



September 16th, 2021 11:00 - 13:00

PARALLEL SESSION 14 - LUNG 3

ID 157. Dose reduction of antenatal betamethasone in women at risk of very preterm delivery

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Objective: To demonstrate the noninferiority of half compared to full antenatal betamethasone dose regimen to prevent severe respiratory distress syndrome in preterm neonates.

Methods: In this multicenter double-blinded, randomized controlled, noninferiority trial, women with a singleton fetus at risk of preterm delivery before 32 gestational weeks, already treated with the first 11.4 mg betamethasone injection were randomly assigned to receive 24 hours later either placebo (half dose group) or the second 11.4 mg betamethasone injection (full dose group). The primary outcome was severe respiratory distress syndrome, defined as the need for exogenous intra-tracheal surfactant within 48 hours of life. The noninferiority was tested with a margin of 4 percentage points.

Results: Among the 3244 women enrolled between January 2017 and October 2019 in 37 French level-3 perinatal centers, 46 women retrieved consent, 29 had stillborn fetuses and 17 were lost to follow-up, leaving 3150 newborns for analysis. For the intention-to-treat (ITT) analysis, the primary outcome occurred in 317/1574 (20.1%) neonates in the half dose group and in 279/1576 (17.7%) neonates in the full dose group. The between-group difference was 2.4 percentage points (upper boundary of one side 97.5% Confidence Interval 5.4%), which was above the noninferiority margin. Per protocol analysis for the primary outcome performed in 2992 neonates was consistent with ITT analysis. Rates of neonatal death, intraventricular hemorrhage grade 3-4, necrotizing enterocolitis stage ≥ 2 , retinopathy of prematurity requiring anti-VEGF or laser, and neonatal survival without any of these complications did not differ between groups.

Conclusion: Half dose did not show noninferiority to full antenatal betamethasone dose regimen to prevent severe respiratory distress syndrome in preterm neonates. However, neonatal survival and complications did not differ between the two groups (ClinicalTrials.gov [NCT02897076](https://clinicaltrials.gov/ct2/show/study/NCT02897076))

Non declared



ID 533. UTILISING POPULATION DATA TO DEVELOP SAFER PERSONALISED PRETERM INFANT CLINICAL TREATMENTS AND TRIALS

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Background

Preterm birth below 28 weeks gestation is associated with significant mortality and morbidity. Reducing these through randomised controlled trials (RCTs) often requires large numbers of infants recruited over many years. Identifying more accurately those at greatest risk of death or serious morbidity would allow better RCTs targeting those most likely to benefit and reducing potential harm in those least likely to. We aimed to estimate the number of infants excluded from the recent early low-dose hydrocortisone RCT (PREMILOC, Baud, Lancet 2016) who died or developed bronchopulmonary dysplasia (BPD); and those included with minimal likely benefit.

Methods

Routinely collected data from infants <32 weeks gestation admitted to 185 neonatal units in England and Wales from 2010 to 2017 were extracted. The combined prevalence of mortality and BPD by gestation, birthweight and gender was determined. We estimated the number of infants 28-31 weeks gestation who died or developed BPD and those <28 weeks gestation least likely to benefit. We also compared respiratory support requirement on neonatal discharge versus 36 weeks corrected gestational age (CGA).

Results

62,864 infants were analysed. The combined prevalence of death/respiratory support at 36 weeks CGA and on discharge respectively varies with gestation, birthweight and gender (Figure). For example, risk of death/BPD for a small-for-gestational-age 28-week infant changes from 75% to 46% (male) or 61% to 35% (female) for death/respiratory support at discharge.

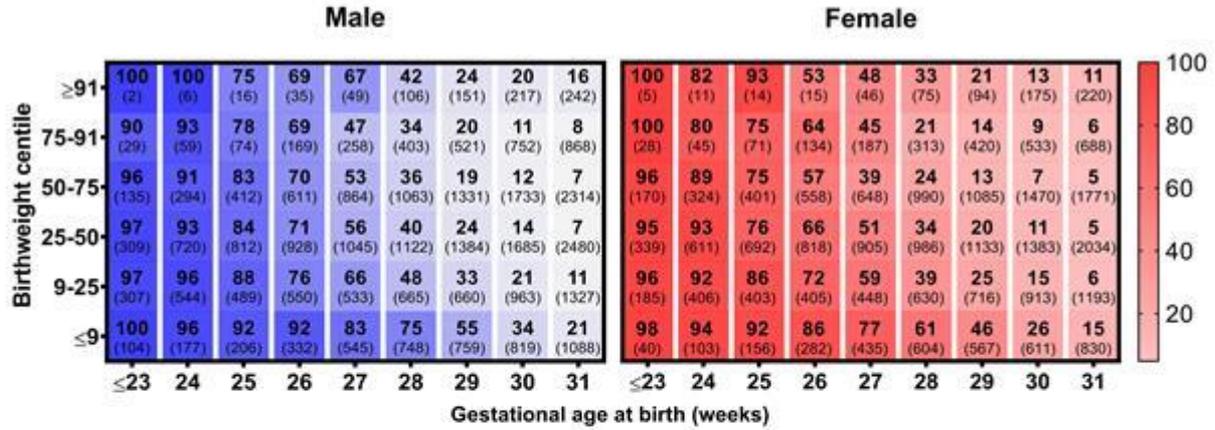
Of the 42,873 infants \geq 28 weeks gestation, 8,368 (19.5%) died or developed BPD and may have benefited from early hydrocortisone. Between 36 weeks and discharge, 283 (1.8%) of the surviving 15,652 infants <28 weeks died, and 4,877 (31.2%) came off all respiratory support.

Conclusion

This study provides novel, contemporary data on mortality and respiratory outcomes across a national population of high-risk infants including at neonatal discharge. Using prophylactic hydrocortisone as an example, we show that about a fifth of very preterm infants could potentially benefit from treatment and nearly a third of extremely preterm infants would get little or no benefit. Utilising a few individual characteristics, it is possible to risk-stratify individual patients for particular treatments or inclusion in RCTs, providing personalised medicine and research.



(A) BPD and death



(B) Respiratory support requirement at discharge and death

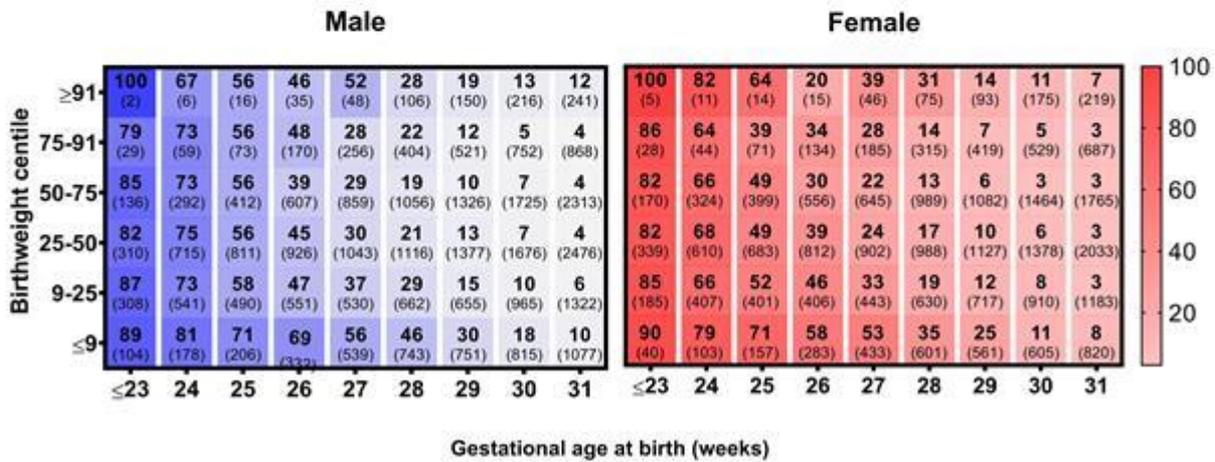


Figure: Heat map depicting the combined (A) BPD and death (n=62,334); (B) post-discharge respiratory support requirement and death (n=62,113) prevalence (%(n)) of very preterm infants by gestation, birthweight and gender.

None declared



ID 203. PREMEDICATION BEFORE LESS INVASIVE SURFACTANT ADMINISTRATION: A SYSTEMATIC REVIEW

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Background

Surfactant therapy is the cornerstone of the management of respiratory distress syndrome. Alternatives to endotracheal intubation for surfactant administration currently include “less invasive surfactant administration”. Its effectiveness was demonstrated by meta-analyses and guidelines now recommend it as the optimal method of surfactant administration in spontaneously breathing babies. While it still requires a direct laryngoscopy, the issue of sedation and analgesia during the procedure remains controversial as 52% of European neonatologists do not use any.

Methods

Medline via Ovid, Embase, Scopus and Cochrane Library of Trials were searched for studies of LISA after sedation without any filters or limits independently by 2 reviewers. Risk of bias (RoB) and quality assessment were evaluated using the RoB2 for RCT or the Newcastle Ottawa Scales (NOS) for cohort studies.

Results

We included eight studies: one RCT, two prospective, three retrospective and two RCT comparing INSURE and LISA after sedation (LISA arms assessed as prospective cohorts), for a total of 908 newborns. Failure, defined as need for intubation or for a second dose of surfactant was no different between sedated and unsedated groups. Infant pain was significantly reduced, with more infants evaluated as comfortable. LISA with sedations led to higher occurrences of intraprocedural desaturation and need for positive pressure ventilation, but need for mechanical ventilation within 24 or 72 hours of life was not significantly different. Clinical tolerance and complications (hypotension, mortality, air leaks, BPD...) were similar. Procedural conditions were evaluated as good or excellent in 83% after sedation.

Discussion and conclusion

This systematic review highlighted that analgesia or sedative drugs increase infant comfort and allow good procedural conditions, with a limited impact on the clinical evolution. Many questions remain about the optimal drug and dosage, given the need to maintain spontaneous breathing and to act only for the shortest duration. Despite limited data, we found no reason to avoid sedative drugs for LISA, given how deleterious awake laryngoscopy can be. Large RCT's should be initiated in units currently not sedating infants prior to LISA.

Other

Prospero registration: CRD42020205365.

No source of funding.

None declared



ID 359. LUNG ULTRASOUND SCORE EVOLUTION IN PREMATURE NEWBORNS WITHOUT BRONCHOPULMONARY DYSPLASIA: A MULTICENTER STUDY

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BACKGROUND: Lung ultrasound score (LUS) has proven as a valuable tool to predict bronchopulmonary dysplasia (BPD) in premature newborns, but the evolution of LUS in infants without moderate-severe BPD (msBPD) has not been studied.

METHODS: We measured LUS in premature newborns born before 32 weeks, at birth, at three days of life (DOL), at one week, and then weekly until 36 weeks' postmenstrual age (PMA). We excluded those with msBPD, and created four groups according to gestational age (GA) at birth: group 1 (23-25 weeks), group 2 (26-27 weeks), group 3 (28-29 weeks) and group 4 (30-32 weeks). To compare LUS between groups in each time evaluated, we calculated repeated measures ANOVA. In order to estimate LUS evolution in each group, we used linear multilevel mixed-effects regression to adjust for repeated measurements.

RESULTS: 256 patients were included: 22 patients (9%) in group 1, 49 (19%) in group 2, 69 (27%) in group 3, and 116 (45%) in group 4. In group 1, LUS were different at 3 DOL, 1, 2, 3 and 4 weeks, versus 11 weeks ($p < 0.02$), and at the same moments, and five weeks ($p < 0.04$), compared to 12 weeks; in group 2, the differences were between birth compared to 11 ($p = 0.018$) and 12 weeks ($p = 0.034$); in group 3, we got significant differences at birth compared to 8 weeks ($p = 0.006$); and in group 4, at birth compared to 3 DOL, 1, 2, 3, 4, 5 and 6 weeks ($p < 0.04$). Model regression was estimated with a spline at one week, and showed statistical significance for the interaction between GA and time ($p < 0.001$), with an increase and a steady phase in the first weeks only in groups 1 and 2, as well as a decrease afterwards until the end of follow up. In the other groups, there was a decrease in LUS from birth until the end of the study, although more immature infants showed higher values of LUS at birth (see figure 1).

CONCLUSION: LUS in premature newborns born before 32 weeks without msBPD, decrease from birth until 36 weeks' PMA, and the evolution is different according to GA at birth.

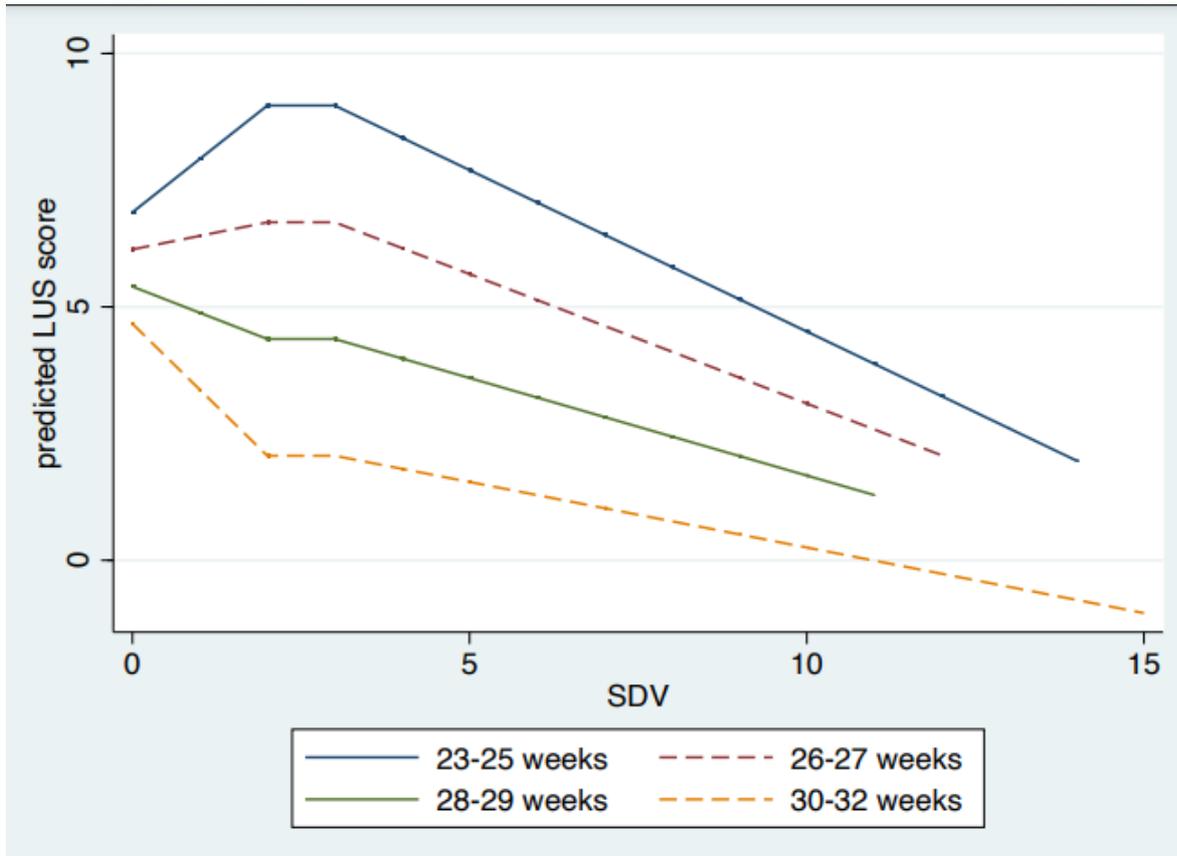


Figure 1. Predicted LUS evolution in premature infants without moderate-severe BPD according to gestational age at birth, by lineal multilevel mixed-effects regression. None declared.