UNIVERSITY OF SÃO PAULO
SÃO PAULO MEDICAL SCHOOL

STUDY PROTOCOL

Official Title of the Study:

Safety and Effectiveness of Different Interface Models for Non-Invasive Ventilation Support in Preterm Infants with a Gestational Age of 28 Weeks or Greater

NCT Number:	NCT Pending
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This document contains official study protocol/statistical analysis information submitted to ClinicalTrials.gov in accordance with 42 CFR 11.48 and ClinicalTrials.gov Results Data Element Definitions.

Study Protocol

Ethics Approval & Team Presentation

Following approval by the Ethics Committee/National Ethics Committee, the multidisciplinary team of the NICU at the Women's Hospital will attend a meeting to present the research and receive the necessary training.

Team Training

The training will be conducted by the study's researcher and directed to the NICU's multidisciplinary team, in person before the pilot study is implemented, ensuring everyone's participation.

The project presentation will include the use of audiovisual devices and practical demonstrations on mannequins, covering the installation of various interfaces, skin assessment, application of adhesives, and completion of data collection forms. The content will cover:

• Study objective;

• Types of interfaces and points of contact/pressure;

• Weaning;

• Procedures for photogrammetry;

• Rating scales and data collection forms;

• Types of adhesives and methods of attachment and removal;

• Evaluation flowchart;

• Data storage.

The materials used will be presented, including interfaces, adhesives, and sprays, as well as the scales and evaluation forms. The data storage process will also be explained.

The in-person training will last 2 hours and will be held in the hospital unit's auditorium on 3 different dates to accommodate the entire team. On-site training will also be conducted in the NICU to consolidate the training.

Randomization and Stratification

After signing the informed consent form, stratification by gestational age will be performed (≥28 weeks and < 32 weeks, and ≥32 weeks and < 37 weeks). After respiratory assessment, if mild to moderate respiratory distress is confirmed (BSA between 1 and 6). Following randomization for allocation to the groups, eligible newborns who had multiple births will be randomized individually. Those who will use mechanical ventilation and will be extubated will be randomized following the same inclusion criteria.

Patients will be randomly allocated into 5 groups, according to the NIV interface:

• Group 1 (G1) - Infant Flow LP® Interface;

• Group 2 (G2) - RAM® Cannula;

• Group 3 (G3) - Dräger Babyflow® nasal mask;

• Group 4 (G4) - Conventional binasal prongs;

• Group 5 (G5) - Fanem® flexible anatomical binasal prongs.

Randomization will be performed using opaque, sequentially numbered, sealed envelopes containing the group allocation, separated into two boxes according to the stratification described above. Vital signs and blood pressure will be collected before the use of ventilatory support on a specific data collection form and will continue at 4-hour intervals at the following times (8:00, 12:00, 16:00, 20:00, 0:00, 4:00) until the non-invasive ventilation (NIV) is withdrawn.

Interventions

Preterm infants (PTNBs) who meet the study inclusion criteria and require non-invasive ventilation as the first choice for ventilatory support or, after tracheal extubation will undergo NIV using Vyaire IX5® or Bellavista® mechanical ventilation devices. Humidifiers (GT2000, GT5000, and GT5000 plus - Globaltec Med®), e Misty 3 (Intermed®, São Paulo Brasil), which do not have servo controls, will be used and adjusted according to the temperature and relative humidity control protocol of the gas delivered to the patient as follows:

• Set the heater initially to power level 5;

• Perform intermittent checks of the supplied gas (every 4 hours);

• Adjust the heater power to target a temperature between 36.5°C and 37°C;

• Top up the water level to the indicated mark (every 4 hours).

Intermittent gas temperature monitoring will be performed using a water-resistant thermometer (G-Tech TH1027) attached to the inspiratory limb of the NIV circuit, via the proximal pressure sensor connection. Allow one minute for the measurement to complete before making any necessary adjustments.

The humidifiers (TR EVOLUTION - TREND Medical), (GT5000S - Globaltec Med®) and (MR850 Fisher & Paykel), should be set to non-invasive mode for the 5 groups according to randomization, also for the use of the humidifier type (servo-controlled or conventional).

The target SpO2 range will be 92% to 96%, following the Unit's routine.