APPENDIX 1. Search strategies for a study of levetiracetam for status epilepticus in adults

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to August 18, 2020

Search Strategy:

#	Searches	Results
1	exp Status Epilepticus/	8243
2	exp Randomized Controlled Trial/	512264
3	exp Levetiracetam/	2163
4	1 and 2 and 3	20
5	limit 4 to humans	18

Database: Embase 1974 to 2020 August 18
Search Strategy:

#	Searches	Results
1	exp levetiracetam/	7398
2	status epilepticus.mp. or exp epileptic state/	25825
3	exp randomized controlled trial/	616962
4	1 and 2 and 3	34
5	limit 4 to human	34

Database: CINAHL

Tuesday, August 18, 2020 5:31:52 PM

#	Query	Limiters/Expanders	Last Run Via	Results
S1	status epilepticus AND randomized controlled trial AND levetiracetam	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete	19

Database: Cochrane Central Register of Controlled Trials
Date Run: 20/08/2020 03:18:57
Comment:

ID	Search	Hits
#1	MeSH descriptor: [Levetiracetam] explode all trees	207
#2	MeSH descriptor: [Status Epilepticus] explode all trees	106
#3	#1 and #2 in Trials	21

Appendix to: Webb CA, Wanbon R, Otto ED. Levetiracetam for status epilepticus in adults: a systematic review. *Can J Hosp Pharm*. 2022;75(1):46-53.

APPENDIX 2 (part 1 of 2). Cochrane risk-of-bias assessment[1]

Chakravarthi et al. (2015)[2]		
Domain	**Risk**	**Description**
Random sequence generation	High	Systematic method of randomization: odd numbered patients received PHT, even numbered patients received LEV
Allocation concealment	High	Given not true randomization, assignment could be anticipated Participants or investigators could possibly foresee assignments, as allocation based on order of recruitment
Blinding of participants and personnel	High	No blinding described
Blinding of outcome assessment	Unclear	No blinding of outcome assessment described
Incomplete outcome data	Low	Many patients randomized (76/120) were excluded from the study as seizure terminated with lorazepam. Only 44/120 went on to receive the treatment they were randomized to. Of these patients, all were accounted for in the outcomes assessment
Selective reporting	Low	All outcomes reported in methods were included in Table 2
Other bias	Low	

Mundlamuri et al. (2015)[3]		
Domain	**Risk**	**Description**
Random sequence generation	Low	Computer generated randomization
Allocation concealment	Unclear	Not reported if or how allocation was concealed
Blinding of participants and personnel	High	No blinding described
Blinding of outcome assessment	Unclear	No blinding of outcome assessment described
Incomplete outcome data	High	All randomized patient data included in 24 hour outcomes. However, one month follow-up data was only available for 73% of patients and reasons for missing data was not reported.
Selective reporting	Unclear	Primary and secondary outcomes not clearly outlined in methods section, so completion of reporting unknown
Other bias	Low	

Gujjar et al. (2017)[4]		
Domain	**Risk**	**Description**
Random sequence generation	High	Computer-generated list of random numbers; randomization encompassed both groups of patients together, then results assessed separately.
Allocation concealment	Unclear	Not reported if or how allocation was concealed, randomization failure occurred in 10 of the SE group due to discretion of treating physician choosing alternate therapy
Blinding of participants and personnel	High	No blinding described
Blinding of outcome assessment	Unclear	No blinding of outcome assessment described
Incomplete outcome data	Low	All defined outcomes for randomized patients were reported
Selective reporting	Low	All outcomes reported
Other bias	Low	

Appendix to: Webb CA, Wanbon R, Otto ED. Levetiracetam for status epilepticus in adults: a systematic review. *Can J Hosp Pharm*. 2022;75(1):46-53.

APPENDIX 2 (part 2 of 2). Cochrane risk-of-bias assessment[1]

Nene et al. (2019)[5]		
Domain	**Risk**	**Description**
Random sequence generation	Low	Computer-generated random numbers
Allocation concealment	Unclear	Not reported if or how allocation was concealed
Blinding of participants and personnel	High	States single blind, but no description of who or how this blinding was completed
Blinding of outcome assessment	Unclear	States single blind, but no description of who or how this blinding was completed
Incomplete outcome data	Low	A small number of patients were lost to follow-up or incorrectly assigned. However, this appears balanced between groups and was both an intention-to-treat and a "Completed Study" analysis was reported.
Selective reporting	Low	Appear to report all outcomes per protocol on clinical trial registry (CTRI/2016/05/006932).
Other bias	Low	

Kapur et al. (2019)[6]		
Domain	**Risk**	**Description**
Random sequence generation	Low	Central randomization through computer program
Allocation concealment	Low	Blinded drug box used throughout
Blinding of participants and personnel	Low	Methods of double blinding clearly described. Unmasking of trial drug allowed for purposes of patient care. 200 of 400 enrollments were unblinded, however unblinding only occurred after the primary outcome had been determined at 60 minutes, or after a criterion for failure to the primary outcome had been met
Blinding of outcome assessment	Low	"Adjudicators were unaware of the treatment assignments and made determinations by medical record review."
Incomplete outcome data	Low	Clear description of all patient flow. Intention to treat, per-protocol, and safety analysis groups clearly described and outcomes in each group reported
Selective reporting	Low	Outcomes clearly stated in methods, reported in results. Full study protocol available and was registered on clinical trials registry (NCT01960075)
Other bias	Low	

References

1. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
2. Chakravarthi S, Goyal MK, Modi M, Bhalla A, Singh P. Levetiracetam versus phenytoin in management of status epilepticus. *J Clin Neurosci*. 2015;22(6):959-63.
3. Mundlamuri RC, Sinha S, Subbakrishna DK, Prathyusha PV, Nagappa M, Bindu PS, et al. Management of generalised convulsive status epilepticus (SE): a prospective randomised controlled study of combined treatment with intravenous lorazepam with either phenytoin, sodium valproate or levetiracetam—pilot study. *Epilepsy Res*. 2015;114:52-8.
4. Gujjar AR, Nandhagopal R, Jacob PC, Al-Hashim A, Al-Amrani K, Ganguly SS, et al. Intravenous levetiracetam vs phenytoin for status epilepticus and cluster seizures: a prospective, randomized study. *Seizure*. 2017;49:8-12.
5. Nene D, Mundlamuri RC, Satishchandra P, Prathyusha PV, Nagappa M, Bindu PS, et al. Comparing the efficacy of sodium valproate and levetiracetam following initial lorazepam in elderly patients with generalized convulsive status epilepticus (GCSE): a prospective randomized controlled pilot study. *Seizure*. 2019;65:111-7.
6. Kapur J, Elm J, Chamberlain JM, Barsan W, Cloyd J, Lowenstein D, et al. Randomized trial of three anticonvulsant medications for status epilepticus. *N Engl J Med*. 2019;381(22):2103-13.

Appendix to: Webb CA, Wanbon R, Otto ED. Levetiracetam for status epilepticus in adults: a systematic review. *Can J Hosp Pharm*. 2022;75(1):46-53.