NEEDLE ASPIRATION OR CHEST DRAIN INSERTION FOR PNEUMOTHORAX IN NEWBORNS: PROTOCOL FOR A RANDOMISED CONTROLLED TRIAL

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HYPOTHESIS
Aspirating air with a needle reduces the need for chest drain insertion in newborn infants with pneumothoraces.

RESEARCH QUESTION
(Population) In newborn infants with respiratory distress with a pneumothorax on chest x-ray,
(Intervention) does needle aspiration (Comparison) compared to chest drain insertion
(Outcome) result in fewer infants having chest drains inserted within 6 hours of diagnosis?

BACKGROUND
Symptomatic pneumothorax occurs in 0.08% of all live births and in 5% to 7% of infants with birth weight of <1500 g.¹,² The risk for pneumothorax is increased in infants with respiratory distress syndrome, meconium aspiration syndrome, and pulmonary hypoplasia and in infants who are resuscitated at birth.³,⁴ Treatment options of spontaneous pneumothorax differ greatly between different countries and centres and to date there is no international standard protocol. Options include expectant treatment, needle aspiration and chest drain insertion. While the majority of practitioners favour immediate insertion of a chest drain, a retrospective cohort study on the management of pneumothorax in ventilated neonates suggests that it may be possible to treat a selected group of ventilated neonates with pneumothorax expectantly without chest tube placement.⁵ However to date there has been no randomized controlled study to review this. In adults, it is recommended that pneumothorax be treated with needle aspiration in the first instance as it may be successful treatment in 30 – 80% of cases.⁶

We propose to perform a prospective multicentre randomised controlled trial to address whether all newborn infants with a pneumothorax should have prompt chest tube insertion or is trial of needle aspiration appropriate initially. Infants randomised to ‘chest tube insertion’ will have chest tube inserted promptly following diagnosis of pneumothorax. Infants randomised to ‘needle aspiration’ will have trial of needle aspiration initially. If this fails these infants will then proceed to have chest tube inserted. The primary outcome is chest drains insertion for treatment of pneumothorax within 6 hours of diagnosis.
PATIENTS AND METHODS

INCLUSION CRITERIA

Infants (term and preterm) will be eligible for enrolment in the study if they

- Have a pneumothorax diagnosed on chest x-ray by treating clinicians
- Are receiving respiratory support
  - Mechanical ventilation (conventional or high frequency oscillation)
  - Continuous positive airway pressure (CPAP)
  - Supplemental oxygen FiO2 > 40% by head box or nasal cannulae to keep SpO2 >90%
- The treating clinicians deem the pneumothorax requires treatment

EXCLUSION CRITERIA

Infants will be excluded from the study if they

- Do not have respiratory distress
- Have significant pulmonary hypoplasia, e.g. Potter’s sequence

CONSENT

Treatment of pneumothorax is performed as an emergency procedure. It is well described how the distress and time constraints associated with obtaining consent for emergency neonatal research may compromise understanding and voluntariness, essential components of adequately informed consent. We, therefore, propose that we will enrol infants using a waiver of consent. The waiver of consent is a well-recognised approach to the difficulties encountered in the enrolment of human adults, children and infants to studies of emergency procedures. This approach has been used in many trials in many countries that have yielded important information that has changed clinical practice.

The UK Medical Research Council state that “provided that the specific approval of a research ethics committee has been obtained for the project overall, it is ethical to carry out research involving children on occasions of extreme urgency without obtaining prior consent” and that “the parents and child must be informed about the research as soon as possible afterwards and their consent for future involvement sought.” They also state that the research should only be carried out with the aim to improve understanding of the subject’s condition, that it entails only minimal risk and that it must be made clear to the parent/child that they can withdraw from the study at any point. This is also supported by Article 19 of the ‘Additional protocol on the Convention of Human Rights and Biomedicine on Biomedical Research’ affirmed by the Council of Europe in 2004.

We believe that our study fulfils these criteria as:

- The clear objective of the research is to improve our understanding of which method of treatment of pneumothorax results in fewer chest drain insertions
- We will inform parents as soon as is practicable that their infant was enrolled in the study and ask their permission to collect their infant’s information
- We will inform parents that they may withdraw their child from the study at any time without explanation
Since January 2012, we have used waivers of consent to enrol infants into several studies (the NEDI, BREL ISRCTN74486341 and WorM ISRCTN17864069 trials) with the approval of the Research Ethics Committee at the NMH. No issues have arisen with families or staff by using this approach to enrolment.

**INTERVENTION**

**NEEDLE ASPIRATION**

Needle aspiration of a pneumothorax will be conducted as outlined below:

- **Site:** 2nd intercostal space in the mid-clavicular line, inserting the needle as close as possible to the upper edge of the lower rib
- **Equipment:** Attach a 23G or 25G butterfly needle to a 3-way tap attached to a 20ml or 50ml syringe
- **Procedure:** Prepare the skin with an alcohol wipe and let dry. Insert the needle perpendicular the chest wall 0.5-1cm in a small baby and 1-2cm in a large baby. Open the tap to the syringe and needle and aspirate. Open the syringe to the atmosphere (i.e. closed to the needle). Empty the syringe. Repeat until you are unable to aspirate any more gas. Remove needle.

Needle aspiration will only be performed once. If there is still a pneumothorax seen on chest x-ray following needle aspiration that the clinician deems treatment is necessary, the infant will proceed to have a chest drain inserted.

**CONTROL**

**CHEST DRAIN INSERTION**

Chest drains will be inserted in 5th intercostal space in the mid-axillary line in a sterile fashion using either a traditional type drain with a trochar or a “pig-tail” drain using the Seldinger technique according to physician preference.

**RANDOMISATION**

Infants will be randomized to either the needle aspiration group or chest drain insertion group in a 1:1: ratio. To ensure balance between the groups, the randomisation will be stratified based on gestational age < 32 weeks and ≥ 32 weeks. Infants will be randomized in blocks of four. The treatment allocation of “NEEDLE ASPIRATION” or “CHEST DRAIN INSERTION” will be written on cards and placed in sequentially numbered sealed opaque envelopes. These envelopes will be placed in two boxes for the two gestational age strata and kept in the Neonatal Intensive Care Unit (NICU). An envelope will be selected from the appropriate box just prior to treatment for pneumothorax in the NICU.

**OUTCOMES**

**PRIMARY OUTCOME**

The primary outcome is chest drain insertion for management of pneumothorax on chest x-ray within 6 hours of diagnosis.
SECONDARY OUTCOMES

We will record the following clinically relevant secondary outcomes:

- Duration of chest drain
- Number of chest drain insertions
- Duration of ventilation post intervention
- Duration of ventilation
- Duration of nasal continuous positive airway pressure
- Duration of supplemental oxygen
- Bronchopulmonary dysplasia – oxygen treatment at 28 days
- Chronic lung disease – oxygen treatment at 36 weeks post menstrual age
- Nosocomial infections
- Pleural effusions
- Duration of hospital stay
- Death before discharge from hospital

SAMPLE SIZE ESTIMATION AND POWER CALCULATION

To demonstrate a reduction in the rate of chest drains inserted from 100% to 80% (relative reduction of 20%) with needle aspiration of pneumothorax as an initial management step, we need to recruit a total of 70 infants (35 infants in each arm of the study). Approximately 10 infants have a pneumothorax at NMH each year; thus this study will need to be a multi-centre study. We have already approached several colleagues who are willing to participate pending approval by the research Ethics Committee.

DATA COLLECTION AND 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 collected, anonymised and stored securely on a password-protected computer in accordance with Good Clinical Practice recommendations.

STATISTICAL ANALYSIS

Data will be analysed using SPSS software (SPSS Inc., IBM, Armonk NY, USA). The primary outcome – the proportion of infants with chest drain inserted for treatment of pneumothorax within 6 hours of diagnosis – will be compared using non-parametric tests (e.g. $\chi^2$ test). Other dichotomous (yes/no) outcomes will be compared using non-parametric tests. Continuous (measured in a scale) outcomes will be compared using parametric tests (e.g. Student’s t-test).
Data will be analysed using SPSS software (SPSS Inc., Chicago IL, USA). The primary outcome – the proportion of infants who have a chest drain inserted within 6 hours of diagnosis for management of the pneumothorax – will be compared using non-parametric tests (e.g. $\chi^2$ test). Other dichotomous (yes/no) outcomes will be compared using non-parametric tests. Continuous (measured in a scale) outcomes will be compared using parametric tests (e.g. Student’s t-test).

CONFLICTS OF INTEREST
We have no relationships, personal or financial, with any company whose products are being studied. We will make all decisions regarding data collection, interpretation and presentation.

FINDINGS OF THIS STUDY
The findings of this study will have important implications for premature infants and the nurses and doctors who care for them around the world. We will thus aim to disseminate our findings as widely as possible. If we receive ethical approval to proceed with this study, we will register the study 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 (e.g. North American Pediatric Academic Societies/Society for Pediatric Research, European Society for Paediatric Research); and for publication in a peer-reviewed scientific journal.

REFERENCES