ID: 70

**TITLE:** DOSE-RESPONSE INVESTIGATION ON PORACTANT ALFA NEBULIZATION TREATMENT DURING NCPAP VENTILATION IN SPONTANEOUSLY-BREATHING SURFACTANT-DEFICIENT NEWBORN PIGLETS

**AUTHORS:** Rey-Santano C1, Mielgo V1, Gomez MA1, Salomone F2, Bianco F2, Ricci F2, Loureiro B3

**AFFILIATIONS:** 1Animal Research Unit, Biocruces Health Research Institute, Barakaldo, Bizkaia, Spain.
2Department of Preclinical Pharmacology, R&D, Chiesi Farmaceutici S.p.A., Parma, Italy;
3NICU, Cruces University Hospital, Barakaldo, Bizkaia, Spain.

**CONTENT:**

The current clinical treatment of neonate with respiratory distress syndrome (RDS) includes endotracheal intubation and rapid intratracheal instillation of exogenous surfactant. Nebulization of surfactant offers an attractive alternative. The aim of this study was to test the nebulization as noninvasive method of administering surfactant, and to determine the optimal dose for the treatment of neonatal RDS.

Thirty-six spontaneously breathing newborn piglets with surfactant-deficiency were assigned to one of six treatment groups (n=6/group): poractant alfa (100, 200, 400 or 600 mg/kg) nebulized via a customized eFlow Neos vibrating-membrane nebulizer system, bolus administration using InSurE technique (200 mg/kg), or no surfactant treatment during nCPAP ventilation (180 min). Pulmonary (gas exchange, lung mechanics), hemodynamic (arterial blood pressure, heart rate) and cerebral effects (carotid blood flow) were evaluated. Lung and brain histological analysis were also performed.

After bronchoalveolar lavages, newborn piglets developed mild respiratory distress syndrome (FiO2:1, pH70 mmHg, PaO2<70 mmHg, Cdyn<0.5 ml/cmH2O/kg). Rapid improvement in pulmonary status was observed in the InSurE group, while a dose-related effect was observed in nebulized groups. Nebulized poractant alfa was effective at a dose higher than 100 mg/kg, showing pulmonary, hemodynamic and cerebral behavior similar to the InSurE group (and significantly better than no surfactant treatment group), but showing lower lung injury score.

In newborn piglets with mild RDS, our results indicate that the administration of nebulized poractant alfa using a customized eFlow Neos nebulizer system is an effective and safe way of non-invasive surfactant administration technique. Supported by: ISCIII-PI18/00166-FEDER/FSE, IT583-13 and Chiesi-Farmaceutici S.p.A.

**COI:** This study was supported by: ISCIII-PI14/024-FEDER/FSE, IT583-13 and Chiesi-Farmaceutici S.p.A.
ID: 219

TITLE: ASSESSMENT OF NEWBORN BREATH SOUNDS USING DIGITAL STETHOSCOPE TECHNOLOGY

AUTHORS: Ashwin Ramanathan 1; Faezeh Marzbanrad 2; Kenneth Tan 1,3; Fatema-Tuz Zohra 2; Robert Roseby 1,4; Ajay Kevat 1; Atul Malhotra 1,3

AFFILIATIONS: 1 Dept of Paediatrics, Monash University, Melbourne, Australia
2 Dept of Electrical & Computer Systems Engineering, Monash University, Melbourne, Australia
3 Monash Newborn, Monash Children’s Hospital, Melbourne, Australia
4 Dept of Paediatric Respiratory Medicine, Monash Children’s Hospital, Melbourne, Australia

CONTENT:

Digital stethoscopes (DS) offer a convenient, cost-effective and easy to use device, designed to enhance the auscultation capabilities of the modern-day clinician. DS have been used to record and study normal and abnormal breath sounds in the paediatric population, including in conjunction with machine learning to accurately produce automated diagnoses for respiratory pathologies (1). Currently there are no studies documenting the use of this technology to assess breath sounds at birth. We aimed to determine whether DS is a feasible method to capture breath sounds in the transitioning newborn and determine whether there is an identifiable change in sound characteristics with time. Reference (1) Ramanathan A, et al. Digital stethoscopes in paediatric medicine. Acta Paediatr 2018; 108(5): 814-822.

A commercially available DS (Clinicloud Pty Ltd, AUS) and sound acquisition software were used to record breath sounds of term infants (37-40 weeks) born via normal vaginal delivery (NVD) and elective caesarean section (CS) at 1 minute and 2 hours of life. Two 1-minute recordings were taken at each time point from the anterior and posterior chest. Recordings had crying segments removed, a bandpass filter 100-1000 Hz was applied to isolate respiratory sound, and analysis was conducted using MATLAB R2018a (MathWorks Inc, MA, USA). Features such as mean frequency (MF), frequency percentiles (p25, p75), and power within frequency bands: low 100-200 Hz (LBF), medium 200-400 Hz (MBF), high 400-800 Hz (HBF) were used to describe the frequency spread and concentration of the breath sound profile.

A total of 61 newborns were studied. Mean (SD) gestation and weight of 32 NVD infants was 38 (0.9) weeks and 3165.6 (447.1) grams, and 29 elective CS infants was 38 (0.9) weeks and 3222.1 (297.1) grams. 83.6% of 1 minute and 100% of 2-hour recordings were analysable. We found a clear shift in frequency profile to lower range over the first 2 hours with decrease in MF and an increase in the proportion of power in the low frequency band 100-200 Hz. Mean change in NVD cohort: MF 40.50 Hz (p<0.001), p25 46.82 Hz (p<0.001), and LBF 0.16 (p<0.001). Mean change in CS cohort: MF 17.46 Hz (p=0.06), p25 24.66 Hz (p=0.03), and LBF 0.07 (p=0.06). Additionally, in a small number of newborns who developed respiratory distress (RD), we found significant differences in frequency profiles compared to those without RD. Mean difference RD vs no RD: MF 64.05 Hz (p=0.002), LBF 0.15 (p=0.02).

It is feasible to use digital stethoscope technology to assess breath sounds in the newborn during the transition period. We were able to depict a change in breath sound characteristics over the first 2 hours of life in newborns delivered via elective CS and NVD as well as suggesting a recognisable difference in infants with respiratory distress. This may be associated with lung fluid clearance over time and be of clinical importance.

IMAGES:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=d03230d158ad2489e3351e19295642f3-MjAxOS0wNSM1Y2UyNjY2YzAxYzI2

Average power spectrum comparison for NVD and Elective CS cohorts at 1 minute and 2 hours of life.
COI: None Declared. No author holds any interest in the commercially available stethoscope manufacturer. Dr Atul Malhotra is supported by a Royal Australasian College of Physicians Research Fellowship.
ID: 407  
TITLE: CAN WHOLE BODY VIBRATION, AS EXPERIENCED DURING NEONATAL AMBULANCE TRANSPORTATION, CAUSE LUNG INJURY?  
AUTHORS: Saleh Algarni 1; Dr Lara Shipley 2; Dr Ian Bloor 3; Dr Shalini Ojha 4; Dr Jon Dorling 5; Dr Don Sharkey  
AFFILIATIONS: Division of Child Health., School of Medicine, Nottingham University, Nottingham, United Kingdom  

CONTENT:  
In 2016 there were ~16,000 neonatal inter-hospital transports in the UK (NTG Annual Transport Data, 2016). The aim for each transport is to keep the infant stable. However, whole body vibration (WBV) during transport can compromise the infant’s stability (Shenai et al. Pediatrics, 1981). The EPICure 2 study demonstrated an increase in mortality and morbidity following preterm inter-hospital transfer (Marlow et al. BMJ, 2014). The only study examining the impact of WBV on the respiratory system, exposed rat pups to WBV of 27m/s^2, far in-excess of that seen in most neonatal transfers (Shah et al. Perinatal medicine, 2010), which resulted in significant lung injury. We aimed to recreate WBV, at normal levels experienced by neonatal patients during ambulance transfer, to examine the impact on the neonatal rat lung.  

Sprague-Dawley rat pups at postnatal day 4 and 7 were randomly divided into two groups: Control (n=26) and WBV exposure (n=28). WBV animals were exposed to moderate (0.9m/s^2, Mod) or high (2m/s^2, High) WBV for 90 minutes. All exposures simulated ranges, in vibration intensity and time, observed during an average UK ambulance transfer (Blaxter et al. Journal of engineering in medicine, 2017). Twenty-four hours after exposure the lung tissues were obtained for QPCR mRNA expression of surfactant proteins A, B, C and D, and inflammatory genes NF-κb, TLR4, MCP1, TGFB1, IL-1β and TNFα. Lung tissues were also stained for histological analysis using an established lung injury scoring system (Matute-Bello et al. American journal of respiratory cell and molecular biology, 2011).  

There were no significant differences between the control and vibration groups in the gene expression of any of the lung surfactant proteins (SPA, SPB, SPC, and SPD) or inflammatory genes NF-κb, TLR4, TGFB1, MCP1, IL-1β and TNFα (Table 1). The histological analysis of haematoxylin and eosin stained lung slides revealed no presence of lung injury observed following vibration in all groups. Moreover, the recruitment and infiltration of neutrophils, a key marker of acute lung injury, in either alveolar or interstitial space was not observed histologically after vibration. No significant increase in alveolar septal thickness, hyaline membranes, and proteinaceous debris filling the air spaces.  

Lungs of neonatal rat pups exposed to real-world WBV, as experienced during neonatal inter-hospital transport, do not have any adverse histological or inflammatory gene changes. These results are contrary to previously published results which used 10 times the amount of WBV with pressure ventilation. Our data suggest real-world WBV does not induce lung injury in this model.  

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Table1: The effect of WBV on QPCR expression of lung mRNA surfactant proteins and inflammatory genes for rat pups at age of 4 & 7 days.  

COI: None declared
ID: 467

TITLE: A NOVEL ECG ELECTRODE PLACEMENT METHOD FOR IMPROVING HEART RATE MEASURES AT BIRTH

AUTHORS: Caroline Henry 1; Lara Shipley 1; Carole Ward 1; Siavash Mirahmadi 2; John Crowe 2; Barrie Hayes-Gill 2; James Carpenter 3; Don Sharkey 1

AFFILIATIONS: 1 Division of Child Health, Obstetrics & Gynaecology, University of Nottingham, Nottingham, UK
2 Department of Electrical and Electronic Engineering, University of Nottingham, Nottingham, UK
3 SurePulse Medical Limited, Nottingham, UK

CONTENT:

In the first few golden minutes of newborn resuscitation, accurate heart rate (HR) is a key and a guiding principle for resuscitation algorithms. The 2015 ILCOR guidelines recommend using electrocardiogram (ECG) when available. The challenge is to ensure quick placement of monitoring technology and minimising electrode detachment without delaying the appropriate first resuscitation steps. The normal method of ECG monitoring requires the skin to be dried and electrodes placed individually, taking a median time of 26s (Katheria et al Pediatrics 2012). We aimed to evaluate the application time of pre-set ECG electrodes on the chest by exploiting the wet properties of the newborns’ skin.

Prior to delivery, the ECG electrodes were attached to a small square of plastic wrap normally used for thermoregulation in preterm infants (see figure). Small holes were made in the plastic wrap to allow the electrodes contact with the skin with ECG conduction gel placed onto the electrodes and so avoid adhesive attachment to the skin. Three time points were calculated from video analysis on the resuscitaire: 1) Time to apply pre-set electrodes from when they were picked up ready to be sited until placement; 2) Time taken to detect recognisable QRS complexes after placement; 3) Time after placement until HR value output by the device (GE B450 monitor). Ethical approval was given and the study funded by the Innovate UK.

57 newborns were studied (20 term infants, 30 32-37wks GA and 7 <32wks GA) with 8 born by vaginal birth. 23 needed stabilisation/resuscitation at birth with at least mask positive pressure ventilation. The median ECG application time was 9s (IQR 6-11s). The median time for a recognizable QRS to be displayed after application was 8s (IQR 2-12s) with all babies displaying a QRS signal by 46s. The median time for a visible HR output from the ECG monitor was 24s (IQR 15-47s). Within 1 minute of arrival on the resuscitaire, all babies had a recognisable QRS signal and 79% had an HR value output which increased to 96.5% (55 of 57) by 90s. There were no electrode detachments.

Pre-set chest ECG electrodes allow faster HR detection and output with fewer ECG failure rates than seen in previous studies. From the time of handling the ECG electrodes, our method typically outputs a QRS signal within 17s, far quicker than Katheria’s 26s to apply. This simple technique avoids detachment of single electrodes and potential skin stripping injury from adhesives. We believe this approach is worthy of further evaluation.

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Figure: Pre-set ECG electrodes on the chest

COI: None declared
ID: 491
TITLE: RESPIRATORY TREATMENT BURDEN AND MEANINGFUL CHANGE: INTERVIEWS WITH CAREGIVERS OF EXTREMELY PREMATURE INFANTS TO INFORM A PHASE 2B CLINICAL TRIAL ENDPOINT
AUTHORS: Sujata P. Sarda 1, Magdalena Vanya 2, Linda Han 3, Ethan J. Schwartz 4, Keira Sorrells 5, Alexandra Mangili 6.
AFFILIATIONS: 1 Takeda, Lexington, MA, USA; 2 ICON, South San Francisco, CA, USA; 3 Takeda, Cambridge, MA, USA; 4 ICON, Gaithersburg, MD, USA; 5 Preemie Parent Alliance, Madison, MS, USA; 6 Takeda, Zug, Switzerland.

CONTENT:

Extremely premature (EP) infants (born at 23 to <28 weeks gestation age [GA]) who continue to experience respiratory complications post-discharge from the neonatal intensive care unit (NICU) may utilize multiple medical resources, including visits to the emergency room (ER), inpatient hospital admissions, home respiratory technology support (RTS), and respiratory medications. This study explored post-NICU-discharge respiratory burden and perceptions of meaningful change among caregivers of extremely premature infants in the United States (US) and Europe to inform the primary endpoint of a Phase 2b study (NCT03253263).

Adult primary caregivers of EP infants in the US, Northern Ireland, and Germany were recruited through patient advocacy organizations and interviewed by phone. Caregivers were included if their infant (3–14 months corrected age [CA]), post-NICU discharge, experienced ≥1 of these: ER visit/rehospitalization due to respiratory diagnosis, RTS (eg: supplemental oxygen, breathing/heart rate monitor, tracheostomy), respiratory medications (eg: nebulizer, steroids, diuretics).

Interviews explored caregiver experiences related to infants with respiratory issues, associated treatment burden, and meaningful change in terms of reducing burden of treatment modalities. Sociodemographic data were summarized using descriptive statistics, and qualitative analysis of the interview data was performed.

40 caregivers (95% female; mean ± SD age, 31.7 ± 5.0 years) of infants (65% female) 3–14 months CA were interviewed. Respiratory morbidities reported by caregivers post-NICU discharge included difficulty/changes in breathing (82.5%), bronchopulmonary dysplasia (60%), respiratory infections (60%), and apnea (32.5%). Infants with respiratory morbidities experienced medication use (92.5%), RTS (82.5%), hospitalizations (37.5%), and ER visits (35%). Table lists the top 3 self-reported negative impacts of each of these. Based on their own experiences, caregivers considered supplemental oxygen as the most burdensome treatment. They most wanted to avoid RTS (tracheostomy and home ventilator use), hospitalizations, and ER visits. Reduced need for oxygen, less frequent administration of medications, and reduced hospitalizations were considered to be the most meaningful treatment changes.

In this study we found that all of the respiratory treatment modalities explored (RTS, ER visits, hospitalizations, and use of respiratory medications) carried a negative impact and were burdensome. A reduction in the use of these treatment modalities would be a meaningful benefit to patients and their caregivers. It should be noted that the small sample size, drawn from only 3 countries, limits the broader generalizability of our results.

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Table: Top 3 Respiratory Treatment Negative Impacts by Treatment Modality

COI: This study was funded by Takeda. S. P. Sarda, L. Han, and A. Mangili are employees of, and own stock/stock options in Takeda. E.J. Schwartz and M. Vanya are employees of ICON and performed contracted research for Takeda in connection with this study. K. Sorrells is an employee of Preemie Parent Alliance and performed contracted consulting in connection with this study. The authors thank I. Probodh, PhD, of Excel Medical Affairs, who provided medical writing assistance funded by Takeda.
TITLE: APNOEIC OXYGENATION TIME IN PRETERM NEONATES

AUTHORS: Dr Radhika Kothari 1; Dr Eoin O’Currrain 1, 2, 3, 4; Dr Kate Hodgson 1, 2, 4; Dr Brett Manley 1, 2, 5; Dr Joyce E O’Shea 6; Dr Lorraine McGrory 7; Dr Louise S Owen 1, 2, 5; Dr Omar Kamlin 1, 2, 5; Dr Jennifer A Dawson 1, 2, 5; Dr Marta Thio 1, 2, 5; Prof Peter G Davis 1, 2, 5

AFFILIATIONS: 1 Neonatal Services and Newborn Research Centre, Royal Women’s Hospital, Melbourne, Victoria, Australia
2 Department of Obstetrics and Gynaecology, The University of Melbourne, Melbourne, Victoria, Australia
3 University College Dublin, Dublin, Ireland
4 Paediatric Infant Perinatal Emergency Retrieval, Neonatal Retrieval Services Victoria, The Royal Children’s Hospital, Melbourne, Australia
5 Murdoch Children’s Research Institute, Melbourne, Victoria, Australia
6 Royal Hospital for Children, Glasgow, UK
7 Neonatal Department, University Hospital Wishaw, Lanarkshire, UK

CONTENT:

Clinical deterioration with desaturation or bradycardia is common during neonatal intubation attempts [1,2]. The NRP recommends a 20-second time limit for intubation attempts; however, attempts often take longer. The time until onset of desaturation in neonates has not previously been reported. Kinouchi et al. [4] examined apnoea time in infants and concluded that SpO2 decreases to < 95% more quickly in younger ones. Patel et al. [5] measured the time until SpO2 <90% after apnoea in healthy children and showed a similar trend in age-related desaturation (94–214 sec). Aim of this study was to determine the apnoeic oxygenation time in preterm infants undergoing elective intubation.

This was an observational study of very preterm neonates born ≤32 weeks’ gestation undergoing elective endotracheal intubation at the Royal Women’s Hospital (RWH), Melbourne, Australia. Data were acquired from a previous randomised trial [6]. All infants received premedication for intubation. Continuous SpO2 and heart rate data were recorded using a pulse oximeter. Apnoeic oxygenation time was defined as the time from the last positive pressure or spontaneous breath, until desaturation (SpO2 <90%), in keeping with other studies [5, 7, 8]. Video recordings of the intubations were retrospectively reviewed and apnoeic oxygenation time was determined for the first intubation attempt only. Measurements of SpO2 and heart rate were recorded every 2 seconds during the apnoeic period.

Data from 119 patients were available from the original trial. Infants were excluded (n=41) if they did not have continuous saturation data, or if intubation occurred in the delivery room. The remaining 78 infants were included. The mean (SD) gestational age was 27 (2.2) weeks and birth weight 1022 (359) g. Median (IQR) age at intubation was 36 (10–312) hours. All but 5 neonates had SpO2 <90% during apnoea (73/78, 94%). The mean (SD) apnoeic oxygenation time was 25.3 (19.4) seconds. The mean (SD) time to desaturation <80% was 37.0 (21.9) seconds, and to desaturation <60% was 58.2 (20.2) seconds. Percentile charts were produced to demonstrate SpO2 changes with time after apnoea. No bradycardia <100 beats per minute was seen. There was no correlation between apnoeic oxygenation time and gestational age (r=-0.04, p=0.71), birth weight (r=-0.19, p=0.11) or starting FiO2 (r=-0.25, p=0.03).

To our knowledge this is the first study to report apnoeic oxygenation time in preterm neonates, and to characterise the changes in oxygen saturation and heart rate after apnoea. Apnoeic oxygenation time is substantially shorter in preterm neonates, compared with pediatric and adult patients. These data provide important clinical information for the development of clinical guidelines and studies to improve neonatal intubation safety.
COI: None declared

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ID: 714
TITLE: INTRAOSSEOUS NEEDLE USE IN NEONATES IN THE UK
AUTHORS: Alexandra Scrivens* 1; Alexandra Doerr* 2; Adrian Sayers 3; Alessandra Glover 2; Faith Emery 4; Charles Christoph Roehr 1
*joint first author
AFFILIATIONS: 1 Newborn Services, Oxford University Hospitals, Oxford, UK. University of Oxford, Oxford, UK
2 St Michael's Hospital, Bristol, UK
3 University of Bristol, UK
4 Southmead Hospital, Bristol, UK

CONTENT:

Intraosseous (IO) devices form a mainstay of resuscitation in paediatric departments, but do not feature so prominently in neonatal units, possibly because most neonatal unit inpatients have an accessible umbilical vein or existing vascular access. However, this is not always the case. A literature search found 41 documented cases where IO needles were used in neonatal units, but only 75% of neonatal units have IO devices available.

Aim:
.To identify recent UK cases where IO access has been used or attempted in patients <28 days of age, or resident on a neonatal unit.
.To ascertain which devices were used, whether they were sited successfully and whether any complications occurred.

An online survey was sent out via trainee representatives to trainee paediatricians in the UK.

Ninety-three responses were received. Thirty-eight respondents (41%) had attempted IO access in the year 2017-8, 12 more than once. Of 65 attempts amongst respondents, 13 were on infants <28 days of age, or neonatal unit inpatients (Table 1). Of these 13 attempts, 10 (77%) were successful. Devices used were: EZ-IO® (12) and Cook needle (1). Complications occurred in 23% of cases (dislodged (2), extravasation (1), thromboembolism (1)).

This survey demonstrated that intraosseous needles have been used successfully in neonates. Whilst not a first choice form of vascular access, IO devices may be considered during neonatal resuscitation situations. Wider IO device training and availability on neonatal units may offer a rare but lifesaving alternative form of IV access in an emergency situation. Further work is needed to determine optimal position and type of IO device in infants.

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Table 1: Features of all IO attempts in neonates or neonatal unit inpatients. NNU – neonatal unit, ED – emergency department, PICU – paediatric intensive care, PW – paediatric ward, CGA – corrected gestational age (weeks)

COI: None declared
ID: 715

TITLE: THE FEASIBILITY OF TRANSCUTANEOUS ELECTROMYOGRAPHY OF THE DIAPHRAGM AS MONITORING TECHNIQUE IN THE DELIVERY ROOM

AUTHORS: Eline Kho 1, 5; Ruud W. van Leuteren 1; Cornelia G. de Waal 1; Frans H. de Jongh 1, 3; Arjan B. te Pas 4; Hylke Salverda 4; Anton H. van Kaam 1, 2; Gerard J. Hutten 1;

AFFILIATIONS: 1 Department of neonatology, Emma Children’s Hospital, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands
2 Department of neonatology, Emma Children’s Hospital, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands
3 Faculty of Science and Technology, University of Twente, Enschede, The Netherlands
4 Department of neonatology, Leiden University Medical Centre, Leiden, The Netherlands
5 Technical Medicine, University of Twente, Enschede, The Netherlands

CONTENT:

To assess cardio-pulmonary transition of (preterm) infants in the delivery room (DR), heart rate (HR) and oxygenation are monitored using either chest impedance (CI) and/or pulse oximetry (PO). However, CI and PO do not provide information on the respiratory effort of the patient, an essential factor to titrate the level of respiratory support. Electromyography of the diaphragm (dEMG) measures the activity of the diaphragm and might be helpful to determine respiratory effort. In addition, it measures HR and RR, so dEMG might improve monitoring compared to CI. However, first it needs to be established if dEMG provides accurate data on HR compared to standard techniques available in the DR.

Infants with a gestational age (GA) > 26 weeks, in need for cardio-respiratory support and monitoring, but without congenital anomalies, were enrolled. CI and PO (standard care monitoring), and dEMG measurement equipment was applied as soon as possible after birth and recorded during the cardio-respiratory stabilization. Time between device application and the first read out of the corresponding HR was calculated (∆t).

HR was calculated based on the dEMG signal and the raw CI waveform. Numerical HR, based on CI and PO data, was acquired from the patient monitor. All HR readings were compared during periods of noise-free recordings using intra-class correlation coefficient (ICC) and Bland-Altman (BA) analysis, including the limits of agreement (LOA).

Fourteen preterm infants (GA 32.5 ± 3.0 weeks; birth weight 1743 ± 790 grams) were included in this ongoing study. Due to errors in data storage, for some patients not all CI tracings were recorded (missing n = 6 for raw CI and n = 1 for numeric CI), so groups size differed for HR-readings.

Time between device application and the first HR read out was equal for dEMG and raw CI signal (both with median (IQR): 10.1 (10.1-10.3) seconds). The median (IQR) ∆t based on numeric CI was 12.0 (8.1-13.7) seconds. HR detection of PO was slower compared to dEMG and CI with a median of 35.9 (16.3-67.7) seconds.

Heart rate monitoring could be executed with high accuracy (all p < 0.01) with an ICC of 0.98 for dEMG vs. raw CI; 0.96 for dEMG vs. numerical CI; and 0.96 for dEMG vs. numerical PO. BA analysis showed the best agreement between dEMG and raw CI (mean difference (LOA): -0.5 (6.8) beats/minute).

This study suggests that dEMG monitoring during cardio-pulmonary transition in the DR is feasible and provides fast and accurate data on HR, similar to CI and faster than PO. Future studies should now investigate the additional value of dEMG in assessing respiratory effort and titrating respiratory support in the DR.
COI: None declared
ID: 796
TITLE: DO SURFACTANTS IMPROVE NONRESPIRATORY OUTCOMES IN PRETERM BABIES? META-ANALYSIS AND REVIEW OF PHYSIOPATHOLOGICAL PLAUSIBILITY
AUTHORS: Silvia Foligno, Daniele De Luca
AFFILIATIONS: Division of Pediatrics and Neonatal Critical Care, Medical Center “A. Béclère”, South Paris University Hospitals, Assistance Publique–Hôpitaux de Paris (APHP) and South Paris-Saclay University, Paris – France
CONTENT:

While porcine seems to be superior to bovine surfactants in terms of respiratory outcomes, it is unclear if a surfactant can also improve non-respiratory outcomes in preterm neonates with respiratory distress syndrome. It is also unknown if there is any physiopathological mechanism linking surfactant therapy to these outcomes. We aim to fill these knowledge gaps.

Systematic pragmatic review and meta-analysis following PRISMA guidelines. Animal or human translational studies about mechanisms linking surfactant replacement to non-respiratory neonatal outcomes were also systematically reviewed. We considered common non-pulmonary outcomes registered in neonatal intensive care units.

Porcine surfactant is associated with lower incidence of PDA (OR:0.655; 95%CI:0.460-0.931;p=0.018;12 trials;1472 patients); prenatal steroids (coef.: -0.009, 95%CI: -0.03 - 0.009, p=0.323) and gestational age (coef.: 0.079, 95%CI: -0.18 - 0.34, p=0.554) did not influence the effect size. No significant differences were found between porcine and bovine surfactants on NICU stay (mean difference (days): -2.977; 95%CI: -6.659 - 0.705; p=0.113;8 trials; 855 patients), IVH of any grade (OR:0.860; 95%CI:0.648-1.139;p=0.293;15 trials;1703 patients), severe IVH (OR:0.852; 95%CI:0.624-1.163;p=0.313;15 trials;1672 patients), NEC (OR:1.190; 95%CI:0.785-1.803); p=0.412;9 trials;1097 patients) and ROP (OR:0.801; 95%CI:0.480-1.337;p=0.396;10 trials;962 patients). Physiopathological mechanisms explaining the effect of surfactant have been found for PDA, while are lacking for all other endpoints (Tab.1).

Porcine surfactant is associated with lower incidence of PDA than bovine surfactants. As there are no differences in terms of other non-respiratory outcomes and no physiopathological plausibility, these endpoints should not be used in future trials.

REGISTRATION: PROSPERO n.CRD42018100906

COI: A/Prof. D. De Luca has received grants for research and educational projects from Chiesi Pharmaceuticals spa and ABBVIE inc. He also received travel grants from ABBVIE inc. He served as consultant and lecturer for both Chiesi Pharmaceuticals spa and ABBVIE inc. Finally, he was member of the advisory boards for both Chiesi Pharmaceuticals spa and ABBVIE inc. These companies produce two surfactants analysed in the paper, but they had no role in design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review, approval of the manuscript or decision to submit it for publication. The other author declares no competing interests.
ID: 801
TITLE: RISK FACTORS FOR NASAL-BILEVEL POSITIVE AIRWAY PRESSURE FAILURE FOR INITIAL RESPIRATORY MANAGEMENT IN PRETERM INFANTS
AUTHORS: Heekwor Son 1; Jaewook Ha 2; Mi-ji Lee 3; Eui Kyung Choi 4; Kyuwee Park 5; Jeonghee Shin 6; Byung Min Choi 7
AFFILIATIONS: 1 Paediatric Dept., Korea University Ansan Hospital, Ansan, Gyeonggi-do, Republic of Korea

CONTENT:
Non-invasive ventilation (NIV) has been increasingly used with the purpose of reducing the risk of adverse pulmonary outcome associated with invasive mechanical ventilation (IMV). Nasal bilevel positive airway pressure (n-BiPAP) has been introduced as an alternative to conventional nasal continuous positive airway pressure (nCPAP) in recent years. Superiorities of n-BiPAP in function of oxygenation and ventilation compared to nCPAP were reported in some studies, however, n-BiPAP failure had been reported in 12.9-26.6%. The aim of our study is to investigate risk factors for n-BiPAP failure for initial respiratory management in preterm infants.

A hundred and twenty two preterm infants (≥ 30 weeks of gestation and >1,250 gram of birth weight) who required respiratory support by n-BiPAP after birth were included. The success group included infants who were weaned from n-BiPAP in 7 days. The failure group included infants who required IMV despite the application of n-BiPAP.

The rate of n-BiPAP failure was resulted in 10.6% (13/122). Incidence of respiratory distress syndrome (RDS) (76.9 vs 24.8%, P < 0.001) and need for surfactant administration (69.2% vs 0%) were significantly higher in the failure group compared to the success group. Increased oxygen requirement, lower pH and higher pCO2 on blood gas analysis within 2 hours after commencing n-BiPAP were also shown in the failure group. However, significant differences were not found in gestational age and birth weight between the two groups. After adjusted for gestational age, incidence of RDS, and increased oxygen requirement during n-BiPAP support remained significantly associated with n-BiPAP failure.

N-BiPAP failure in preterm infants are expected when they have any evidence for RDS. Increased oxygen requirement during n-BiPAP support may also help to identify high-risk preterm infants for n-BiPAP failure. Strategies to avoid n-BiPAP failure should be investigated, and further multi-centered well-designed randomized studies are needed to access efficacy and safety of n-BiPAP for initial respiratory management in preterm infants.

COI: None declared
ID: 814

TITLE: PHYSICAL STIMULATION OF NEWBORN INFANTS IN THE DELIVERY ROOM: A RETROSPECTIVE ANALYSIS

AUTHORS: Vincent D. Gaertner 1,2; Sophie A. Flemmer 1,2; Laila Lorenz 1; Peter G. Davis 1,3; C. Omar F. Kamlin 1,3

AFFILIATIONS: 1 Neonatal Services, The Royal Women’s Hospital, Melbourne, Australia
2 University Hospital Regensburg, Regensburg, Germany
3 Department of Obstetrics and Gynaecology, University of Melbourne, Melbourne, Australia

CONTENT:

Neonatal resuscitation guidelines recommend that newborn infants should be dried, warmed and stimulated within the first minute after birth to assist with the establishment of regular respirations. However, the mode, site of application and frequency of stimulations are not stipulated in these guidelines. Although stimulation is the most common intervention during neonatal stabilisation in the delivery room, its characteristics and effectiveness are insufficiently described. Thus, the aim of our study was to describe timing, frequency, different methods and effects of tactile stimulation of newborn infants.

We conducted a retrospective observational study using video recordings of neonatal resuscitations performed at The Royal Women’s Hospital, Melbourne. The video captured the resuscitaire from above allowing to see the treating clinicians' stimulations as well as the infants’ reactions. Four different types of stimulation (drying, chest rub, back rub and foot flick) were defined a priori and the frequency and infant response were documented. Data were summarised as medians (IQR) or as numbers (%). The difference in medians was assessed using a Wilcoxon test. Infants were grouped by gestational age (GA): infants <30 weeks’ gestation and infants ≥30 weeks’ gestation.

A total of 120 video recordings were reviewed. 75 infants (63%) received at least one episode of stimulation and 70 (58%) infants were stimulated within the first minute after birth. The median (IQR) time to first stimulation was 19 (15–24) seconds. Stimulation was less commonly provided to infants <30 weeks’ gestation (median (IQR) number of stimulations: 0 (0–1)) than infants born ≥30 weeks’ gestation (1 (1–3); p<0.001). The most common response to stimulation was limb movement (71% of stimulations) followed by infant cry and facial grimace (37% and 36% of all stimulations, respectively). Truncal stimulation (drying, chest rub, back rub) was associated with more crying and movement than foot flicks.

Less mature infants are stimulated less frequently than more mature infants and many very preterm infants do not receive any stimulation. If stimulation occurs, it is mostly performed within the first minute after birth. Truncal stimulation appears to be more effective than foot flicks and may be beneficial during neonatal transition. Further prospectively conducted studies investigating specific modes of stimulation are required.

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Number and timing of stimulations divided by gestational age. Part (A) shows infants <30 weeks’ gestation and part (B) shows infants ≥30 weeks’ gestation.

COI: None declared
ID: 818

TITLE: THE MANAGEMENT OF RESPIRATORY DISTRESS SYNDROME IN PRETERM INFANTS: THE CHANGING EXPERIENCE IN WALES

AUTHORS: Christopher William Course1, Mallinath Chakraborty1,2

AFFILIATIONS: 1: Welsh Regional Neonatal Intensive Care Unit, University Hospital of Wales, Cardiff, United Kingdom
2: Cardiff University, Cardiff, UK

CONTENT:

Respiratory Distress Syndrome (RDS) is the commonest diagnosis after premature birth, a result of structural and functional immaturity of the lungs. These preterm infants often require invasive and non-invasive respiratory support, supplementary oxygen and surfactant therapy. A proportion of these infants will go on to develop chronic lung disease of prematurity, with abnormal respiratory function and increased respiratory morbidity persisting through childhood and into adult life. There exists a wealth of high-quality evidence on optimal management of RDS. We aimed to describe trends in management before and after introduction of a national guideline in Wales on RDS management.

Anonymised, prospective data from all participating neonatal units (level two and level three) in Wales were collected in two six-month time periods in 2015 and 2018 for all inborn infants <34 weeks’ gestation using a standardised proforma. A national guideline for management of RDS in preterm infants was introduced in 2016 by the Wales Neonatal Network. Data collection included areas of antenatal management, delivery room stabilisation, invasive and non-invasive respiratory support, surfactant treatment and elements of supportive care. Univariate and multivariate methods were used to compare data between the two epochs. Odds ratios and 95% confidence intervals (CI) were adjusted for gestational age at delivery and level of unit of delivery. Statistical significance was set at p < 0.05.

Data on 225 infants from 2015 and 276 infants in 2018 was analysed. Mean gestational age and birthweight were comparable between the epochs (p > 0.05). Comparing care before and after introduction of the guideline, there was overall improvement in use of targeted tidal volume ventilation (aOR 7.94 [3.75,16.8]), caffeine therapy (aOR 2.49 [1.4,4.6]), oxygen therapy post-surfactant (aOR 2.16 [1.23,3.82]) and early use of parenteral nutrition (aOR 2.75 [1.66,4.58]). Areas of poorer management included use of high positive end expiratory pressures (aOR 0.58 [0.35,0.96]) and stabilisation in FiO2 <30% (aOR 0.29 [0.17,0.47]). Little variation was seen between level two and three units, although more mature infants had significantly higher rates of delayed cord clamping (DCC) (aOR 1.44 [1.23,1.68]), stabilisation on CPAP (aOR 1.85 [1.65,2.07]), and early enteral feeding (aOR 1.22 [1.12,1.32]).

We present novel data from Wales collected around the implementation of a new national RDS guideline. Significant improvements in management of RDS in preterm infants were seen, particularly regarding mechanical ventilation. Yet some practices such as DCC, struggle to be embraced. Despite large volumes of high-quality evidence, some elements of best practice are yet to be adopted consistently. Further work should focus on education and training.

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Summary of main results with adjusted odds ratio comparing the 2018 cohort with the 2015 cohort. (* = statistically significant results)

COI: None declared.
ID: 827

TITLE: PRE- AND POSTNATAL RISK FACTORS FOR PULMONARY INTERSTITIAL EMPHYSEMA IN PRETERM INFANTS ≤32 WEEKS OF GESTATION

AUTHORS: Judith Behnke (First Author) 1,3
Markus Waitz 1
Klaus-Peter Zimmer 1
Lars Daniel Berthold 2
Harald Ehrhardt 1,3

AFFILIATIONS: 1 Department of General Pediatrics & Neonatology, Justus Liebig University Giessen, Germany.
2 Department of Pediatric Radiology, Institute for Diagnostic and Interventional Radiology, Justus Liebig University of Giessen, Germany.
3 Member of the German Lung Research Center (DZL), Giessen, Germany.

CONTENT:

Pulmonary interstitial emphysema (PIE) is one of the most severe respiratory complications in preterm infants belonging to the group of air leak syndromes. Typically mechanically ventilated extremely low birth weight infants (ELBWIs) with respiratory distress syndrome (RDS) are affected. We aimed to determine the association of further important pre- and postnatal risk factors (e.g., diabetes during pregnancy, preeclampsia/HELLP, intrauterine growth restriction (IUGR), antenatal steroids (ANCS), gender) which are well accepted to increase the risk of the preterm infant for BPD and long-term pulmonary sequelae with the occurrence of PIE as well as their contribution to severe complications.

n=226 preterm infants ≤32 gestational age (GA) discharged between 2016-2017 from the neonatology of the Justus Liebig University of Giessen with chest x-ray examination within the first 5 days of life were retrospectively classified as non-PIE (n=142) or PIE (n=37) with the subgroup of severe PIE cases (n=12). Additionally, PIE cases were matched with 37 non-PIE cases by GA, birth weight (BW) and gender. Pre- and postnatal risk factors were identified by univariate analysis (SPSS Statistics 25). Data presented as median (interquartile range) and differences assessed for statistical significance using the Mann-Whitney U rank sum test or χ² test as appropriate.

Previously known risk factors including GA and BW and the association of PIE with adverse outcome parameters of intraventricular hemorrhage (IVH) and mortality were confirmed, but PIE did not impact the frequency of BPD (PIE 54.1% vs. 59.4% non-PIE). Preeclampsia/HELLP (PIE 24.3% vs. non-PIE 8.1%) was identified as additional risk factor (p≤0.05). In PIE cases, severe impairment in lung gas exchange correlated with the presence of RDS (PIE 51.3% vs. non-PIE 29.7%), insulin requirements (PIE 54.1% vs. non-PIE 29.7%) and the higher maximum inspired fraction of oxygen (FiO2) (PIE 0.50 (0.40-0.72) vs. non-PIE 0.37 (0.25-0.53)), but PIE was not fostered by differences in ventilator settings (PIP, PEEP). Any diabetes during pregnancy, chorioamnionitis, antenatal corticosteroid use (ANCS) and male gender had no significant effect on the incidence of PIE.

Pulmonary interstitial emphysema (PIE) is a severe complication in infants born ≤32 GA that poses a high risk for adverse outcome in preterm infants. We identified pre-eclampsia/HELLP as important additional risk factor for PIE that should be included in future risk calculations to identify infants at high risk for PIE directly after birth.

COI: None declared.
Continuous Positive Airway Pressure (CPAP) was first described by Gregory in 1971 as a non-invasive respiratory support of preterm infants. The first dedicated variable flow system for nasal use was developed by K Nilsson and G Moa in Sweden, later known as Infant Flow. Compared to other systems it was pressure stable with a low resistance to breathing and low imposed work of breathing. The Infant Flow type of geometry has been used in a new system for neonatal resuscitation (rPAP) with a marked reduction in resistance to breathing. The aim of this study was to describe the flow and function of the Infant Flow geometry using simulated breathing and computational fluid dynamics.

To resolve the flow characteristics within the Infant Flow device during the breathing cycle, the 3D unsteady and incompressible Navier-Stokes equations were solved. A breathing flow profile of a 3.4 kg healthy infant was applied at the position of the nasal prongs. At the jet inlet, constant flows of 3, 4 and 5 L/min, corresponding to CPAP pressure in the range of 3 – 9 cm H2O, were imposed along with a constant pressure boundary condition at the outlet boundaries. The results were presented for analysis as videos of the complete breath cycle and examples of expiration and expiration.

The simulation fully resolved the flow phenomena occurring in the Infant Flow geometry using breath flow profile recorded from an infant. The high resolution needed to resolve the field requires extensive computational power. The CFD simulations for the breathing cycle and the geometry (time plus three dimensions) were calculated and selected cross sections of inspiration and expiration presented in figure 1. The main flow feature during inspiration was support by gas entrainment and mixing. During expiration the jet deflected towards the exhaust with unstable impingement of the jet at the opposing edge. The results confirm the previously suggested function of a high velocity jet that deviate during expiration and produce a fluidic flip.

The Infant flow device was designed thirty years ago and a similar design has recently been used in a new resuscitation system. The delivered CPAP has low resistance to breathing, pressure stable CPAP and low imposed work of breathing. We have previously shown that on these aspects, the design still has an advantage over other CPAP system. The Infant Flow supports inspiration by gas entrainment and expiration by impingement at the opposing edge.

**IMAGES:**
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Figure 1: Top row display early developments of the Infant Flow geometry (initially called Jet Piece). The left prototype was the first used in an infant. To the right the is the EME Infant Flow device similar to the devices manufactured today by other co
COI: Kjell Nilsson is one of the inventors of Infant Flow. Thomas Drevhammar and Kjell Nilsson have invented a new resuscitation system based on a geometry similar to Infant Flow. Pilot results have been presented at the World Congress of Biomechanics 2018, Dublin.
ID: 871
TITLE: CHORIOAMNIONITIS AS A RISK FACTOR FOR BRONCHOPULMONARY DYSPLASIA: A META-ANALYSIS AND META-REGRESSION
AUTHORS: Eduardo Villamor-Martinez 1, María Álvarez-Fuente 2, Amro M. T. Ghazi 1, Mohammed A. Kilani 1, Pieter Degraeuwe 1, Luc J. I. Zimmermann 1, Boris W. Kramer 1, Eduardo Villamor 1
AFFILIATIONS: 1 Department of Pediatrics, Maastricht University Medical Center (MUMC+), School for Oncology and Developmental Biology (GROW), Maastricht, the Netherlands. 2 Hospital Ramón y Cajal, Madrid, Spain
CONTENT:
Bronchopulmonary dysplasia (BPD) remains one of the major complications of very preterm birth. Inflammatory and infectious events are suggested to play a key role in the initiation, progression, and severity of BPD. The inflammatory response may have been initiated in utero, in the setting of chorioamnionitis (CA). We aimed to perform a systematic review, meta-analysis, and meta-regression of clinical studies exploring the association between CA and BPD.

PubMed/MEDLINE and EMBASE databases were searched. Studies were included if they examined preterm infants and reported primary data that could be used to measure the association between exposure to CA and the presence of BPD. A random-effects model was used to calculate odds ratios (OR) and 95% confidence intervals (CI). Sources of heterogeneity were determined by subgroup and meta-regression analyses.

We found 3,168 potentially relevant studies, of which 158 met the inclusion criteria (185,676 infants). Meta-analysis showed that CA exposure was significantly associated with BPD28 (OR 2.10, 95% CI 1.76-2.51), and BPD36 (OR 1.29, 95% CI 1.16-1.42). The association between CA and BPD remained significant for both clinical and histological CA. Exposure to funisitis was not significantly associated with a higher risk of BPD when compared to exposure to CA in the absence of funisitis. In addition, we found significant differences between CA-exposed and CA-unexposed infants in GA, BW, and other infant characteristics. CA was not significantly associated with RDS (OR 1.10, 95% CI 0.92-1.34) but multivariate meta-regression with backward elimination revealed that a model combining difference in GA and odds of RDS explained 64% of variance in the association between CA and BPD36 across studies.

Our results confirm that preterm infants exposed to CA have a higher risk of developing BPD, but the pathogenic effect of CA on BPD may be modulated by the effect of CA on GA and risk of RDS.

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Figure 1. Meta-analysis of the association between chorioamnionitis (CA) and bronchopulmonary dysplasia (BPD), grouped by definition of CA. k: number of studies; PMA: post-menstrual age.

COI: None declared
ID: 895

TITLE: AN IN VITRO MODEL TO UNDERSTAND THE IMPROVEMENT IN LUNG SURFACANT ACTIVITY DURING WHOLE BODY HYPOTHERMIA

AUTHORS: Chiara Autilio 1
Mercedes Echaide 1
Daniele De Luca 2
Jesus Perez-Gil 1

AFFILIATIONS: 1 Department of Biochemistry and Molecular Biology, Faculty of Biology and Research Institute Hospital 12 de Octubre, Complutense University, Madrid, Spain
2 Division of Pediatrics and Neonatal Critical Care, South Paris University Hospitals, APHP, and South Paris-Saclay University, Paris, France

CONTENT:

Pulmonary surfactant (PS) is a lipid-protein complex that reduces the surface tension at the respiratory air-liquid interface of alveoli, minimizing the work of breathing[1]. The composition and structure of PS are directly responsible for its mechanical properties in a healthy lung or under pathological conditions. We previously demonstrated that PS activity improves after 72h of Whole Body Hypothermia (WBH) in neonates with and without lung injury[2,3]. PS performance is significantly better when samples are tested under cooling condition (33.5°C). To better understand the molecular mechanisms at the basis of this temperature-dependent improvement, we designed a surfactant in vitro model.

We combined synthetic lipids and porcine surfactant protein-B(SP-B), preparing 2 protein/lipid mixtures characterized by higher or lower surface active properties: 1) DPPC (35% w/w), POPG (35% w/w) and SP-B (1% w/w) in the presence of POPC (30% w/w) or 2) DPPC (35% w/w), POPG (35% w/w) and SP-B (1% w/w) in the presence of a lower surface active lipid, namely DOPC (30% w/w). We studied their biophysical activity upon breathing-like conditions at the Captive Bubble Surfactometer, analyzing each sample in triplicates (8 mg/mL of phospholipid) at both 37°C and 33.5°C.

We did not find any significant differences along compression-expansion dynamics in the performance of the more active mixture containing POPC [37°C: minimum gamma=13 +/- 4 mN/m; 33.5°C=16 +/- 2 mN/m]. Conversely, we obtained a significant decrease in surface tension, testing the mixture with DOPC at 33.5°C [37°C: minimum gamma=18 +/- 2 mN/m; 33.5°C=7 +/- 2 mN/m, p<0.001].

Conclusions: Our in vitro data suggests that the improvement in PS activity upon WBH may partially depend on a better and preferential exclusion from the air-liquid interface of less active phospholipids during expiration.


COI: no conflict of interest
**ID:** 933  
**TITLE:** NEONATAL INTUBATION SUCCESS RATES AMONG PAEDIATRIC TRAINEES  
**AUTHORS:** Gemma Edwards 1; Khadija Belkhatir 2; Andrew Brunton 3; Hilary Conetta 4; Joyce O'Shea 5.  
**AFFILIATIONS:**  
1 Princess Royal Maternity, Glasgow, Scotland, UK  
2 Neonatal Unit, Royal Berkshire Hospital, Reading, England, UK  
3 Neonatal Unit, Royal Hospital for Children, Glasgow, Scotland, UK  
4 Neonatal Unit, Royal Alexandra Hospital, Paisley, Scotland, UK  
5 Neonatal Unit, Royal Hospital for Children, Glasgow, Scotland, UK  

**CONTENT:**  
Neonatal intubation is a mandatory competency for paediatric trainees. It is however a challenging skill to learn and maintain, and one with risk of serious complications. Advances in obstetric care, discontinuation of routine intubation for infants born through meconium stained liquor, increased use of non-invasive respiratory support, less invasive surfactant administration and increased numbers of trainees have all resulted in fewer opportunities to learn and practice intubation. Success rates have been reported to be falling and the likelihood of infants requiring multiple attempts at intubation rising. We sought to measure intubation success rates in three sites in the United Kingdom.

Over a 12 month period, May 1st 2018 until April 30th 2019, information was collected prospectively about all intubations carried out in one level three and two level two neonatal units in the United Kingdom. The setting and indication for each intubation, the level of experience of the intubator, the equipment and premedication used, the weight, corrected gestation and physiological stability of the infant for each attempt were recorded. Data sheets were completed after each intubation by the intubator. Patient notes, x-rays and electronic notes were checked weekly by study investigators to ensure all intubations were included. Primary outcome was the first attempt intubation success rate.

There were 140 intubations during the 12 month period across the three sites. First attempt success rate overall was 55% (77/140) and 48% (16/33), 54% (25/46) and 59% (36/61) in the three different sites. First attempt intubation success rate for intubations during stabilisation at delivery without premedication was 45% (20/44). First attempt intubation success rate for elective premedicated intubations in the neonatal intensive care unit was 59% (56/95). Success rates by level of intubator are displayed in Table 1; junior trainees have 1-3 years of paediatric experience and middle grade have 4-6 years experience. The median number of attempts before successful intubation was 1, with a range of 1 – 7 attempts. There were 34 occasions (24% of intubations) where 3 or more attempts were necessary before successful intubation.

Rates of neonatal intubation on first attempt are low across junior and middle grade paediatric trainees especially for emergency non-premedicated intubations. This highlights a requirement for high quality teaching of this skill to all levels of trainee in the neonatal unit before progressing to more challenging emergency intubation. The middle grade group require plentiful opportunity to intubate as success rates are similar to junior trainees.

**IMAGES:**  
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Table 1; Success rates by level of intubator

**COI:** None declared.