

September 20th, 2023 08:30 - 9:00

## POSTER WALK – LUNG 2

### ID 701. Less invasive surfactant administration (LISA) in preterm infants on different modes of non-invasive respiratory support

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#### Background

A common complication of prematurity is respiratory distress syndrome, caused by surfactant deficiency. The LISA (less invasive surfactant administration) method delivers surfactant to the lungs via a thin catheter as the infant spontaneously breathes whilst being supported by non-invasive respiratory support.

We describe the experience of two tertiary neonatal intensive care units (NICUs) in the UK who both provide LISA to very preterm infants, but use different non-invasive respiratory support.

#### Methods

We conducted a retrospective study on the provision of LISA to preterm infants in John Radcliffe Hospital (JRH), Oxford and Imperial College Healthcare NHS Trust (ICHT), London. Data were collected from medical records of preterm infants born <36 weeks' gestation who received LISA between 1st October 2019 – 1st September 2020 at JRH and from 1st October 2021 to 15th January 2023 at ICHT.

Infants were supported by nasal high flow therapy (nHFT) at JRH and predominantly nasal continuous positive airway pressure (nCPAP) at ICHT.



LISA was indicated when  $FiO_2$  requirement was  $> 0.30$ . Surfactant (Curosurf, Chiesi Pharmaceuticals) was administered at a standard dose of 200 mg/kg. Procedure was considered successful if  $FiO_2$  decreased  $< 0.30$ . Intubation rate was assessed in the first 48 hours after LISA procedure. Premedication was given as per clinician's discretion. Infants from the 2 centres were compared as two groups. (SPSS 27, software USA).

## Results

Forty-six infants received surfactant with LISA technique at JRH and 84 infants at ICHT.

There were no differences in the mean GA and birthweight between centres.

LISA was given later at ICH (14.8 hours at ICH vs 6.2 hours at JRH,  $p < 0.001$ ). There were significant differences in the  $FiO_2$  prior to and post procedure, but not in the  $FiO_2$  difference achieved. There was no difference in the proportion of infants intubated at 48 hours and those that needed repeat LISA. There was no difference in the number of attempts during the procedure or the use of premedication.

## Conclusion

Our findings suggest that LISA procedure is equally successful in infants supported with nHFT or nCPAP. The optimal timing of LISA and use of premedication needs to be further investigated.

Table 1, Differences in the main characteristics, respiratory support and respiratory outcomes between the two centres (JRH and ICHT), results presented as mean (SD) or proportions (%)

	Oxford N=46	Imperial College N=84	Mean diff (95% CI)	p value
GA (weeks)	29.9 (3.4)	30.2(3.3)	-0.33 (-1.5, 0.87)	0.59
BTWT (g)	1371 (718)	1423 (711)	-51 (-310, -207)	0.69
Age when LISA given (hours)	6.2 (4.6)	14.8 (12.7)	-8.6 (-12.6, -4.6)	<0.001
Respiratory support at the time of LISA	nHFT 46/46	nCPAP 78/84 BiPAP 4/84 Facial CPAP 2/84		<0.001
FIO2 prior LISA	0.45 (0.1)	0.54 (0.2)	-0.09 (-0.16,-0.02)	0.02
FIO2 post LISA	0.29 (0.2)	0.35 (0.2)	-0.06 (-0.12,0.001)	0.05
FIO2 difference achieved	0.16 (0.1)	0.19 (0.1)	-0.04 (-0.1, 0.02)	0.2
Intubated at 48 hours (%)	5/46 (11%)	16/84 (19%)	8%	0.32
Repeat LISA (%)	4/46 (9%)	8/84 (10%)	1%	0.88
No of attempts Mean (SD)	1 (0.5)	1 (0.3)		Overall 0.1
Pre-Medication used (%)	20/46 (44%)	40/84 (48%)	4 %	0.72
Fentanyl used (%)	14/46 (30%)	39/84 (46%)	16%	0.09

## ID 999. Midazolam as premedication for Less Invasive Surfactant Administration: a prospective audit

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### Background

Less invasive surfactant administration (LISA) to treat respiratory distress syndrome reduces mechanical ventilation and risk of bronchopulmonary dysplasia in preterm infants. Premedication can relieve procedural pain associated with laryngoscopy, thereby facilitating LISA, but may have side effects. The optimal premedication for LISA remains unknown. We reviewed our centre's use of midazolam as preferred LISA premedication drug.

### Methods

Prospective audit of neonates who routinely received midazolam for LISA within our tertiary-level NICU between July 2019 and December 2022. Under our Unit's guideline neonates received midazolam 50–100 µg/kg intravenously 2–5 minutes prior to laryngoscopy. Atropine 20 mcg/kg was optional. Surfactant (Curosurf) 200 mg/kg was administered via a dedicated LISA catheter (Surfcath or Vygon). Data regarding each LISA procedure were recorded contemporaneously by the operator on a bespoke audit proforma and in the medical records. We reviewed rates of procedural success (defined as successful LISA catheterisation and surfactant administration), physiological stability, and side effects during the LISA procedures, and numbers needing endotracheal intubation within 24 hours.





## Results

61 neonates received midazolam premedication for LISA in the study period: n=36 received 50 µg/kg; n=24 received 100 µg/kg in total; n=1 received 150 mcg/kg in total. Median gestational age was 29.4 weeks (IQR: 28.0–33.6, range 24.2–39.0 weeks). Median postnatal age at LISA was 6 (IQR: 3–10.5) hours. Median FiO<sub>2</sub> immediately preceding LISA was 0.42 (IQR: 0.36–0.50) and 1-hour post LISA was 0.30 (IQR: 0.26–0.40). For 60/61 (98%) the procedure was deemed successful. In the sole case where it was considered unsuccessful, a 34.6 week gestation baby, 100mcg/kg provided inadequate sedation and LISA was abandoned after two attempts. Only 2 babies required endotracheal intubation and ventilation within 24 hours of first LISA dose. Rates of recorded side effects during LISA were: surfactant reflux n=8 (13%); bradycardia (heart rate <100/min) n=11 (18%); apnoea n=17 (28%); oxygen desaturation (SaO<sub>2</sub> <80%) n=31 (51%).

## Conclusion

In our experience routine Midazolam premedication for LISA was safe, well tolerated, and was associated with a high rate of procedural success. Midazolam may be a worthy candidate for formal study in future comparative trials of LISA premedication drugs, and against non-pharmacological LISA administration.

None declared

## ID141. A national survey on use of less invasive surfactant administration in Uzbekistan

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A national survey on use of less invasive surfactant administration in Uzbekistan

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### ABSTRACT

**Background.** The aim of the study was to assess the rate of utilization, policy of premedication, technique, equipment, experience on safety and efficacy for less invasive surfactant administration or minimally invasive surfactant therapy (LISA/MIST) use in Uzbekistan.

**Methods.** An online survey was designed and distributed via Google Forms tool to 107 neonatologists from 15 units through the mailing list of the Uzbekistan Neonatal Society. Participants were asked to answer the survey for their own neonatal intensive care unit (NICU).

**Results.** LISA/MIST use rate was 81.6% among 15 NICUs which responded (response rate was 80.2%). LISA was used regularly in all of the units (26.4%), occasionally in 35 (40.2%), rarely in 12 (13.8%), and only for clinical trials in 1 (1.1%). LISA/MIST has been never applied in 16 units (18.4%).



Conclusions. LISA/MIST is more widely used in Uzbekistan in comparison with several regions in Europe and rarely in the USA. Future studies are expected to further clarify some questions about LISA/MIST procedure, especially on its efficacy and safety.

Key words: less invasive surfactant administration, minimally invasive surfactant therapy, respiratory distress syndrome, surfactant, survey.

None declared

## ID 156. A MULTICENTER, RANDOMIZED TRIAL OF SURFACTANT THERAPY GUIDED BY MEASUREMENT OF SURFACTANT IN GASTRIC ASPIRATE: A STUDY PROTOCOL

### FAST TRIAL 2: FAST ASSESSMENT OF SURFACTANT DEFICIENCY IN PRETERM INFANTS TO SPEED UP TREATMENT

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#### Introduction

Respiratory Distress Syndrome (RDS) in preterm infants is caused by surfactant deficiency. Treatment with surfactant reduces the rate of mortality and bronchopulmonary dysplasia (BPD). Early treatment improves prognosis, but selection of whom and when to treat remains unknown. Presently treatment is based on clinical criteria such as need for supplemental oxygen and supported only by observational studies. Recently we developed a point-of-care test based on the lecithin/sphingomyelin ratio in gastric aspirate sampled immediately at birth. This



L/S–test can predict the need for surfactant treatment within 10 minutes and before RDS symptoms develop with sensitivity and specificity of approximately 90% and 80%, respectively. This study aims to compare survival without moderate to severe BPD in preterm infants when treated with surfactant guided by point of care measure of the L/S–ratio versus routine treatment.

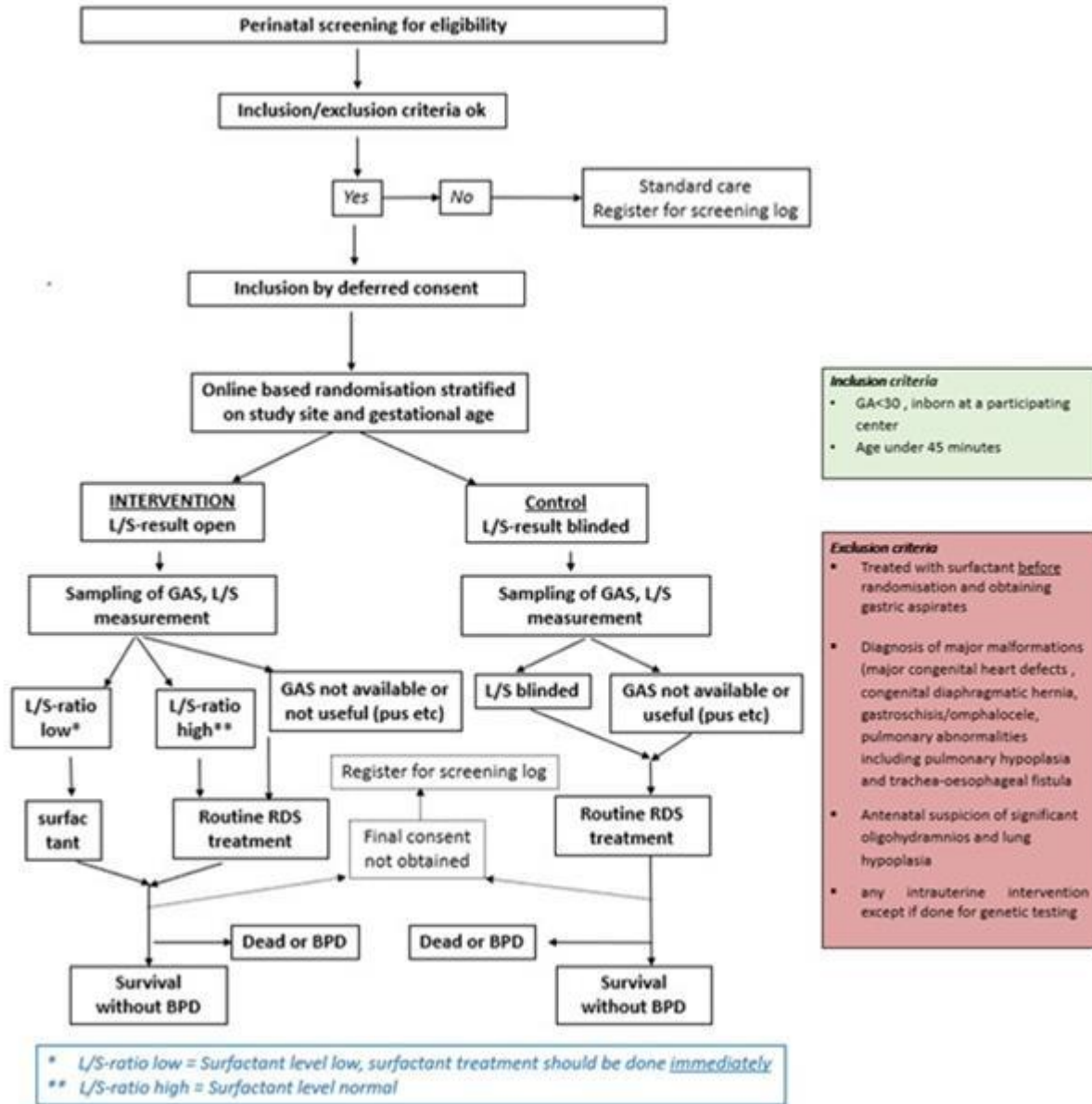
### Methods and analysis

The study will be conducted at 4 Danish university hospitals with in–house neonatal intensive care units as an open label randomized controlled trial. 372 infants born at less than 30 weeks’ gestation will be randomized and allocated in a 1:1 ratio at birth before sampling a gastric aspirate. All infants will have a gastric aspirate sampled and the L/S–ratio analyzed within 45 minutes from birth. Infants in the intervention group will receive surfactant treatment immediately a L/S–test is positive for surfactant deficiency. The staff remains blinded to the result of the L/S test results in the control group, and control infants will be treated based on routine criteria (Figure 1). In both groups surfactant can be administered via thin catheter or an endotracheal tube. The primary outcome is “survival without moderate to severe BPD”. Data will be analyzed according to intention–to–treat.

Before the study starts recruitment the diagnostic accuracy of the point of care L/S test will be revalidated in a new cohort of preterm infants. The re–validation study results will be presented if available at the time of JENS 2023.

### Ethics

This is the first study in Denmark to receive ethical approval by the Danish Committee on Biomedical Research Ethics to recruit newborn preterm infants immediately at delivery by deferred consent.



Henrik Verder, Peter Schousboe are consultants and shareholders in Sime Diagnostics Ltd who developed the L/S POC Device. They were involved in the trial design and protocol development.



## ID 510. Prediction of need for surfactant treatment using gastric aspirates at birth – clinical validation of a new a point-of-care method

### Fast Assessment of surfactant deficiency in preterm infants to Speed up Treatment (FAST Trial 2 Validation)

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#### Background

Respiratory Distress Syndrome (RDS) in preterm infants is caused by surfactant deficiency. Treatment with surfactant reduces mortality and the risk of bronchopulmonary dysplasia (BPD). At present, treatment is guided by clinical criteria such as the level of supplemental oxygen needed. This is supported only by observational studies.

The lecithin/sphingomyelin ratio (L/S–ratio) in gastric aspirates reflects lung maturity. We have developed a fast method using mid–infrared spectroscopy to measure the L/S–ratio in gastric aspirates sampled immediately at birth and showed the ability of the L/S–test to predict the need for surfactant enabling very early targeted treatment. The L/S–test has been continuously improved and is now available as a fully automated point–of–care (POC) test. This study aims to assess the diagnostic accuracy of the POC L/S–test and to define the optimal cut–off L/S–ratio for surfactant treatment.

#### Methods and analysis

Fresh gastric aspirates will be sampled immediately at birth from n=75 preterm infants born before 30 weeks gestational age. The L/S–ratio will be measured by the POC L/S–test and compared to relevant clinical respiratory data including treatment with surfactant, timing of the treatment and fraction of inspired oxygen at the time of treatment.

The primary outcome is the optimal cut–off L/S ratio to predict subsequent treatment with surfactant. This will be analysed with receiver operating characteristics to calculate sensitivity, specificity and the likelihood–ratio.

The researchers analysing the L/S–ratio will be blinded to clinical data and clinical staff will be blinded to the result of the L/S ratio.

#### Results

The study is expected to complete recruitment late July 2023, and preliminary results will be available for jENS 2023.

#### Conclusion

The POC L/S test is expected to show a high diagnostic accuracy and will be used to guide surfactant treatment in a subsequent randomized clinical trial aiming to





determine if early targeted surfactant treatment guided by the L/S test can improve the rate of survival without BPD.

Henrik Verder, Peter Schousboe are consultants and shareholders in Sime Diagnostics Ltd who developed the L/S POC Device. They were involved in the trial design and protocol development.



## ID 100. The NON-pharmacological Approach to Less Invasive Surfactant Administration trial (NONA-LISA): Protocol for a randomised controlled trial

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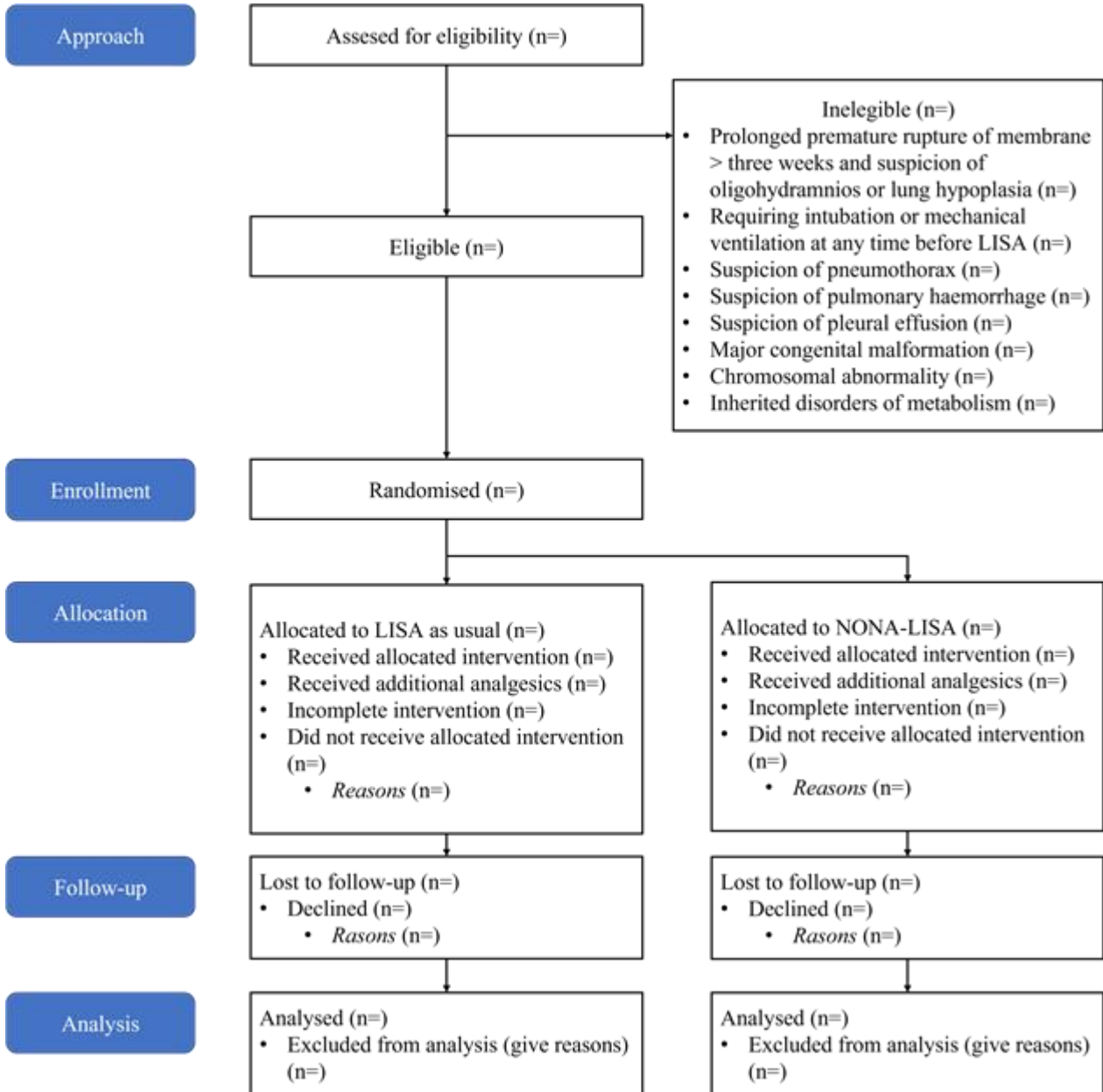
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Background and aims: Less Invasive Surfactant Administration (LISA) is a technique to apply surfactant in the lungs via a tracheal catheter during spontaneous breathing. However, using pre-procedure analgesia with the risk of apnoea may complicate the procedure or reduce the effect of LISA. This randomised controlled trial aims to compare LISA after administration of either fentanyl or saline.

**Methods:** This multicentre, blinded, randomised controlled trial will include 324 infants born before 29 completed gestational weeks, meeting the criteria for surfactant treatment by LISA. Infants will be randomised to LISA after administration of fentanyl 0.5–1 mcg/kg intravenously (control group) or LISA after administration of isotonic saline solution intravenously (intervention group). Both groups will receive the unit's standard level of care before and after the procedure. Both groups will receive an identical, protocolised, non-pharmacological approach, including light and noise reduction, sucrose, swaddling/wrapping, and tucking. Additional analgesics will be provided at the discretion of the clinician. The primary outcome is the need for endotracheal intubation and mechanical ventilation for at least 30 minutes (cumulated) within 24 hours after the procedure. Secondary outcomes include the number of attempts, duration of the procedure, COMFORTneo score during the procedure, and mortality and bronchopulmonary dysplasia at 36 weeks.

**Results:** This is a protocol for the NONA–LISA randomised controlled trial. We expect to start inclusion during the summer of 2023. Preliminary results will not be ready for presentation during jENS 2023.

**Conclusions:** This randomised controlled trial addresses an essential aspect of surfactant treatment by LISA; the use of analgesic premedication. This trial will improve the evidence supporting preterm infants during the LISA procedure. The trial may point towards supportive measures to reduce morbidity and potentially result in new clinical recommendations.



None declared.



## ID 503. POINT-OF-CARE MEASUREMENT OF LUNG SURFACTANT AT BIRTH: PART OF FAST TRIAL 2

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Background. Early treatment of respiratory distress syndrome (RDS) with nasal continuous positive airway pressure and early surfactant treatment decreases neonatal mortality and incidence of bronchopulmonary dysplasia (BPD). Measuring and treating according to lung surfactant content immediately after birth is likely to optimize treatment and improve outcome.

Recently, we developed a lab-based method to measure lung surfactant content in gastric aspirate (GAS) from premature infants. This method was able to predict RDS with a high sensitivity and specificity, as described in *Acta Paediatr* 2020;109:280–4 and 285–90. The method has now been developed into a point-of-care device able to measure surfactant content in premature infants 10–15 min after birth.

The aim of this study is to describe the technical process from a lab-based method to a fully automated CE marked point-of-care device.



**Methods.** Surfactant was measured by mid-Infrared (MIR) spectroscopy as the lecithin dipalmitoylphosphatidylcholine (DPPC), the most surface-active lung molecule, and as lecithin-sphingomyelin ratio (L/S). Each measurement is performed with 100  $\mu$ L of GAS injected into a custom disposable via a standard feeding syringe. If necessary, lower volumes can be measured. The algorithms developed earlier by analysing MIR-spectra of DPPC and sphingomyelin are now trained with 70 GAS-samples by the point-of-care device. Each sample is applied onto a 13 mm CaF<sub>2</sub> disk, dried and then measured by MIR. The material is extracted with dichlormethane-methanol and measured as reference values by mass spectroscopy.

**Results.** Repeted concentrations of DPPC and sphingomyelin are very stable estimated by the new algorithms and the point-of-care device.

**Conclusions.** Lung surfactant can now be measured in GAS 10-15 min after birth by a point-of-care method, enabling early targeted surfactant treatment.

The point-of-care device is currently undergoing clinical validation to define a cut-off value and diagnostic accuracy. Preliminary results will be present at jENS 2023. Furthermore, a randomised study is planned to compare the BPD incidence in 372 very premature infants treated at birth with targeted surfactant predicted with the point-of-care device vs. treatment when FiO<sub>2</sub> is > 0.30 (FAST Trial 2).

HV, NS, PS and PV are consultants and shareholders of SIME Diagnostics, and Holbaek Hospital and SIME has entered into a public-private partnership. The other authors have

none to declare

## ID 455. USAGE OF SURFACTAN AND EVALUATION OF LUNG PROBLEMS IN LATE PRETERM INFANTS

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**Aim:** Respiratory distress syndrome in premature newborns can lead to serious morbidities or even death. Our study aimed to evaluate surfactant delivery frequency and surfactant indications, as well as lung problems in late-preterm infants.

**Materials and Methods:** This retrospective and cross-sectional study was carried out by HSU Izmir Dr. Behçet Uz Pediatric Diseases and Surgery Research and Training Hospital. Infants who were born late preterm between January 2016 and December 2021 and were hospitalized in the NICU of our hospital due to respiratory distress in the first 24 hours. Lung problems and surfactant requirement of these infants were evaluated. On both a short-term and long-term prognosis level, the frequency of surfactant dosages, their indications, and their effects were examined. As the control group, patients who were admitted to the NICU in the same period due to respiratory distress with similar indications but did not receive surfactant were considered.

**Results:** 211 late preterm infants were included in the study within the specified period. It was observed that surfactant was not given to 105 babies and surfactant was given to 106 babies. The mean gestational week of the infants included in the study was 35 (34/36) weeks and the birth weight was 2185 (1780/2590) grams. A significant difference was observed in birth weight between the groups ( $p < 0,001$ ). Invasive ventilation was required in 52.1% of all cases and noninvasive ventilation was



required in 33.6%. Especially in the delivery room, the need for resuscitation and intubation were higher in the group requiring surfactant ( $p=0,001$ ). The most common lung pathology in the surfactant group was RDS. The frequency of PDA, inotropic use and BPD was also higher in those who needed surfactant ( $p<0,001$ ). In the multilogistic regression analysis of our study, AUC was calculated as 0.735 at birth weight  $\leq 1690$  g.

Conclusion: Surfactant deficiency is an important problem in late preterm infants. For this reason, it should not be forgotten that infants born at these gestational weeks are preterm babies and the evaluation of antenatal steroid administration should not be ignored.

Key words: Late preterm, respiratory distress syndrome, surfactant, transient tachypnea of the newborn.

not declared





## ID 941. DELAYED SURFACTANT ADMINISTRATION IN NEONATES 32-36 WEEKS: PROBABLE CAUSE OF PNEUMOTHORAX

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Background. Defining the most appropriate timing of surfactant administration in preterm neonates with respiratory distress syndrome (RDS) has long been the subject of a debate. According to the recent European Consensus guidelines on the management of RDS, the administration of surfactant is recommended when oxygen requirements exceed 30%, in all the preterm neonates. Neonates of 32–36 weeks gestational age (GA) with RDS, despite their relative maturity, have an increased risk of pneumothorax or pneumomediastinum. The aim of the study was to assess whether a delay in surfactant administration to neonates of 32–36 weeks of GA with RDS increased the risk of pneumothorax.

Methods. A total of 271 neonates (32–36 weeks GA), hospitalized in our Neonatal Intensive Care Unit during a 4–year period, were included in the study. Presence of RDS, timing of surfactant administration (<12 hours, >12 hours), development of pneumothorax, and its management were recorded. The timing of surfactant administration was correlated with the presentation of pneumothorax. Spss 25.0 was used for statistical analysis.

Results. Sixty-six (24%) of our study neonates developed RDS, with a pneumothorax occurring in 10 of them (15.2%). A scalp vein placement was required in 6 neonates, while a chest tube drainage system was necessary for the remaining 4. Analysis demonstrated that a delay in surfactant administration significantly increases ( $p < 0.000$ ) the risk of pneumothorax.

Conclusions. Delayed surfactant administration in moderate and late preterm neonates with RDS possibly increases the risk of complications, including pneumothorax.

None declared

## ID 795. Less Invasive Surfactant Administration - a single centre experience

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Doctor Sophie Reynolds<sup>1</sup>

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Background: Less Invasive Surfactant Administration (LISA) introduced to the Trust  
~April 2017 •No specific gestation cut-off •Indicated in all babies with a persistent  
O<sub>2</sub> requirement of >30%

Aim : overview of all patients receiving surfactant from July 2020 to July 2022  
•Comparison of babies receiving surfactant via LISA and those receiving via  
Endotracheal tube (ETTS)

Results: Total patients receiving surfactant by any means: 149 babies •LISA = 93  
•ETTS = 56 •Total babies receiving LISA = 93 •Number requiring 2nd dose of  
surfactant = 14 •Required intubation after LISA = 38 (total) •15/38 <24 hours after  
LISA •23/38 >24 hours after LISA LISA cohort – Outcome based on dose/kg (n=93)  
Outcome Overall survival •91% of babies receiving LISA survived to discharge •72%  
of babies receiving surfactant and ventilated survived to discharge

Discussion (1) •There is experience internationally for use of LISA >15y •Locally  
experience spans 5 years •LISA is safe and long term outcome is reported to be  
better for preterm infant morbidity and mortality •Over the study period of 2 years,  
~150 babies received surfactant, 2/3 of which was via LISA •The earliest gestation  
was 24+1/40 who received LISA which is comparable to the group receiving  
surfactant via ETT. •Weight is NOT a limiting factor, as LISA cohort was received by  
an infant weighing just 465g (compared to ETT surfactant at 525g). •There were no

ethnicity or gender bias between both groups •In the 23, 24 and 25/40 infants more received surfactant via ETT •From 26/40 onwards the majority had LISA •At gestations of 38/40+ LISA was almost exclusively used •LISA was administered by all grades of staff. •Nearly 1/5 of procedures carried out by junior level staff •91% of babies receiving LISA survived to discharge •23% had a final diagnosis of CLD •13% went home on oxygen •77% of babies who were intubated for surfactant survived to discharge •58% had a final diagnosis of CLD •46% were discharged on home oxygen

Conclusion •LISA is safe and long term morbidity and mortality is improved.

None declared





## ID 819. Less Invasive Surfactant Administration (LISA)

Results in applying this method in our NICU (between April 2019-December 2022)

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Background:

Less invasive surfactant administration (LISA) is widely and increasingly used in Europe for the treatment of respiratory distress syndrome. There is a growing body of evidence that LISA-treated infants are at a decreased risk for BPD compared to intubation and mechanical ventilation.

The results of LISA in our NICU over the last 3 years are presented below.

Methods:

We compared the standard procedure of surfactant administration via endotracheal intubation, while the infant was ventilated with a gentler approach called LISA. With LISA technique, surfactant was applied via a thin catheter, while the infant was breathing spontaneously on CPAP.

We have administrated surfactant at 750 infants over the period April 2019–

December 2022.

The infants were further classified in 3 categories according to their gestational age (GA).

Category 1: mature infants, >37 GA

Category 2: late preterm infants, 34+0–36+6 GA

Category 3: preterm infants, <34 GA

We used Curosurf at a dose of 200mg/kg.

Results:

350 (47%) of the infants received surfactant with LISA, while 400 (53%) via endotracheal intubation.

36 (5%) of the infants that received surfactant with LISA needed secondary intubation due to lack of respiratory improvement

181 children of Category 1 (mature infants > 37 GA) received surfactant, 173 (96%) via intubation, while 8 (4%) via LISA

294 children of Category 2 (late preterm infants) received surfactant, 173 (59%) via intubation, while 121 (41%) via LISA

275 children of Category 3 (preterm infants) received surfactant, 54 (20%) via intubation, while 221 (80%) via LISA.

Comments:

Complications: Pneumothorax at 4 mature infants after LISA

The majority of Category 1 has received surfactant via intubation because nCPAP is not preferred as a method of RDS therapy in mature infants at our NICU and that is why LISA was performed less in this group.

Conclusion:

Without doubt, LISA patients showed an immediate improvement of the oxygenation, a shorter duration of any other form of ventilatory support as a lower percentage of intubation and mechanical ventilation in the first 72 hours.

Data on long-term outcome after LISA compared to intubation are rare. Further follow-up is mandatory .

None declared