BLUI Blanket Trial (Blue Light Universitas Indonesia)

The Effectiveness of the "Blui Blanket" Light Emitting Diode Phototherapy Blanket Model Against Decreased Bilirubin in Physiological Jaundice Gestational Age ≥ 35 Weeks - a Randomised Control Trial

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Protocol

Research Question

1.3.1 What is the efficacy of the Light Emitting Diode BLUI Blanket phototherapy blanket in reducing bilirubin levels in physiological neonatal jaundice after considering other conditions (Neonatal and Maternal Factors) and the side effects that occur?

1.3.2 How is the efficacy of the Light Emitting Diode BLUI Blanket phototherapy blanket compared to fluorescent phototherapy in reducing bilirubin levels in physiological neonatal jaundice after considering the conditions of Neonatal and Maternal Factors?

1.3.3 Does the BLUI Banket Phototherapy Blanket have good acceptability for doctors, nurses, and parents?

PICO

Population

Inclusion criteria -

1. Infants with gestational age ≥ 35 weeks and birth weight ≥ 2000 grams (p25);
2. Postnatal age > 24 hours – 14 days;
3. No history of birth trauma/cephalhematoma/bleeding;
4. Total serum bilirubin levels are ≥ 10 and less than ≤ 19 mg/dl (cut-off value for medium risk infants, gestational age 35-36 6/7 weeks and fit), and radar serum bilirubin total ≥ 12 less ≤ 22 mg/dl (limit value lower risk infants aged ≥ 38 weeks and fit);

5. Asian race; 64
6. No circulatory disturbances, respiratory disorders, and saturation above 90%.
7. The patient's parents/guardians agree to participate in the study and sign an informed consent.

Exclusion criteria –

1. Genetic, metabolic disorders, hemolytic anemia (examination of GDS levels, blood group, and rhesus, peripheral blood picture);
2. Infection (clinical fever or hypothermia and increased leukocyte laboratory tests);
3. The direct bilirubin level exceeds 2 mg/dl or 20% of the total serum bilirubin level.

Intervention

BLUI Blanket

Control

Conventional (Fluorescent) Phototherapy

Outcome

Primary - The proportion of physiologic jaundice neonates whose bilirubin levels decreased by or more than 3 mg/dL from the initial bilirubin level within 24 hours of neonates receiving therapy with LED BLUI blankets was more significant than the proportion of neonates receiving treatment with fluorescent phototherapy.

Method/Design

Trial design - The trial is a single-centre two-armed randomised controlled trial. The intervention group will be treated with a *BLUI Blanket* on the post-natal ward. The control group will have convensional phototherapy (fluorescent overhead lamp). Both groups will have serum bilirubin levels monitored 24 hours until they reach a safe level for their age and gestation. A safe level is defined as serum bilirubin level below the treatment line.

Ethical approval – Ethical approval will be sought from the Research Ethics Committee in the Faculty of Public Health, Universitas Indonesia.

Eligibility and Consent – After receipt of a serum bilirubin level near or above the treatment line when compared with age on an appropriate treatmentnomogram, the parents or guardians of the infant will be approached for informed consent by a member of the research team or a neonatal doctor. The investigator will explain the study fully to the patient's parent(s)/guardian(s) using the Patient Information Sheet. Parents will be informed that they may withdraw their child from the study at any time should they wish; and that a decision not to consent their child's participation in the study or to withdraw their infant from the study once enrolled will not affect their infants accessto the best available care at the RSAB Harapan Kita. Consent forms will be kept securely, and a copy will be provided in the patients' chart. Fully informed written consent will be obtained prior to enrolment.

Randomisation and Allocation Concealment - Randomisation will occur on receipt of informed consent. A computer-generated random number list will be used, prepared by an investigator with no clinical involvement in the trial. Sequences will be grouped based on the

type of phototherapy used - BLUI Blanket and conventional (fluorescent) phototherapy. Once generated the randomisation lists will be sealed in opaque envelopes. Once the patient is consented to enter the trial, the investigator(s), doctor on duty or ANP will open the next sequential opaque envelope in the correct strata and provide the allocated interventions.

Blinding – Blinding of parents or research staff will not be possible due to the nature of the intervention.

Methods

Infants will be randomised after having an serum bilirubin sample which is 'near' the treatment line for their age or less from the treatment line on a treatment nomogram. Both groups will have serum bilirubin samples taken 24 hours until they cross the treatment line and require phototherapy, or until they are deemed to be at a safe level from the line and suitable for discharge home. Infants in the control group may also be discharged for repeat sample as an outpatient if deemed appropriate.

Sample Size Calculation

A sample size for each group with α is degree of confidence (95%), β is test strength (80%). Proportion of physiologic jaundice neonates receiving conventional phototherapy and having decreased bilirubin levels ≥ 3 mg/dL in 24 hours. Assumption/estimation of the probable proportion of physiologic jaundice neonates receiving LED blankets versus conventional phototherapy for decreased bilirubin levels ≥3 mg/dL in 24 hours = 2 times, proportion of diseased population 2 (P0 x RR). Ratio of population 2 to population 1.

In this study, the hypothesis will be tested at the 95% confidence level ($\alpha = 0.05$) and the power of the test ($1 - \beta$) is 0.8.

The sample calculation formula is determined based on a comparison of 2 proportions. Because the average decrease in bilirubin levels from Maharoof et al. 2017, on conventional phototherapy = 3.29 mg/dL, it is estimated RR 1,6-1,8. Based on the results of the calculation of the sample size described above, a total sample of 50 subjects was obtained, so that the total sample size was 100 subjects to facilitate block 4 randomization with 6 permutations so that there were 25 randomized blocks.

Assignment of Intervention

The process of determining the allocation of subjects to the intervention or control group is carried out by the principal investigator (PI). Intervention officers are not involved in determining the assignment of subjects. The random allocation method used is block

randomization. Each block consists of 4 subjects so that 6 variations of the permutation result blocks are obtained (AABB, ABAB, ABBA, BBAA, BABA, BAAB), then the researcher randomizes block variations for a number of 100 participants by doing a simple lottery. The order in which patients enter the hospital determines the order of the draw results. Patients who came for an eligibility assessment were assessed as study subjects based on medical record data, after proper PI came to the patient to explain the study and ask for consent. If the patient agrees, then then phototherapy is given based on the results of the randomization whether the patient gets fluorescent phototherapy or phototherapy blankets.

Data collection

Basic data were collected in the form of demographic data (age, gender, birth weight, gestational age), data related to the reaserch (Monitoring breastfeeding models; frequency & volume breast-feed; therapy pause; long therapy; side effect: rash skin, body temperature, dehydration, stool consistency) and outcome measurement data, bilirubin serum level. Demographic data and data related to the reaserch were obtained from patient medical record documents, bilirubin serum level was measeured.

Data management

Data entry was carried out by the main researcher under the supervision of a supervisor from the University of Indonesia, the data was entered into excel format which was locked with 2 security times, then the researcher coded the categorical scale variables. The researcher submitted the excel data format to an independent data analyst for analysis.

Statistical Methods

The statistical analysis plan used was the dependent and independent mean difference test if the baseline data between groups did not show any significant differences. If the baseline data shows a significant difference, then perform the average difference test by controlling the variables that show the difference.

Monitoring Data

Data monitoring was carried out by Prof. Asri Adisasmita and Prof. Purwanty Astuti as supervisors in this study.

Ethical Clearence

This research has received ethical approval from the research and community engagement ethical committee, faculty of public health at the University of Indonesia with number: Nomor: Ket- 38/UN2.F10.D11/PPM.00.02/2023 on February 23rd 2023 signed by the chairman Prof. Dr. dr. Ratna Djuwita, MPH.

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Confidentiality

We will record data that is routinely collected for each infant in their medical records as part of their routine care. Participation in the study will not necessitate extra investigations or intervention over and above those indicated as part of their routine care. The data will be recorded on dedicated Case Report Forms (CRFs). These CRFs will not contain identifying information of individual infants and will be stored securely. Data which is extracted from these CRFs will be anonymised and entered intodatabases on password protected computers.

Conflicts of Interest

We have no conflicts of interest to declare.

Findings of this study

The findings of this study will have important implications for infants and families, health workers and government, and we will aim to publish the data and disseminate it as widely as possible. If we receive ethical approval to proceed with this study it will be registered with the International Standard Randomised Controlled Trials Number Register (http://www.controlled-trials.com/isrctn/). Once complete we will submit our findings for presentation at national and international scientific meetings and for publication in a peer-reviewed scientific journal.

Consort Diagram