

Background & Objectives:

- Drugs such as phenobarbital and phenytoin usually fail to control seizures in neonates
- Levetiracetam has proven efficacy and excellent safety profile in older patients
- These qualities and availability of intravenous preparation of levetiracetam have led to its widespread use in neonates
- However, randomized studies have not been performed
- **Objective:** To study the efficacy and safety of levetiracetam compared with phenobarbital as a first-line treatment of neonatal seizures

ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet



Levetiracetam Versus Phenobarbital for Neonatal Seizures : Which is better?

Methods :

- Multicenter, randomized, blinded, controlled, phase IIb trial
- Inclusion criteria: Infants with gestational age 36–44 weeks, weight > 2.2 kg and at risk or suspected to have neonatal seizures
- Exclusion criteria: Prior use of any anti-convulsant, serum creatinine > 1.6 mg/dl, seizures due to correctable metabolic cause (hypoglycemia, hypocalcemia)
- 106 participants were enrolled and randomly assigned to receive levetiracetam (40 mg/kg+20 mg/kg; n = 53), or phenobarbital (20 mg/kg+20 mg/kg; n = 30).
- Eligible enrolled infants were on continuous EEG monitoring
- Primary outcome measure: Complete seizure freedom for 24 hours, assessed by independent review of the EEGs by 2 neurophysiologists

Results :

- Eighty percent of patients (24 of 30) randomly assigned to phenobarbital remained seizure free for 24 hours, compared with 28% of patients (15 of 53) randomly assigned to levetiracetam (P < 0.001; relative risk 0.35 [95% confidence interval: 0.22–0.56]; modified intention-to-treat population)
- More adverse effects (hypotension, respiratory suppression, sedation) were seen in subjects randomly assigned to phenobarbital (not statistically significant)

Conclusion: Phenobarbital was more effective than levetiracetam for the treatment of neonatal seizures. Higher rates of adverse effects were seen with phenobarbital treatment.

EXPERT COMMENT



“This study has revealed greater efficacy of phenobarbital than levetiracetam in controlling neonatal seizures. Adverse effects were more frequent with phenobarbital. Higher-dose studies of levetiracetam are warranted, and definitive studies with long-term outcome measures are needed.”

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Reference

Sharpe C, Reiner GE, Davis SL, Nespeca M, Gold JJ, Rasmussen M, et al. Levetiracetam Versus Phenobarbital for Neonatal Seizures: A Randomized Controlled Trial. *Pediatrics*. 2020;145(6):e20193182.

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