Research Media Watch:

Nonintubated Surfactant Application vs Conventional Therapy in Extremely Preterm Infants A Randomized Clinical Trial

Continuous positive airway pressure (CPAP) as a first-line respiratory intervention in extremely low-gestational-age (GA) neonates who have respiratory distress syndrome has been shown to be at least as efficient as intubation, surfactant treatment, and mechanical ventilation. CPAP failure, defined as the need for mechanical ventilation, should be avoided because it is associated with increased mortality and morbidity compared with CPAP success.

The Nonintubated Surfactant Application (NINSAPP) trial was a multicenter, randomized, clinical parallel-group study conducted at 13 level III neonatal intensive care units in Germany between April 15, 2009, and June 21, 201. The study was performed in accordance with Good Clinical Practice guidelines 2

Infants with GA between 23 weeks 0 days and 26 weeks 6 days were eligible. Inclusion criteria were spontaneous breathing, age 10 to 120 minutes, and signs of respiratory distress (fraction of inspired oxygen [FiO2] >0.3 for saturation of peripheral oxygen [SpO2] >83%, and/or Silverman score ≥5); written informed consent had to be given by legal guardians prior to birth or immediately thereafter, but in any case before randomization. Infants were excluded if they had a prenatally diagnosed severe underlying disease, had primary cardiopulmonary failure, or were enrolled in any other interventional trial.

Participants included 211 of 558 eligible (37.8%) spontaneously breathing preterm infants born between 23.0 and 26.8 weeks' gestational age with signs of respiratory distress syndrome. In an intention-to-treat design, infants were randomly assigned to receive surfactant either via a thin endotracheal catheter during CPAP-assisted spontaneous breathing (intervention group) or after conventional endotracheal intubation during mechanical ventilation (control group). Analysis was conducted from September 6, 2012, to June 20, 2013.

Main Outcomes and Measures Survival without BPD at 36 weeks' gestational age. Of 211 infants who were randomized, 104 were randomized to the control group and 107 to the LISA group. Of the infants who received LISA, 72 (67.3%) survived without BPD compared with 61 (58.7%) of those in the control group. The reduction in absolute risk was 8.6% (95% CI, −5.0% to 21.9%; P = .20). Intervention group infants were less frequently intubated (80 infants [74.8%] vs 103 [99.0%]; P < .001) and required fewer days of mechanical ventilation. Significant reductions were seen in pneumothorax (5 of 105 intervention group infants [4.8%] vs 13 of 103 12.6%]; P = .04) and severe intraventricular hemorrhage (11 infants [10.3%] vs 23 [22.1%]; P = .02), and the combined survival without severe adverse events was increased in the intervention group (54 infants [50.5%] vs 37 [35.6%]; P = .02; absolute risk reduction, 14.9; 95% CI, 1.4 to 28.2).

LISA did not increase survival without BPD but was associated with increased survival without major complications. Because major complications are related to lifelong disabilities, LISA may be a promising therapy for extremely preterm infants.

Source : JAMA Pediatr. 2015;169(8):723-730

Comments : LISA was not superior concerning

the primary end point of the study, but it was associated with benefits in important secondary outcomes that are closely related to lifelong disabilities. LISA is a promising new therapy for extremely preterm infants with respiratory distress synsdrome, but it certainly deserves further investigation.

Cerebral Palsy after Neonatal Encephalopathy: How Much Is Preventable?

Using the Canadian Cerebral Palsy Registry (CCPR), study aimed to investigate term-born children with later CP after moderate or severe NE. The objectives were: (1) to determine the expected proportion of term CP after NE that could theoretically be prevented by hypothermia; and (2) to elucidate the perinatal factors associated with CP after NE in those who do not meet the clinical criteria required to qualify for hypothermia.

The CCPR captures cases of CP identified through both pediatric rehabilitation centers and university hospitals at which provincial pediatric neurology and developmental pediatric services are located, from the birth year of 1999 until 2011. The registry covers most of Quebec, the greater Toronto area of Ontario, and the entire provinces of British Columbia, Alberta, Nova Scotia, and Newfoundland, and includes more than one-half (approximately 18 million individuals) of the Canadian population. These data are supplemented by a standardized parental interview and physical examination of the child by a pediatric neurologist, developmental pediatrician, or child physiatrist.

To be enrolled in the CCPR, a child must be at least 2 years of age and meet current diagnostic consensus criteria for CP, which include a clinical diagnosis of a nonprogressive motor impairment resulting from a presumably early insult to the

developing brain.The diagnosis is confirmed whenever possible at 5 years of age, and the children without CP were removed from the registry. Patients within the CCPR included for analysis in this study: (1) were born at <36 weeks; (2) had a birth weight of <1800 g; and (3) fulfilled criteria for moderate or severe NE during the first week of life. We then categorized the neonates according to the

presence or absence of currently used clinical criteria required to qualify for hypothermia ("cooling criteria"). Criteria for NE were derived from the Sarnat score.

Among the 543 term-born children with CP, 155 (29%) had moderate or severe NE. Sixty-four of 155 (41%) met cooling criteria and 91 of 155 (59%) did not. Shoulder dystocia was more common in those who did not meet cooling criteria (OR 8.8; 95% CI 1.1-71.4). Low birth weights (20% of all singletons), small placentas (42%), and chorioamnionitis (13%) were common in both groups

The majority of children with CP after NE did not meet cooling criteria. An estimated 5.1% (95% CI 2.4%-6.9%) of term CP after NE may be theoretically prevented with hypothermia. Considering shoulder dystocia as an additional criterion may help recognize more neonates who could potentially benefit from cooling. In all cases, a better understanding of the antenatal processes underlying NE is essential in reducing the burden of CP.

Source: J Pediatr2015;167:58-63

Comments : estimate of the proportion of term CP after NE that could be prevented by hypothermia should encourage further research on the antenatal processes underlying NE to develop other preventative strategies to reduce the burden of CP.

Neurodevelopmental outcomes following late and moderate prematurity: a population-based cohort study

There is a paucity of data relating to neurodevelopmental outcomes in infants born late and moderately preterm (LMPT; 32+0–36+6 weeks). This study present the results of a prospective, population based study of 2-year outcomes following LMPT birth.

1130 LMPT and 1255 term-born children were recruited at birth. At 2 years corrected age, parents completed a questionnaire to assess neurosensory (vision,

hearing, motor) impairments and the Parent Report of Children's Abilities-Revised to identify cognitive impairment. Relative risks for adverse outcomes were adjusted for sex, socio-economic status and small for gestational age, and weighted to account for oversampling of term-born multiples. Risk factors for cognitive

impairment were explored using multivariable analyses

Parents of 638 (57%) LMPT infants and 765 (62%) controls completed questionnaires. Among LMPT infants, 1.6% had neurosensory impairment compared with 0.3% of controls (RR 4.89, 95% CI 1.07 to 22.25). Cognitive impairments were the most common adverse outcome: LMPT 6.3%; controls 2.4% (RR 2.09, 95% CI 1.19 to 3.64). LMPT infants were at twice the risk for neurodevelopmental disability (RR 2.19, 95% CI 1.27 to 3.75). Independent risk factors for cognitive impairment in LMPT infants were male sex, socioeconomic

disadvantage, non-white ethnicity, preeclampsia and not receiving breast milk at discharge

Compared with term-born peers, LMPT infants are at double the risk for neuro-developmental disability at 2 years of age, with the majority of impairments

observed in the cognitive domain. Male sex, socio-economic disadvantage and preeclampsia are independent predictors of low cognitive scores following LMPT birth.

Source : Arch Dis Child Fetal Neonatal Ed 2015;100: F301–F308.

Comments : Prematurity remains one of the major causes of infant mortality and lifelong morbidity worldwide. Study had demonstrated that babies born at 32–36 weeks of gestation are at double the risk for neurodevelopmental disability at 2 years of age, with the vast majority of identified impairments in the cognitive domain