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Nasal Continuous Positive Airway Pressure with Heliox in Preterm Infants with Respiratory Distress Syndrome

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STUDY QUESTION
To assess the therapeutic effects of breathing a low density helium and oxygen mixture (heliox, 80% helium and 20% oxygen) in premature infants with respiratory distress syndrome (RDS) treated with nasal continuous positive airway pressure (NCPAP).

METHODS
A multicenter pilot randomized controlled trial conducted over 2 years (between February 2008 and September 2010) in Italy.

Population
Inclusion
Infants born between 28 and 32 weeks of gestational age with radiologic findings and clinical symptoms of RDS and requiring respiratory support with NCPAP within the first hour of life.

Exclusion
- Congenital malformations.
- Grade 2 or higher intraventricular hemorrhage.
- Intubation in the delivery room and requiring FiO2 0.4 to maintain oxygen saturation between 88% and 95% before randomization.

Interventions
Intervention group infants
Were treated with NCPAP by using the Infant Flow SiPAP (VIASYS Healthcare Palm Springs, CA). The patients assigned to the heliox group were treated for 12 hours after randomization with NCPAP plus Heliox21 (BOC Medical, The LindeGroup, Munich, Germany), a mixture of 80% helium and 20% oxygen, stored in 10-L cylinders. Seven to eight cylinders were required for each patient.

Control group
Received NCPAP with standard medical air. In both groups, the starting NCPAP level was set at 4 to 6 cm H₂O and FiO₂ adjusted to maintain oxygen saturation levels between 88% and 95%.

Outcomes
Primary
Primary outcome was the requirement of mechanical ventilation within the first 7 days of life.

Secondary
- Treatment with surfactant
- Duration of ventilator support (both mechanical ventilation and NCPAP)
- Number of surfactant doses
- Length of stay
- Mortality
- Incidence of major complications of prematurity (pneumothorax, necrotizing enterocolitis, patent ductus arteriosus, retinopathy of prematurity, bronchopulmonary dysplasia (BPD), Intraventricular hemorrhage (IVH), and periventricular leukomalacia).

Allocation
Enrolled infants were randomly assigned by block randomization (block size of 4), using a closed-envelope method. Randomization was stratified at each center by gestational age into the following two strata: 28+0 to 29+6 weeks and 30+0 to 32+6 weeks.

Follow-up
Complete.

Blinding
No! Clinicians were blind only to the list of randomization but not to intervention. This perhaps due to delivered heliox was via cylinders and standard air via the central wall supply, blinding the clinicians was therefore quite difficult.

RESULTS
51 newborn infants were randomly assigned to two groups, 24 in the control group and 27 in the heliox group. There were no differences in clinical characteristics at birth and prenatal conditions between the 2 groups.

NCPAP with heliox treatment significantly decreased the risk of intubation for mechanical ventilation (14.8% vs 45.8%; \(P=0.029\), RR 0.32, 95% CI 0.12–0.88) and decreased the surfactant need (11.1% vs 43.5%; \(P=0.021\), RR 0.26, 95% CI 0.08–0.82).

This effect was still significant even after adjusting to baseline factors.

The total duration of NCPAP was 26±37 days in the heliox group versus 33±6 days in the control group (\(P=0.681\)). The length of stay was 52±30 days in the heliox group vs 47±33 days in the control group (\(P=0.627\)).

There were no side effects and no significant differences between groups for any secondary outcomes; however, the study was not powered to detect a difference in those outcomes.

CONCLUSION
Heliox increases the effectiveness of NCPAP in the treatment of RDS in premature infants.
COMMENTARY

Although the combination of Heliox therapy with CPAP may offer a potentially promising synergistic protective lung strategy for preterm infant with RDS to reduce the need for intubation and the rate of ventilation induced lung injuries; this RCT however is the only study addressing this question, with very small sample size which makes definitive conclusions difficult to be drawn, in addition there is still knowledge gaps with the respect of the following: Safety and consistent efficacy about the application of Heliox in premature infants with respiratory distress syndrome (RDS), in addition to the best time of initiation and best treatment duration? Is there a time frame beyond which no benefit can be discerned? What is the best method of mixing with oxygen (Heliox 70:30) versus (Heliox 80:20), the applicability of this therapy to extreme premature infants <28 week of gestational age is also not clear.

This is the only randomized pilot study that tested the combined role of Heliox with CPAP to reduce the need for intubation or mechanical ventilation, other trials have focused on ventilated infants, one RCT conducted by Elleau et al.,[1] in the pre surfactant era, showed reduction in ventilation days, death and BPD when heliox used with ventilation in preterm infants with RDS. A recent but small study by Migliori et al.[2] proved that heliox reduces the resistive work of breathing and ventilation days while improving gas exchange in mechanically ventilated preterm infants.

In summary, with the above mentioned limitation and until further randomized controlled data are available, treatment with such a costly therapy cannot be recommended.

Abstracted from
Colnaghi M, Pierro M, Migliori C, Ciralli F, Matassa PG, Vendettuoli V, et al. Nasal Continuous Positive Airway Pressure with Heliox in Preterm Infants with Respiratory Distress Syndrome. Pediatrics 2012;129:2 e333-e338.

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