Cover page

Official Title:
Effect of Foot Reflexology on Comfort and Physiological Parameters in Neonates with Hypoxic-Ischemic Encephalopathy Undergoing Therapeutic Hypothermia: A Randomized Controlled Trial

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STUDY PROTOCOL WITH SAP

1. Background and Objective

Hypoxic-ischemic encephalopathy (HIE) is a major cause of neonatal mortality and long-term neurodevelopmental morbidity. Therapeutic hypothermia is the standard neuroprotective treatment; however, it is associated with stress, discomfort, and prolonged intensive care exposure. Non-pharmacological interventions may improve comfort and physiological stability.

This study aims to evaluate the effects of foot reflexology on comfort level and physiological parameters in neonates with HIE undergoing therapeutic hypothermia.

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2. Study Design

This study is a prospective, parallel-group, randomized controlled trial.

Participants will be randomly assigned into:

- Experimental group: Therapeutic hypothermia + foot reflexology
- Control group: Therapeutic hypothermia + standard care

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3. Study Setting

The study will be conducted in a tertiary-level neonatal intensive care unit.

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4. Participants

Inclusion Criteria:

- Gestational age ≥ 36 weeks
- Diagnosed with hypoxic-ischemic encephalopathy
- Undergoing therapeutic hypothermia
- Hemodynamically stable
- Written informed consent obtained from parents/legal guardians

Exclusion Criteria:

- Major congenital anomalies
- Severe intracranial hemorrhage
- Multi-organ failure
- Hemodynamic instability
- Uncontrolled seizures
- Skin conditions preventing reflexology
- Need for active resuscitation

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5. Sample Size

Sample size was calculated using G*Power software.
Based on:

- $\alpha = 0.05$
- Power = 0.80
- Effect size = 0.65

A minimum of 38 neonates per group was required.
Considering potential data loss, 42 neonates per group (total n=84) will be included.

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6. Randomization and Blinding

Participants will be randomized using a computer-generated block randomization method (1:1 ratio). Allocation will be concealed using sealed opaque envelopes.

Due to the nature of the intervention, blinding of the practitioner is not possible. Outcome assessors and data analysts will be blinded.

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7. Intervention

Foot Reflexology (Experimental Group):

- Initiated at least 3 hours after therapeutic hypothermia begins
- Applied 3 times daily
- Each session: 15 minutes
- Total duration: 72 hours
- Standardized protocol applied to both feet
- Performed by trained researcher

Control Group:

- Standard therapeutic hypothermia care only
- No additional non-pharmacological intervention

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8. Outcome Measures

Primary Outcome:

- Comfort level assessed using COMFORTneo scale
- Measured at:
    - Baseline
    - 24 hours
    - 48 hours
    - 72 hours

Secondary Outcomes:

- Heart rate
- Respiratory rate
- Oxygen saturation
- Mean arterial pressure
- Body temperature

Measured:

- Immediately before and within 10 minutes after each session

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9. Data Collection

Data will include:

- Demographic and clinical characteristics
- COMFORTneo scores
- Physiological parameters

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10. Safety Monitoring

Each session will be monitored for:

- Bradycardia
- Oxygen desaturation
- Temperature instability
- Hemodynamic instability
- Seizure activity

Sessions will be terminated if any adverse event occurs.

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11. Ethical Considerations

Ethical approval will be obtained prior to study initiation.
Written informed consent will be obtained.
The study will comply with the Declaration of Helsinki.

Statistical Analysis Plan (SAP)

Data will be analyzed using SPSS software.

Continuous variables will be expressed as mean ± standard deviation, and categorical variables as frequency and percentage.

Normality will be assessed using appropriate tests.

Between-group comparisons will be performed using independent samples t-test or Mann–Whitney U test, as appropriate.

Within-group comparisons will be analyzed using paired t-test.

Repeated measures will be analyzed using repeated measures ANOVA to evaluate time, group, and interaction effects.

Post-hoc analyses will be conducted using appropriate multiple comparison tests.

A p-value of <0.05 will be considered statistically significant