

What is the inspired oxygen fraction that better predicts the need for surfactant administration for the lungs of preterm neonates with neonatal distress syndrome?

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Registration date 16/10/2023	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 16/10/2023	Condition category Pregnancy and Childbirth	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Current international guidelines on neonatal respiratory distress syndrome (RDS) recommend continuous positive airway pressure (CPAP) stabilization as the primary treatment. RDS occurs from a deficiency of surfactant, due to either inadequate surfactant production, or surfactant inactivation in the immature lungs. Surfactant replacement is indicated for those babies still requiring a fraction of inspired oxygen (FiO₂) > 0.3 (above the normal atmospheric level or 20%) regardless of the gestational age (GA). The research team will explore the accuracy of decreasing FiO₂ thresholds as early predictors of surfactant replacement in babies stratified by GA.

Who can participate?

Neonates aged 1 day to 6 months of age with RDS

What does the study involve?

This study is a pragmatic, observational study set in 12 Italian and Spanish neonatal intensive care units (NICUs). This is a secondary analysis of data from a derivation and a validation cohort of preterm babies suffering from RDS, stratified by gestational age (250-276; 280-306; 310-336 days) and stabilized on CPAP. FiO₂ was collected soon after stabilization and its prognostic accuracy was evaluated on the subsequent surfactant administration by a rigorously masked physician.

What are the possible benefits and risks of participating?

It is hoped that future patients will benefit from the findings that FiO₂ is a GA-dependent predictor of early surfactant administration. Neonates participating in the study have no possible risks because they will not undergo new procedures because of the study itself. It is an observational study without interventions on patients.

Where is the study run from?
University of Naples Federico II (Italy)

When is the study starting and how long is it expected to run for?
May 2017 to April 2023

Who is funding the study?
University of Naples Federico II (Italy)

Who is the main contact?
Prof Francesco Raimondi, raimondi@unina.it (Italy)

Contact information

Type(s)

Public, Scientific, Principal investigator

Contact name

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

Nil known

Study information

Scientific Title

Inspired oxygen fraction thresholds accuracy to predict surfactant administration in neonatal RDS is gestational age dependent: a pragmatic, multi-center study

Study objectives

The inspired oxygen fraction (FiO₂) has been described as a significant predictor of CPAP failure and subsequent surfactant administration. Current European recommendations are to deliver surfactant if the infant has been stabilized with CPAP 6 cm H₂O and still requires a FiO₂>0.3 while Canadian guidelines recommend waiting until the oxygen requirement meets an FiO₂>0.5. While the American Academy of Pediatrics would only recommend an early (i.e. within 2 hours of life) individualized surfactant administration without citing the FiO₂>0.3 cut-off, the latter has been considered by a recent expert consensus from the United States.

Indeed, the choice of any FiO₂ threshold is not supported by indisputable evidence. A recent meta-analysis showed no significant difference in major neonatal outcomes (i.e. BPD, ventilation etc) within the FiO₂ 0.3-0.59 interval. However, it remains unclear whether a FiO₂ ≤0.3 threshold may be equally or more beneficial.

We hypothesized that decreasing FiO₂ thresholds as predictors of CPAP failure would improve early surfactant replacement.

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 15/06/2017, Ethics Committee "Carlo Romano" at the Università Federico II di Napoli (Via Pansini 5, Napoli, 80131, Italy; + 39 331 2642920; segreteria@comitatoeticofedericoiicardarelli.it), ref: 187/17

Study design

Pragmatic observational secondary analysis cohort study

Primary study design

Observational

Study type(s)

Diagnostic

Health condition(s) or problem(s) studied

Inspired oxygen fraction as a predictor of need for surfactant in respiratory distress syndrome of preterm neonates

Interventions

This is a secondary analysis of prospectively collected data from 12 NICUs (Università Federico II, Naples; Ospedale Pineta Grande, Castelvoturno; Ospedale Careggi, Università di Firenze, Florence; Ospedale Buzzi, Milan; Università di Milano, Fondazione Policlinico, Milan; Ospedale Salesi, Università Politecnica delle Marche, Ancona; Fondazione Policlinico Gemelli, Roma; Hospital Gregorio Marañón, Madrid; Hospital San Juan de Dio, Barcelona; Hospital Basurto, Bilbao; and, Hospital Puerta del Mar, Cadiz).

Two cohorts of preterm infants 250-336 weeks of gestational age (GA) were investigated after validating their homogeneity. Neonates were stratified by gestational age calculated from the first day of the last menstrual period: 25-27; 28-30; 31-33 weeks. Written parental consent was obtained and the study was approved by the Ethics Committee "Carlo Romano" at the Università Federico II di Napoli (prot # 1621/17). Formal approval was also obtained by the Ethics Committee of each participating center. The study was conducted in accordance with the TRIPOD statement guidelines.

Preterm neonates were stabilized after birth as per the individual NICU protocol. After CPAP stabilization and within 120 minutes of life, a local investigator who was not in charge of the patient recorded the quantity of respiratory support in cm H₂O, her/his FiO₂ and the post-natal age. SpO₂ was recorded at the right hand by pulse oximetry, and it was maintained in the 90-95% range by adjusting FiO₂. Natural surfactant (poractant alfa 200 mg/kg for the first dose and 100 mg/kg for the following doses, Chiesi Farmaceutici, Parma, Italy) was prescribed by an attending neonatologist, unaware of the purpose of the study, based on radiographic and clinical signs suggestive of respiratory distress syndrome (RDS) as per the individual NICU protocol. For each patient, the local investigator also recorded the subsequent respiratory support history, the clinical complications from birth to discharge/exitus, and the presence of BPD.

Intervention Type

Other

Primary outcome(s)

FiO₂ thresholds recorded within the first 3 hours of life as predictors of later surfactant administration in preterm neonates by a masked attending physician measured using a secondary analysis of prospectively collected data at one timepoint

Key secondary outcome(s)

The following secondary outcome measures were measured using prospectively collected data at one timepoint:

1. Gestational age, birth weight, type of delivery, chorioamnionitis, maternal hypertension, PROM, IUGR, Apgar score at 5 min ≤ 5 , and antenatal steroids recorded within 120 minutes of life
2. First surfactant dose administered (number of infants)
3. Age at first surfactant dose (minutes)
4. FiO₂ at first surfactant dose
5. Death or BPD at NICU discharge

Completion date

30/04/2023

Eligibility

Key inclusion criteria

Premature neonates with respiratory distress syndrome (RDS) enrolled at birth and before the administration of the first surfactant dose. RDS in the preterm infant was defined as the presence of intercostal and subcostal retractions with expiratory grunting shortly after birth in the presence of typical radiographic features.

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Neonate

Lower age limit

1 days

Upper age limit

6 months

Sex

All

Total final enrolment

412

Key exclusion criteria

1. Infants who were intubated in the delivery room
2. Neonates with major congenital malformations

Date of first enrolment

01/05/2018

Date of final enrolment

31/10/2022

Locations**Countries of recruitment**

Australia

Italy

Spain

Study participating centre**Federico II University Hospital**

Division of Neonatology, Department of Translational Medical Sciences

Via Pansini 5

Naples

Italy

80131

Study participating centre**NICU Casa di Cura Pineta Grande**

Via Domitiana

Castel Volturno (CE)

Italy

81030

Study participating centre

Neonatology Division, Instituto de Investigación Sanitaria Hospital General Universitario Gregorio Marañón, Complutense University of Madrid
C/ O´Donnell, 48-50
Madrid
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Study participating centre

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Study participating centre

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Study participating centre

Department of Clinical Sciences and Community Health, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Cà Granda Ospedale Maggiore Policlinico, University of Milan
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Study participating centre

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Study participating centre

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Study participating centre
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Montevideo Etorb., 18,
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Study participating centre
Newborn Research Centre, The Royal Women's Hospital, University of Melbourne
Grattan Street
Parkville. Victoria
Australia
3010

Study participating centre
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Via Conca, 71 - Torrette
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Study participating centre
TIN Fondazione Gemelli. Università Cattolica del Sacro Cuore
Largo Agostino Gemelli 8
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Sponsor information

Organisation

University of Naples Federico II

ROR

<https://ror.org/05290cv24>

Funder(s)

Funder type

University/education

Funder Name

Università degli Studi di Napoli Federico II

Alternative Name(s)

University of Naples Federico II, University of Naples, Federico II University of Naples, Università di Napoli, Università di Napoli Federico II, UNINA

Funding Body Type

Government organisation

Funding Body Subtype

Universities (academic only)

Location

Italy

Results and Publications

Individual participant data (IPD) sharing plan

The dataset generated and /or analyzed during the current study will be available upon request from Prof Francesco Raimondi, raimondi@unina.it. Anonymized data will be available for sharing for one year after the publication of the study.

IPD sharing plan summary

Available on request