neurocritical care Society and American epilepsy society 2012	Hong Kong Epilepsy Society Society 2017
Midazolam	0.2 mg/kg (maintenance 0.05-4 mg/kg/h)	0.2 kg/kg (initial rate 2 mg/min) (maintenance 0.05-2 mg/kg/hr increase CI 0.05-0.1 mg/kg/hr q 2-4 h	0.1-0.2 mg/kg - (maintenance 0.05-3 mg/kg/h) -
Propofol	2-3 mg/kg bolus 1-2 mg/kg (maintenance 4-10 mg/kg/h)	1-2 mg/kg (initial rate 20 mcg/kg/min) (maintenance 30-200 mcg/kg/hr ถ้าให้นานกว่า 48 h ระวังไม่ควรเกิน 80 mcg/kg/min	3-5 mg/kg (maintenance 2-15mg/kg/h)

Initial or emergent or early status epilepticus

AEDs	European Foundation Neurology Society 2010	American Neurocritical care Society and American epilepsy society 2012	Hong Kong Epilepsy Society Society 2017
Thiopental	3-5 mg/kg bolus 1-2 mg/kg q 2-3 min (maintenance 3-7 mg/kg/h)	2-7 mg/kg (< 50 mg/min) (maintenance 0.5-5 mg/kg/h) Increase CI 0.5-1 mg/kg/h q 12 h with bolus 1-2 mg/kg)	2-3 mg/kg (maintenance 3-5 mg/kg/hr)
Pentobarbital	5-10 mg/kg (> 1 hr) (maintenance 0.5-1 mg/kg/h Increase 1-3 mg/kg/hr)	5-15 mg/kg add 5-10 mg/kg (< 50mg/min) (maintenance 0.5-5 mg/kg/h)	-

Guideline: Super-refractory

Ketamine	1-3 mg/kg CI up to 5 mg/kg/hr	[4]
Immunotherapy: methylprednisolone	1g/d 3-5 d	[4]
IVIg	0.4 g/kg/d x 5 d	
Ketogenic diet		[4]
Magnesium	2-6 g/h (obtain serum level 3.5 mmol/L	[4]
Pyridoxime (young children)		[4]
Hypothermia		[4]
Lacosamide		[4]
Electroconvulsive therapy		[4]
Epileptic surgery		[4]

[4]Hong Kong Epilepsy Society Society 2017

คำถาม

- Lorazepam ดีกว่า diazepam จริงหรือ
- Second-line treatment status epilepticus: LEV vs. PHT vs VPA
- การศึกษาของ valproate พบว่าดีกว่า phenytoin ในการรักษาแบบ first line นอกจากนั้นพบว่าเมื่อ failure ต่อ phenytoin แล้ว มาใช้ valproate จะได้ผลดีกว่าเมื่อ failure ต่อ valproate แล้วมาใช้ phenytoin (25% vs. 71%)
- ความแตกต่างของ efficacy ระว่างยากันชักที่ใช้รักษาผู้ป่วย benzodiazepine resistance status epilepticus ?
- lacosamide มีข้อมูลที่สามารถนำมาเขียนใน guideline ได้หรือยัง

Is IV LZP more efficacy than DZP or MZP as a first-line treatment status epilepticus

- Basic knowledge of pharmacokinetics
- Study population
- Pre-hospital or hospital treatment
- Outcome of study: the proportion of patients with clinical seizure cessation

Is IV LZP more efficacy than DZP or MZP as a first-line treatment status epilepticus: Meta-analysis

- Seizure cessation: RR 0.64; 95% CI 0.45-0.90 Prasad et al. Cochrane Database Syst Rev 2014;9 CD003723

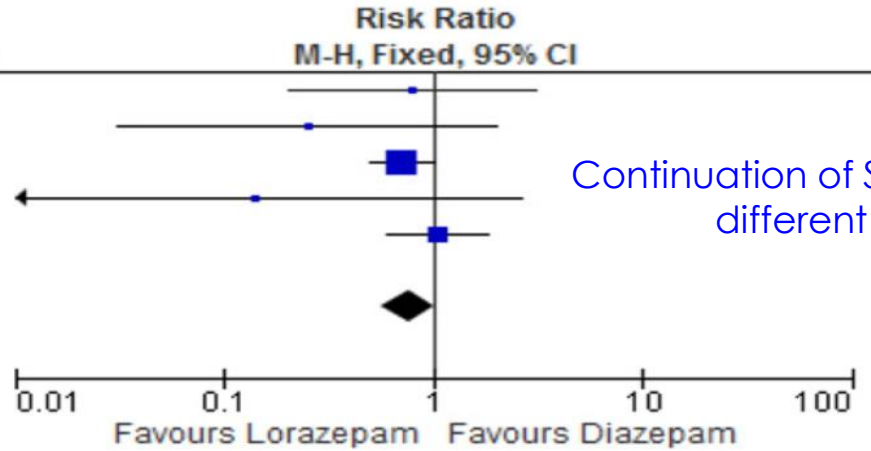
  RR 1.09; 95% CI 1.00-1.20 Brigo et al. Epilepsy & Behav 2016;64:29-36.

Is IV LZP more efficacy than DZP or MZP as a first-line treatment status epilepticus: Meta-analysis

Brigo et al. Epilepsy & Behav 2016;64:29-36.

Study or Subgroup	Lorazepam IV Events	Total	Diazepam IV Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Leppik 1993	3	19	4	20	5.5%	0.79 [0.20, 3.07]	1983
Appleton 1995	1	27	5	34	6.3%	0.25 [0.03, 2.03]	1995
Alldredge 2001	27	66	39	68	54.3%	0.71 [0.50, 1.02]	2001
Gathwala 2012	0	40	3	40	5.0%	0.14 [0.01, 2.68]	2012
Chamberlain 2014	21	133	21	140	28.9%	1.05 [0.60, 1.84]	2014
Total (95% CI)		**285**		**302**	**100.0%**	**0.76 [0.57, 1.02]**	
Total events	52		72				

Heterogeneity: Chi² = 3.77, df = 4 (P = 0.44); I² = 0%
Test for overall effect: Z = 1.84 (P = 0.07)

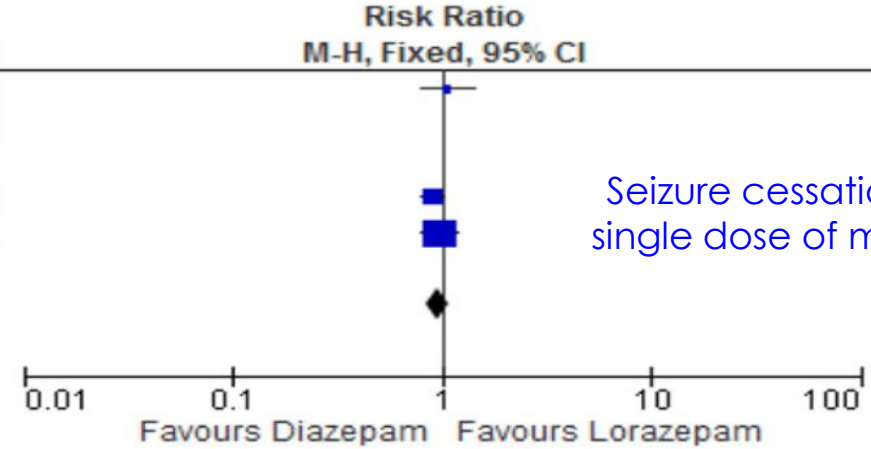


Continuation of SE requiring a different drug

B

Study or Subgroup	Lorazepam IV Events	Total	Diazepam IV Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Leppik 1993	16	19	16	20	11.1%	1.05 [0.79, 1.41]	1983
Appleton 1995	0	0	0	0		Not estimable	1995
Alldredge 2001	0	0	0	0		Not estimable	2001
Gathwala 2012	36	40	40	40	28.8%	0.90 [0.81, 1.01]	2012
Chamberlain 2014	80	133	87	140	60.2%	0.97 [0.80, 1.17]	2014
Total (95% CI)		**192**		**200**	**100.0%**	**0.96 [0.85, 1.08]**	
Total events	132		143				

Heterogeneity: Chi² = 1.54, df = 2 (P = 0.46); I² = 0%
Test for overall effect: Z = 0.68 (P = 0.50)



Seizure cessation after a single dose of medication

Meta-analysis outcome

PHT VS. VPA. LEV

Direct comparison

- PHT VS. VPA : OR 1.07 95% CI 0.57-2.03 ($I^2 = 0$)
- PHT VS. LEV: OR 1.18 95% CI 0.50-2.78 ($I^2 = 26\%$)

Indirect comparison

- LEV VS. VPA: OR 1.16 95% CI 0.45-2.97%

Second-line treatment status epilepticus: LEV vs. PHT vs VPA

Absence of evidence of a statistically significant difference in seizure control between LEV and VPA or between VPA or LEV and PHT

This finding is not synonymous with evidence of no evidence

Sodium valproate vs phenytoin in status epilepticus: a pilot study.

Misra UK[1], Kalita J, Patel R.

Author information

Abstract

Sixty-eight patients with convulsive status epilepticus (SE) were randomly assigned to two groups to study the efficacy of sodium valproate (VPA) and phenytoin (PHT). Seizures were aborted in 66% in the VPA group and 42% in the PHT group. As a second choice in refractory patients, VPA was effective in 79% and PHT was effective in 25%. The side effects in the two groups did not differ. Sodium valproate may be preferred in convulsive SE because of its higher efficacy.

Comment in

Sodium valproate vs phenytoin in status epilepticus: a pilot study. [Neurology. 2007]

The status of intravenous valproate for status. [Epilepsy Curr. 2007]

the critical difference in the response 20%, the efficacy of PHT 40%
The sample size calculate = 85% (the power of the test 90%
Recruit 68 patients power of the test 71%

CRITICAL REVIEW AND INVITED COMMENTARY

Lacosamide in status epilepticus: Systematic review of current evidence

*†[1]Adam Strzelczyk, *[1]Johann Philipp Zöllner, *Laurent M. Willems, †Julie Jost, *Esther Paule, *‡Susanne Schubert-Bast, *†Felix Rosenow, and *†Sebastian Bauer

Epilepsia, 58(6):933–950, 2017
doi: 10.1111/epi.13716

Overall, in 3 of 36 children (age range 4 weeks–17 years), side effects were described; however, no serious adverse events occurred in the studies in pediatric patients,[69–71] suggesting that LCM seems to be a safe and efficacious treatment option in SE in pediatric patients.

Overall Efficacy of LCM in SE

In total, 522 episodes of SE in 486 adults and 36 minors could be extracted from the literature, including the data already evaluated by Höfler and Trinka.[25] Efficacy data were available for a total of 471 episodes (51.7% female). Overall LCM efficacy was 57%, which is similar to the efficacy ranged from 100%[33,73] to 50%,[38] with 92% (34/39) overall, which seems better than in GCSE ($p = 0.013$) and NCSE ($p < 0.001$).

LCM is currently not approved for use in SE. Consequently, most studies used LCM as an adjunctive therapy in patients with refractory SE. This impacts the evaluation of LCM efficacy and may have led to an underestimation of the efficacy of LCM in SE treatment. AEDs are commonly less effective in terminating SE when they are afforded a later position in the succession of anticonvulsive drugs,[74] which is reflected in the findings from several studies. The efficacy with later positioning decreased from 60% to 20%,[35] 100% to 75%,[43] 84.6% to 55.6%,[49] and 72.2% to

- Retrospective study > prospective study
- Small study population
- Adjunctive therapy (4-5 AEDs)

A randomized controlled trial of lacosamide versus sodium valproate in status epilepticus

Usha K. Misra, Deepanshu Dubey, and Jayantee Kalita

Epilepsia, 58(5):919–923, 2017
doi: 10.1111/epi.13706

Usha K. Misra,
Professor & Head of Neurology, Sanjay Gandhi Postgraduate Institutes of Medical Sciences, Lucknow, India.

Summary

Objective: To compare the efficacy and safety lacosamide (LCM) and sodium valproate (SVA) in lorazepam (LOR)–resistant status epilepticus (SE).

Methods: Patients with LOR-resistant SE were randomized to intravenous LCM 400 mg at a rate of 60 mg/kg/min or SVA mg/kg at a rate of 100 mg/min. The SE severity score (STESS), duration of SE and its etiology, and magnetic resonance imaging (MRI) findings were noted. Primary outcome was seizure cessation for 1 h, and secondary outcomes were 24 h seizure remission, in hospital death and severe adverse events (SAEs).

Results: Sixty-six patients were included, and their median age was 40 (range 18–90) years. Thirty-three patients each received LCM and SVA. Their demographic, clinical, STESS, etiology, and MRI findings were not significantly different. One hour seizure remission was not significantly different between LCM and SVA groups (66.7% vs 69.7%; p = 0.79). Twenty-four hour seizure freedom was higher in SVA (20, 66.6%) compared with LCM group (15, 45.5%), but this difference was not statistically significant. Death (10 vs. 12) and composite side effects (4 vs. 6) were also not significantly different in LCM and SVA groups. LCM was associated with hypotension and bradycardia (one patient), SVA with liver dysfunction (six patients).

Significance: In LOR-resistant SE patients, both LCM and SVA have comparable efficacy and safety. SVA resulted in slightly better 24 h seizure remission.

KEY WORDS: Status epilepticus, Lacosamide, Sodium valproate, Antiepileptic drug, Adverse event, Mortality, Lorazepam.

Guideline

แนวทางการรักษานี้เป็นเครื่องมือส่งเสริมคุณภาพในการบริการด้านสุขภาพที่เหมาะสมกับทรัพยากรและเงื่อนไขในสังคมไทย โดยหวังผลในการสร้างเสริมและแก้ไขปัญหาสุขภาพของคนไทยอย่างมีประสิทธิภาพและคุ้มค่า ข้อเสนอแนะต่างๆ ในแนวทางเวชปฏิบัตินี้ ไม่ใช่ข้อบังคับของการปฏิบัติ ผู้ใช้สามารถปฏิบัติแตกต่างไปจากข้อแนะนำได้ ในกรณีที่สถานการณ์แตกต่างออกไปหรือมีเหตุผลที่สมควรโดยใช้วิจารณญาณที่เป็นที่ยอมรับในสังคม