

## **The Delivery Room Management Trial**

The Vermont Oxford Network Clinical Trials Group is embarking on a study of the delivery room management of premature infants. We want to compare three distinct methods of post-delivery stabilization and subsequent early respiratory care on chronic lung disease and survival in premature infants at high risk of respiratory distress syndrome. Specifically, we will compare:

- intubation, prophylactic surfactant administration shortly after delivery, and subsequent stabilization on ventilator support
- early stabilization on Nasal Continuous Positive Airway Pressure (NCPAP) with selective intubation and surfactant administration for clinical indications, and
- intubation, prophylactic surfactant administration shortly after delivery, and rapid extubation to NCPAP

The rationale for these three study arms is detailed in the study protocol. At the outset, participating centers will have different levels of expertise and comfort in implementing the various study arms. In particular, the early application of NCPAP may be a new concept to the staff at participating centers. Given the complexity of introducing changes that may be seen as radical at certain centers, we have structured the study to support the educational needs of participating centers, to allow for time to gain expertise in the application of the more unique approaches to care, and to test the feasibility of introducing these approaches in the delivery room.

The study has been structured in three stages. The first stage will develop and support general competency using nasal CPAP. Units will be provided with instructions on how to create an appropriate CPAP apparatus and given materials about how to use nasal CPAP, how to apply nasal prongs, and how to troubleshoot difficulties in maintaining infants on nasal CPAP. These fundamental issues will be reinforced using web conferencing. Centers that anticipate participating in the formal study will be asked to use nasal prong CPAP in the context of routine care in the Neonatal Intensive Care Unit. Each participating unit would evaluate a minimum of 20 patients and complete data regarding problems encountered with the system, and training of the neonatal staff.

After units have demonstrated basic competency in building and applying nasal CPAP (approximately 3 months), the second stage will begin. In this pilot stage, units will randomize infants to one of the three methods of delivery room stabilization. For different units, aspects of DR stabilization will be more or less difficult. Some units may have more experience with CPAP than with delivery room surfactant administration. Checklists regarding success of stabilizing infants and administration of assigned treatment and any post-treatment complications will be monitored. In addition, data from the run-in period will be used to further refine our definition of chronic lung disease at 36 weeks. Only centers that complete the run-in phase adequately would participate in the third phase. If there are widespread problems during the run-in phase, we will re-evaluate the feasibility of the protocol.

Lastly, if centers demonstrate capability during the run-in phase, we will launch the major trial. We anticipate enrolling approximately 702 infants in each study arm (a total of 2106 infants) in order to demonstrate differences in chronic lung disease or death at 36 weeks adjusted age.

Overall, we anticipate the three phases of the study to be completed within the next three years. Complete sets of educational materials, protocol, and draft data forms are included with this cover letter.

We look forward to starting this ambitious project!

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