September 20th, 2023 09:00 - 11:00

PARALLEL SESSION 2 – LUNG 1

ID 756. Two-year outcomes in a randomised controlled trial of less invasive surfactant administration (LISA) in preterm infants supported with continuous positive airway pressure (CPAP)

Professor Peter Dargaville[1,2], Dr. Omar Kamlin[3], Ms. Francesca Orsini[4], Dr. Xiaofang Wang[4], Dr. Tony De Paoli[1], Prof. Howard Clark[5], Prof. Roger Soll[6], Prof. Samantha Johnson[7], Prof. Jeanie Cheong[3,4], Prof. John Carlin[4,8], Prof. Peter Davis[3], for the OPTIMIST-A study investigators
[1]Royal Hobart Hospital, [2]Menzies Institute for Medical Research, University of Tasmania, [3]Royal Women's Hospital, [4]Murdoch Children's Research Institute, [5]EGA Institute for Women's Health, University College London, [6]Larner College of Medicine, The University of Vermont, [7]Department of Population Health Sciences, University of Leicester, [8]Department of Paediatrics, University of Melbourne

BACKGROUND: Definitive studies of the longer-term effects of LISA are lacking. We aimed to evaluate, in preterm infants 25-28 weeks' gestation, the effect of LISA on neurodevelopment and respiratory health during the first 2 years of life.
METHODS: In this blinded randomised controlled trial (OPTIMIST-A, ACTRN12611000916943), infants supported with CPAP and requiring FiO_2 ≥0.30 before 6 h received LISA (200 mg/kg poractant alfa delivered via thin catheter) or sham treatment (control), with continuation of CPAP thereafter unless predefined intubation criteria were met. Beyond the previously reported in-hospital outcomes (JAMA 2021;326:2478), data were gathered on respiratory health and further hospitalisations in the first 2 years and presence of neurodevelopmental disability (NDD: moderate-severe cognitive or language impairment, cerebral palsy, vision or hearing impairment) at 2 years corrected age (CA). Modes of outcome ascertainment were i) parent-completed online questionnaire including the Parent Report of Children's Abilities – Revised (83%); ii) face-to-face assessment including Bayley III psychometric testing (10%); or iii) abbreviated questionnaire (7%). Primary outcome was the composite of death or NDD. Treatment effects were estimated as relative risk (RR) with 95% confidence interval (CI), adjusted for gestation strata and site clustering.

RESULTS: 485 infants were randomised at 33 sites. Data were available at 2 years CA in 453 infants (LISA: N=224 [29 deaths < 2 years; 195/212 survivors with follow-up data]; control: N=229 [24 deaths; 205/220 survivors with follow-up data]). The treatment groups showed good prognostic balance (Table). Incidence of death or NDD was similar in the two groups, as were the rates of the primary outcome components (death, NDD) (Table). There was, however, an important difference favouring the LISA group in need for hospitalisation in the first 2 years for any illness (RR 0.78; 95% CI: 0.66–0.92) and for respiratory illness (RR 0.66; 95% CI: 0.54–0.81), as well as a reduction in wheezing and breathing difficulty, use of bronchodilator therapy and diagnosis of asthma (Table).

CONCLUSION: Application of LISA in the first 6 h may considerably reduce the burden of respiratory illness in the first two years of life, with no effect on neurodevelopmental outcome at 2 years CA.

Table: Baseline variables and outcomes

BASELINE VARIABLES	LISA	Control		
Gestation, weeks	27.3 (26.3–28.1)	27.3 (26.4–28.0)		
Birth weight (g)	932 (780–1065)	905 (777–1070)		
Male sex	116/224 (52%)	109/229 (48%)		
Multiple birth	84/224 (38%)	71/229 (31%)		
Antenatal steroids (any)	204/224 (91%)	210/229 (92%)		
Caesarean delivery	184/224 (82%)	180/229 (79%)		
Apgar score at 5 min	8 (7–9)	8 (7–9)		
Age at randomisation (h)	2.7 (1.6–4.0)	2.6 (1.7–3.6)		
Immunised <2 yrs against: RSV Influenza	119/175 (68%) 91/173 (53%)	128/185 (69%) 104/184 (57%)		
Family history of asthma (in parents or siblings)	50/177 (28%)	53/188 (28%)		
OUTCOMES	LISA	Control	Adjusted relative risk (95% CI)	P value
Death or NDD*	78/215 (36.3%)	79/219 (36.1%)	1.00 (0.81 to 1.24)	0.99
Death prior to 2 years CA	29/224 (12.9%)	24/229 (10.5%)	1.23 (0.69 to 2.19)	0.48
NDD in survivors to 2 years CA	49/186 (26.3%)	55/195 (28.2%)	0.94 (0.71 to 1.25)	0.69
Cognitive or language impairment	42/183 (23.0%)	47/195 (24.1%)	0.96 (0.73 to 1.27)	0.77
Cerebral palsy (equivalent to GMFCS level ≥2)	9/195 (4.6%)	15/204 (7.4%)	0.63 (0.36 to 1.11)	0.11
Visual impairment	0/193 (0.0%)	5/204 (2.5%)	Not estimable	-
Hearing impairment	4/194 (2.1%)	4/205 (2.0%)	1.06 (0.31 to 3.61)	0.93
One or more hospitalisation† with any illness in first 2 years	77/194 (39.7%)	104/204 (51.0%)	0.78 (0.66 to 0.92)	0.003
One or more hospitalisation† with respiratory illness in first 2 years	49/195 (25.1%)	78/204 (38.2%)	0.66 (0.54 to 0.81)	<0.001
Parent-reported wheezing/breathing difficulty	73/180 (40.6%)	104/194 (53.6%)	0.76 (0.63 to 0.90)	0.002
Any bronchodilator therapy	57/180 (31.7%)	83/194 (42.8%)	0.74 (0.57 to 0.96)	0.026
Parent report of physician diagnosis of asthma	8/180 (4.4%)	23/194 (11.9%)	0.37 (0.19 to 0.73)	0.004

n/N (%) or median (interquartile range).
*Primary outcome not determinable for 9 infants (LISA), 10 infants (control).
†Excluding birth hospitalisation.
GMFCS: gross motor function classification system; RSV: respiratory syncytial virus.
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*Primary outcome not determinable for 9 infants (LISA), 10 infants (control).
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GMFCS: gross motor function classification system; RSV: respiratory syncytial virus.

ID 218. INTERMITTENT SIGH BREATHS DURING HIGH-FREQUENCY OSCILLATORY VENTILATION ARE ASSOCIATED WITH IMPROVED VENTILATION DISTRIBUTION IN PRETERM INFANTS

Doctor Christian Heiring[1], PhD Judith Hough[2], Associate Professor Luke Jardine[3,6], Professor Gorm Greisen[1,5], M. Hough[4], M. Steele[2]
[1]Rigshospitalet, [2]Australian Catholic University, [3]Mather Health, [4]University of Waterloo, [5]Institute of Clinical Medicine, Copenhagen University, [6]The University of Queensland

Background and Aims:
Recruitment maneuvers during high frequency oscillatory ventilation (HFOV) are used to open collapsed alveoli. However, the increase in mean airway pressure could also lead to hyperinflation and volutrauma incurring further lung damage. Using intermittent sigh breaths during HFOV has been proposed as an alternative. The aim of this study was to determine if HFOV with intermittent sigh breaths, compared to HFOV alone, could improve ventilation distribution and oxygenation, in preterm infants with hypoxic respiratory failure (HRF).

Methods:
In this prospective interventional cross-over study, ventilated preterm infants < 30 weeks gestational age randomly received HFOV with sigh breaths followed by HFOV-only for alternating two hour periods. Sigh breaths were delivered with an inspiratory time of 1 second, a peak inspiratory pressure (PIP) of 30 cmH20 and a frequency of 3 breaths/minute. During sigh breath periods the set-mean airway pressure (MAP) was reduced in proportion to the difference between PIP and set-MAP to keep the mean airway pressure constant.
Electrical impedance tomography (EIT) measured ventilation distribution (end-expiratory lung volume (EELV), global inhomogeneity (GI), and amplitude), and physiological variables were recorded to monitor oxygenation.

Results:
Sixteen infants (10 males, 6 females) were included in the study with a median (range) gestational age of 25.5 weeks (23-31), weight of 950 grams (660-1920), and postnatal age of 25 days (3-49).
EIT identified that the addition of sigh breaths resulted in a significantly higher EELV (p=0,04;). This was primarily due to an increase in ventilation in the posterior (dependent) lung.
SpO2 was improved and FiO2 lower (p<0.05) during sigh breaths, and SpO2/FiO2 accordingly higher although not statistically significant (291 +-/ 26 vs 250 +/-27, p=0.17)

Conclusion:
This is the first study to use EIT during HFOV-sigh breaths to assess distribution of ventilation. Intermittent sigh breaths during HFOV were associated with improved distribution of ventilation and lower oxygen requirement in preterm infants with HRF.

	No Sigh	Sigh	Sigh p-value	Baseline	30 min	60 min	Time p-value
	Mean ± SE (95% CI)			Mean ± SE (95% CI)			
EIT							
Amp - Global	0.01 ± 0.002 (0.01-0.02)	0.02 ± 0.01 (0.01-0.03)	0,26	0.01 ± 0.002 (0.004-0.01)	0.01 ± 0.002 (0.01-0.02)	0.02 ± 0.01 (0.01-0.03)	0,05
Amp - R	0.02 ± 0.003 (0.01-0.02)	0.03 ± 0.007 (0.02-0.04)	0,24	0.01 ± 0.003 (0.01-0.02)	0.02 ± 0.004 (0.01-0.03)	0.02 ± 0.007 (0.01-0.04)	0,08
Amp - L	0.01 ± 0.002 (0.01-0.02)	0.01 ± 0.002 (0.01-0.02)	0,07	0.01 ± 0.002 (0.01-0.01)	0.01 ± 0.002 (0.01-0.02)	0.01 ± 0.002 (0.01-0.02)	0,16
Amp - A	0.01 ± 0.003 (0.01-0.02)	0.02 ± 0.004 (0.01-0.03)	0,16	0.02 ± 0.004 (0.01-0.02)	0.02 ± 0.003 (0.01-0.02)	0.02 ± 0.003 (0.01-0.02)	0,63
AMP - P	0.02 ± 0.003 (0.01-0.02)	0.03 ± 0.01 (0.01-0.04)	0,18	0.01 ± 0.004 (0.005-0.02)	0.02 ± 0.003 (0.01-0.02)	0.03 ± 0.007 (0.01-0.04)	0,18
EELV - Global	0.05 ± 0.02 (0.01-0.10)	0.12 ± 0.03 (0.05-0.18)	0.04*	0.00 ± 0.002 (-0.01 - -0.001)	0.08 ± 0.03 (0.02-0.14)	0.11 ± 0.04 (0.04-0.19)	0.03*
EELV - R	0.06 ± 0.03 (0.01-0.12)	0.14 ± 0.05 (0.05-0.24)	0,08	0.00 ± 0.001 (-0.01 - -0.004)	0.10 ± 0.04 (0.02-0.19)	0.14 ± 0.05 (0.05-0.23)	0.02*
EELV - L	0.04 ± 0.02 (-0.01-0.08)	0.09 ± 0.03 (0.03-0.16)	0.01*	0.001 ± 0.001 (-0.004-0.002)	0.06 ± 0.03 (0.01-0.12)	0.09 ±0.04 (0.01-0.16)	0.04*
EELV - A	0.06 ± 0.04 (-0.01-0.14)	0.12 ± 0.05 (0.02-0.22)	0,23	0.00 ± 0.003 (-0.01 - -0.002)	0.09 ± 0.04 (0.01-0.17)	0.13 ± 0.06 (0.001-0.26)	0,18
EELV - P	0.04 ± 0.02 (-0.003-0.08)	0.10 ± 0.04 (0.03-0.18)	0.04*	0.00 ± 0.002 (-0.01 - -0.002)	0.07 ± 0.03 (0.01-0.14)	0.08 ± 0.04 (0.02-0.16)	0,14
Avg GI Index	0.51 ± 0.01 (0.48-0.54)	0.49 ± 0.14 (0.46-0.51)	0,52	0.54 ± 0.03 (0.49-0.59)	0.49 ± 0.01 (0.46-0.51)	0.49 ± 0.01 (0.46-0.52)	0.04*
Physiological							
SpO2	92.16 ± 0.49 (91.19-93.012)	95.02 ± 0.56 (93.93-96.11)	0.00*	93.06 ± 0.74 (91.60-94.51)	93.51 ± 0.54 (92.46-94.56)	93.22 ± 0.53 (92.18-94.26)	0,26
SpO2/FiO2	249.58 ± 26.57 (197.51-301.65)	291.12 ± 25.51 (241.13-341.12)	0,17	251.12 ± 23.54 (204.98-297.27)	262.74 ± 23.21 (217.25-308.22)	277.19 ± 22.30 (233.49-320.90)	0,20
HR	157.58 ± 3.60 (150.53-164.64)	157.01 ± 3.35 (150.45-163.57)	0,80	160.30 ± 4.81 (150.86-169.73)	156.60 ± 3.04 (150.64-162.57)	156.63 ± 3.06 (150.62-162.64)	0,49
SBP	69.33 ± 3.40 (62.68-75.99)	66.07 ± 3.47 (59.27-72.86)	0,24	67.86 ± 3.43 (61.14-74.58)		67.54 ± 3.37 (60.93-74.15)	0,90
DBP	34.89 ± 1.70 (31.56-38.23)	34.66 ± 2.56 (29.65-39.67)	0,91	34.75 ± 2.31 (30.22-39.28)		34.80 ± 1.99 (30.90-38.70)	0,98
Mean BP	49.75 ± 2.46 (44.93-54.58)	48.25 ± 3.31 (41.76-54.74)	0,44	49.22 ± 3.27 (42.81-5564)		48.78 ± 2.68 (43.52-54.05)	0,85
Ventilator settings							
FiO2	40.18 ± 3.29 (33.73-46.63)	37.07 ± 2.85 (31.49-42.65)	0.05*	38.92 ± 2.92 (33.19-44.64)	39.22 ± 3.06 (33.23-45.21)	38.66 ± 3.20 (32.40-44.93)	0,19
MAP-measured	12.72 ± 0.65 (11.44-14.00)	12.50 ± 0.58 (11.36-13.64)	0,41	12.72 ± 0.66 (11.42-14.01)	12.58 ± 0.61 (11.38-13.77)	12.65 ± 0.60 (11.47-13.82)	0,80
MAP-set	12.85 ± 0.62 (11.64-14.06)	11.91 ± 0.60 (10.72-13.08)	0.00*	12.41 ± 0.61 (11.22-13.60)	12.36 ± 0.61 (11.16-13.56)	12.36 ± 0.61 (11.16-13.56)	0,79
Amplitude	18.62 ± 1.02 (16.83-2081)	19.26 ± 0.95 (17.39-21.12)	0,26	18.58 ± 1.09 (16.44-20.72)	18.89 ± 1.00 (16.94-20.84)	19.30 ± 0.95 (17.43-21.17)	0,32
MV	1.27 ± 0.09 (1.11-1.45)	1.32 ± 0.11 (1.11-1.53)	0,63	1.26 ± 0.08 (1.09-1.42)	1.26 ± 0.10 (1.06-1.46)	1.33 ± 0.11 (1.12-1.55)	0,33
DCO2	48.87 ± 5.34 (38.40-59.34)	53.40 ± 7.58 (38.53-68.26)	0,47	46.58 ± 4.96 (36.86-56.30)	50.41 ± 6.62 (37.43-63.40)	53.01 ± 6.86 (39.56-66.45)	0,54
Leak	1.69 ± 1.64 (-1.54-4.91)	0.69 ± 0.67 (-0.62-2.00)	0,31	2.37 ± 2.30 (-2.12-6.87)	1.11 ± 1.09 (-1.02-3.25)	0.92 ± 0.90 (-0.85-2.69)	0,57
Vosc	2.39 ± 0.24 (1.92-2.86)	3.02 ± 0.52 (1.99-4.04)	0,31	2.30 ± 0.17 (1.96-2.63)	2.87 ± 0.53 (1.84-3.90)	2.58 ± 0.33 (1.93-3.23)	0,82
Freq	10,69	10,69	0,00	10,69	10,69		0,00
Hz	10,69	10,69	0,00	10,69	10,69	10,69	0,00
PIP		30,00	0,00		24,00	24,00	
SD GI Index	0.04 ± 0.004 (0.03-0.05)	0.0409 ± 0.004 (0.03-0.05)	0,95	0.0382 ± 0.004 (0.03-0.05)	0.0401 ± 0.004 (0.03-0.05)	0.0419 ± 0.005 (0.03-0.05)	0,62
GC – xGlobal	17.44 ± 0.33 (16.81-18.08)	17.13 ± 0.34 (16.45-17.80)	0,87	18.15 ± 0.67 (16.83-19.47)	17.18 ± 0.28 (16.64-17.72)	17.04 ± 0.36 (16.32-17.75)	0,29
GC – yGlobal	17.44 ± 0.34 (16.76-18.11)	17.65 ± 0.37 16.93-18.37	0,59	17.28 ± 0.53 16.24-18.33	17.54 ± 0.35 16.85-18.23	17.62 ± 0.37 16.90-18.34	0,88

AMP, EELV, Avg GI: EIT meausures. EELV=end expiratory lung volume
SpO2 and FiO2: pulse oximetry and fraction of inspired oxygen
MAP, PIP = mean airway an peak inspiratory pressure

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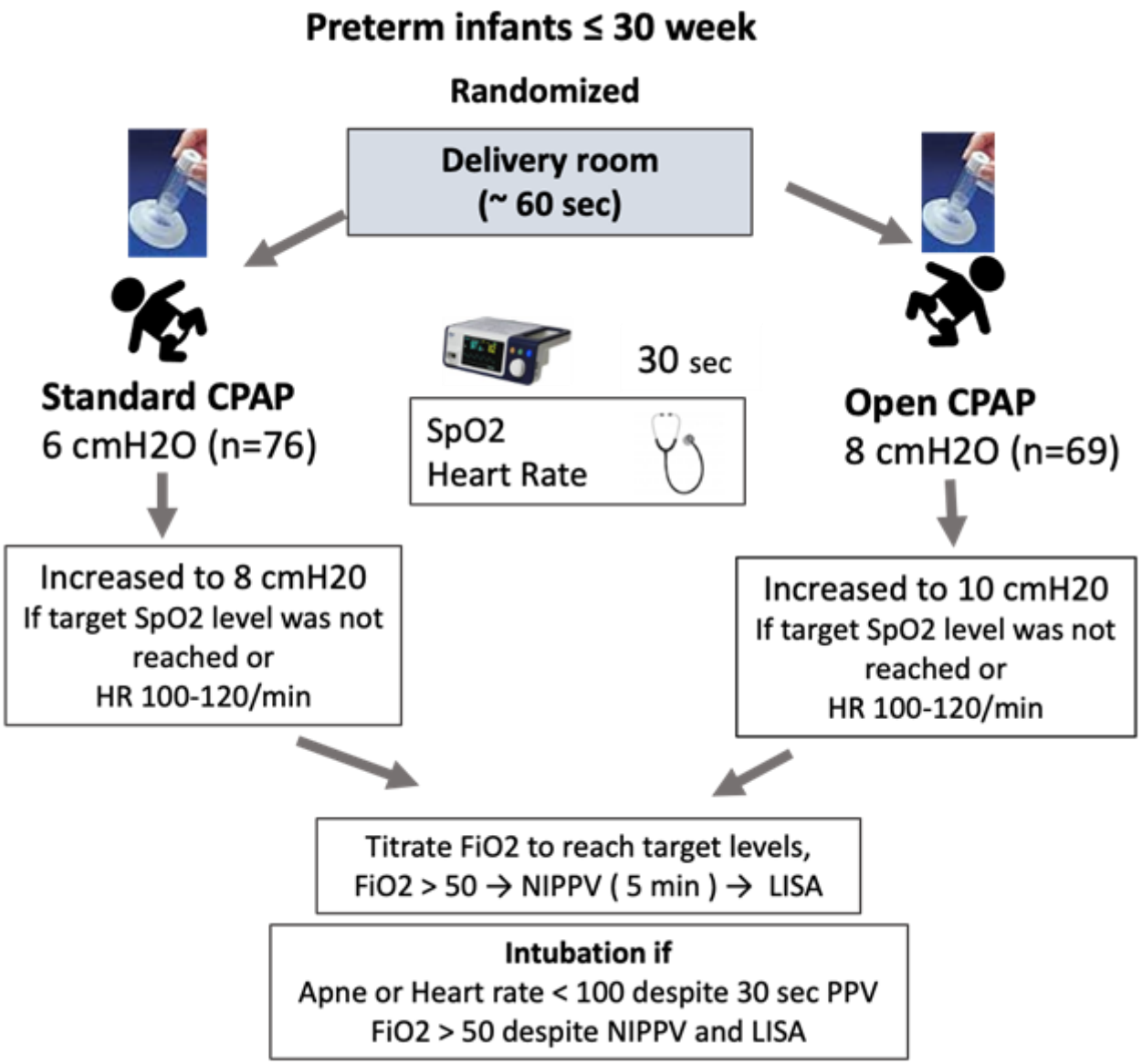
ID 929. Can Open Lung Strategy in the Delivery Room Reduce CPAP Failure in Very Preterm Infants ? Randomized Controlled Trial Using Two Different Pressure Ranges (OpenCPAP-DR)

Prof. Nuray Duman[1], Assoc. Mehtap Durukan Tosun[2], Doctor Funda Erdogan[1], M.D. Tugba Egeli[1], Professor Ahmet Yagmur Bas[3], M.D. Merve Unal[1], M.D. Burak Deliloglu[1], M.D. Can Akyıldız[1], M.D. Coskun Armagan[1], M.d. Ali Haydar Sever[1], M.D, PhD Pembe Keskinoglu[4], M.D. Nihal Demirel[3], M.D. Hasan Ozkan[1]
[1]Dokuz Eylül University- Faculty of Medicine, Department of Pediatrics, Division of Neonatology , [2]Department of Neonatology, Etlik Zubeyde Hanım Women's Health Training and Research Hospital, University of Health Sciences, [3]Department of Neonatology, Ankara Yıldırım Beyazıt University, [4]Department of Biostatistics, School of Medicine, Dokuz Eylul University

Background: Recommended standard CPAP pressures for delivery room management of very preterm infants may not meet the needs of individual babies. In this study, we aimed to compare the influence of individualised CPAP therapy applied with lung recruitment using different PEEP ranges on physiological parameters, and CPAP failure.

Methods: Eligible infants ≤30 weeks of gestation were randomized into standardCPAP or openCPAP groups according to initial CPAP levels of 6 or 8 cmH2O under 30% FiO2 following the initial steps of resuscitation.The heart rate(HR) and preductal saturation(SpO2) were evaluated every 30 seconds. Starting pressures were increased to the upper limit of 8 cmH2O for the standardCPAP group and 10 cmH2O for the openCPAP group if the heart rate and oxygen saturation targets were not achieved. FiO2 level was titrated if the target saturation was not reached with the upper pressure limits, and LISA threshold was FiO2 >50%. CPAP failure was defined as NIPPV, LISA or invasive MV requirement in the first 72 hours. Primary outcomes were FiO2 and SpO2 level at 5th /10th minutes, LISA requirement and CPAP failure within the first 72 hours (Clinical Trial NCT05031650).

Results: Among the 145 successfully randomized infants, 76 were in the standardCPAP group and the remainder in the openCPAP group. Mean gestational age and birth weights were 28.23±1.64 weeks and 1144±306 gram respectively. The need of PEEP adjustment to the upper limit was higher in the standardCPAP group(51.3% vs.30.4%,p=0.012). There were no significant difference between the groups in terms of FiO2 levels at 5th/10th minutes, LISA need in the delivery room or in the NICU. CPAP failure rate was higher in the standardCPAP group (72.4% vs 55.1%,p=0,038). Incidence of morbidities including pneumothorax, and/or mortality were similar.
Conclusion: This is the first clinical trial specifically assessed the effect of lung recruitment strategy using different PEEP levels in the delivery room management of very preterm infants. An individualised PEEP strategy starting with a PEEP level of 8 cmH2O seems to promote better lung aeration, and increased CPAP success. Further studies evaluating individualised PEEP strategy in delivery room accompanied with objective lung volume monitoring are needed.


Preterm infants ≤ 30 week
Randomized
Delivery room
(~ 60 sec)
Standard CPAP
6 cmH2O (n=76)
30 sec
SpO2
Heart Rate
Open CPAP
8 cmH2O (n=69)
Increased to 8 cmH20
If target SpO2 level was not reached or
HR 100-120/min
Increased to 10 cmH20
If target SpO2 level was not reached or
HR 100-120/min
Titrate FiO2 to reach target levels,
FiO2 > 50 → NIPPV (5 min) → LISA
Intubation if
Apne or Heart rate < 100 despite 30 sec PPV
FiO2 > 50 despite NIPPV and LISA

ID 680. HIGHER NCPAP TO PREVENT EXTUBATION FAILURE IN EXTREMELY PRETERM INFANTS: RESULTS OF ÉCLAT

Miss Anna Kidman[1,2,3], A/ Prof. Brett Manley[1,2], Dr Rosemarie Boland[1], A/ Prof. Susan Donath[5], A/ Prof. Atul Malhotra[3], Dr Friederike Beker[4], Professor Peter Davis[1,2], Dr Risha Bhatia[3]
[1]University Of Melbourne, [2]Newborn Research the Royal Women's Hospital, [3]Monash Newborn, [4]Mater Mothers Hospital , [5]The Clinical Epidemiology and Biostatistics Unit Murdoch Children's Research Institute

Background:
Up to 60% of extremely preterm infants (EPIs; <28 weeks) experience extubation failure. Clinicians aim to extubate EPIs to nasal continuous positive airway pressure (nCPAP) as soon as possible. The optimal nCPAP level to reduce extubation failure is unclear.

Methods:
EPIs were randomised to either higher nCPAP (9-11 cmH2O) or standard nCPAP (6-8 cmH2O) at the first extubation attempt following prospective informed consent. The primary outcome was extubation failure within 7 days, defined as 1) FiO2 ≥ 0.20 above baseline FiO2 prior to extubation; 2) pH <7.20 and pCO2 >60 mmHg; 3) > one apnoeic episode requiring intermittent positive-pressure ventilation within a 24-hour period, or ≥ six apnoeic episodes requiring stimulation within six consecutive hours; or 4) an urgent need for reintubation and mechanical ventilation.

Results:
138 infants, mean (SD) gestation 25.7(1.3) weeks with mean (SD) birthweight 777 (201)g were randomised. Extubation to a higher nCPAP range of 9-11 cm H2O reduced the risk of extubation failure from 57% to 35% (RD -0.22, 95% CI -0.38, -0.06). There were no important differences in maternal and infant demographics, or incidence of adverse events between groups: pneumothorax 1% vs. 1% (RD 0.00 95% CI -0.04, 0.04) and spontaneous intestinal perforation 3% vs. 1 % (RD 0.03, 95% CI -0.03, 0.08).

Conclusion:
Extubation of extremely preterm infants to higher nCPAP reduces extubation failure without increasing rates of adverse effects.