STUDY PROTOCOL

1. Study Title

Levetiracetam Versus Phenobarbitone for the Treatment of Neonatal Seizures in a Tertiary Care Hospital

Short title/acronyms: Levetiracetam Versus Phenobarbitone for the Treatment of Neonatal Seizures

2. Protocol ID

DHQ-DIK-IREB NO. 4806

Date: 26 February 2024.

ClinicalTrials.gov Identifier: NCT Not Yet Assigned

3. Background & Rationale

Neonatal seizures are the most common neurological emergency in neonates and are associated with significant morbidity and mortality. Phenobarbitone has traditionally been the first-line anticonvulsant; however, its efficacy is limited and it has significant adverse effects. Levetiracetam is emerging as a safer alternative with promising seizure control rates. This study aims to compare the efficacy and safety of levetiracetam versus phenobarbitone in neonates with seizures.

4. Objectives

Primary Objective

To compare seizure control rates within 24 hours between levetiracetam and phenobarbitone in neonates with clinically diagnosed seizures.

Secondary Objectives

- To compare time to seizure cessation between both drugs.
- To compare the need for second-line anticonvulsant therapy.
- To compare seizure recurrence during hospital stay.
- To compare adverse drug reactions.
- To compare mortality rates.

5. Study Design

A prospective randomized controlled trial conducted at the Neonatal Intensive Care Unit (NICU) and Pediatric wards of a tertiary care hospital.

6. Study Setting

Neonatal Intensive Care Unit (NICU) and Pediatric ward at [Your Hospital Name], Pakistan.

7. Study Population

Neonates (0–28 days) with clinically diagnosed seizures admitted to NICU or Pediatric ward.

8. Sample Size

Based on previous literature, assuming seizure control rates of 70% with levetiracetam and 50% with phenobarbitone, with 80% power and 5% significance level, the calculated sample size is **n = 100 (50 in each group)**. However we will include all the patients accepting the inclusion criteria during one year of study.

9. Inclusion Criteria

- Neonates (0–28 days old) with clinically diagnosed seizures.
- Term and preterm neonates.
- Parents/legal guardians provide informed consent.

10. Exclusion Criteria

- Major congenital anomalies or genetic syndromes.
- Severe renal or hepatic impairment.
- Neonates already receiving anticonvulsants before admission.
- Neonates with metabolic seizures not responding after correction.
- Neonates with CNS infection requiring specific treatment (unless seizures persist).
- Parents refuse consent.

11. Intervention

Arm A: Levetiracetam

- Loading dose: 20 mg/kg IV
- Repeat dose: 20 mg/kg IV after 12 hours if seizures persist
- Maintenance dose: 10 mg/kg IV/PO twice daily until seizure control or discharge

Arm B: Phenobarbitone

- Loading dose: 20 mg/kg IV
- Repeat dose: 10 mg/kg IV after 20 minutes if seizures persist
- Maintenance dose: 5 mg/kg IV/PO once daily until seizure control or discharge

12. Outcome Measures

Primary Outcome

Seizure control rate within 24 hours after first-line treatment.

Secondary Outcomes

- Time to seizure cessation
- Need for second-line anticonvulsant
- Seizure recurrence during hospital stays
- Adverse drug reactions
- Mortality during hospital stay

13. Study Procedures

1. Neonates with clinical seizures will be assessed by pediatric/neonatology team.
2. Eligible neonates will be randomized into either levetiracetam or phenobarbitone group.
3. Baseline data including demographic details, gestational age, birth weight, and clinical status will be recorded.
4. Standard investigations will be done (CBC, blood glucose, electrolytes, ABG, neuroimaging if required).
5. Treatment will be administered as per group allocation.
6. Monitoring of seizure activity and side effects will be done for 72 hours and until discharge.
7. Data will be recorded on a structured proforma.

14. Randomization

Simple randomization using Lottery method.

15. Data Collection

Data will be collected on a structured proforma and entered into SPSS version 25.

16. Ethical Considerations

Approval will be obtained from the Institutional Review Board (IRB). Informed consent will be obtained from parents/legal guardians.

17. **Principal Investigator:**
Dr. Gohar Ali