Combining Two Individualized Lung Recruitment Maneuvers at Birth for Very Preterm Infants: a Retrospective Cohort Study

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Introduction

Current international guidelines recommend starting resuscitation of premature infants with:

- an intermittent positive pressure ventilation (PPV),
- using a PEEP of 5-6 cmH₂O with
- the first insufflations of 2-3 s (but not greater than 5 s)

However, these measures are probably not sufficient for recruiting the optimal functional residual capacity (FRC).

Current knowledge on the respiratory transition at birth:

- **Phase 1** (30 sec to 5min): fetal lung fluid is evacuated. **Sustained inflation (SI)** aerates homogeneously the fluid-filled lungs.

- **Phase 2** (up to 4 h): accumulation of fluid in the interstitial space. **Adequate PEEP** helps to maintain the fluid in the interstitial tissue..

- **Phase 3:** Aerated lungs
(Hooper et al. *ADC Fetal & NN Ed.* 2016;101:F266)

Lung recruitment (LR) maneuvers at birth using SI were assessed in randomized controlled trials with promising but also limited results (Schmölzer et al. *ADC Fetal & NN Ed.* 2015;100:F361).

The **dynamic PEEP strategy**, assessed in animal models, is another maneuver able to establish an optimal FRC, as would an SI strategy optimized by Electrical Impedance

Tomography (Tingay et al. *AJP Lung Cell Mol Physiol.* 2017;312:L32).

As nobody knows what the optimal SI durations and PEEP levels are, we hypothesized that very preterm infants (VPIs) < 32 weeks require an individualized LR combining both maneuvers.

Objective

To evaluate whether combining two individualized LR maneuvers (SI and dynamic PEEP) at birth is superior to current international guidelines.

Methods

In this retrospective cohort study, 100 and 102 inborn VPI were enrolled between 2014 and 2016, before and after introducing LR maneuvers.

Inclusion criteria: Inborn VPI < 32 weeks, need for pulmonary resuscitation.

Exclusion criteria: associated congenital malformations.

Intervention: progressive increase in SI and PEEP (every 1 or 2 SI) in case of apnea and/or HR<100/min and/or FiO₂ > 0.4:

- SI: 3 to 5 to 10 to 15 seconds
- PEEP: 5 to 8 to 10 to 12 to 15 cmH₂O

SI's were stopped when spontaneous breathing was observed, while a gradual decrease in PEEP was performed at an FiO₂<0.4

Results

Very preterm infants < 32 weeks population characteristics	Period 1 (2014/2015) N=100	Period 2 (2016) N=102	p value
Female, n (%)	47 (47%)	41 (40%)	0,40
Birth Weight, g (median) [1 st Qu, 3 rd Qu]	1075 [850;1365]	1022 [888;1361]	0,98
Gestational age, wk (median) [1 ^{er} Qu, 3 ^e Qu]	29 [27;30]	28 [27;30]	0,50
Intrauterine Growth Restriction < 3 rd p, n (%)	25 (25%)	23 (23%)	0,81
Cesarean Section, n (%)	60 (60%)	73 (72%)	0,11
Antenatal corticosteroids, n (%)			
- None	15 (15%)	11 (11%)	0,61
- One dose	21 (21%)	20 (19%)	
- Two doses	64 (64%)	71 (70%)	
Premature birth causes, n (%)			
- Chorioamnionitis	30 (30%)	23 (23%)	0,55
- Preeclampsia + abnormal Fetal Heart Rate	44 (44%)	54 (53%)	
- Others	12 (12%)	13 (13%)	
- Idiopathic	14 (14%)	12 (12%)	

Respiratory Outcomes Black: < 32 weeks Red: < 29 weeks	Period 1 2014/2015 N=100/ N=49	Period 2 2016 N=102/ N=59	P value	Adjusted P value
Intubation in the Delivery Room, n (%)	69 (69%) 44 (90%)	50 (49%) 34 (58%)	0.006 0.0005	0.001 0.005
INSURE Procedure, n (%)	1 (1%) 1 (2%)	7 (6.9%) 4 (6.8%)	0.065 0.37	
MV <72h, n (%)	75 (75%) 45 (92%)	60 (61%) 40 (71%)	0.053 0.012	0.012 0.027
Duration of MV <72h, h (median) [1 st Qu, 3 rd Qu]	12.5 [1.5-48] 42 [9-72]	7 [0-41] 12 [0-48]	0.064 0.009	
2 nd dose of Surfactant, n (%)	18 (18%) 17 (35%)	8 (7.8%) 7 (12%)	0.052 0.009	0.005 0.003
Total Duration of MV, d (median) [1 st Qu, 3 rd Qu]	1 [0-5] 5 [1-20]	1 [0-7] 4 [0-10]	0.86 0.12	
HFO, n (%)	26 (26%) 24 (49%)	34 (33%) 19 (32%)	0,32 0.12	
Postnatal Corticosteroids, n (%)	29 (29%) 24 (49%)	16 (15%) 14 (24%)	0,035 0.011	0,0006 0.002
Physiologic BPD at 36 weeks, n (%)	14 (14%) 10 (20%)	6 (5.9%) 5 (8.5%)	0.09 0.13	0.027 0.091

INSURE: intubation-surfactant-extubation; MV: mechanical ventilation; HFO: high frequency oscillation; BPD: bronchopulmonary dysplasia.

Mortality & Morbidity Black: < 32 weeks Red: < 29 weeks	Period 1 2014/2015 N=100/N=49	Period 2 2016 N=102/N=59	P value
Mortality, n (%)	9 (9%) 7 (14%)	13 (13%) 12 (20%)	0.53 0.57
Bronchopulmonary Dysplasia and/or Mortality, n (%)	23 (23%) 17 (35%)	19 (19%) 17 (29%)	0.55 0.65
Pneumothorax, n (%)	1 (1%) 1 (2%)	1 (1%) 1 (1.7%)	1 1
Treated Patent Ductus Arteriosus, n (%)	15 (15%) 15 (31%)	21 (21%) 17 (29%)	0.4 1
Intraventricular Hemorrhage grade 3-4, n (%)	2 (2%) 2 (4.1%)	6 (5.9%) 6 (10%)	0.3 0.3
Periventricular Leukomalacia, n (%)	4 (4%) 2 (4.1%)	1 (1%) 1 (1.7%)	0.2 0.6
Enterocolitis > 2a, n (%)	4 (4%) 3 (6.1%)	5 (4.9%) 4 (6.8%)	0.6 0.6
Retinopathy of Prematurity > grade 2, n (%)	1 1	0 0	0.36 0.5

Conclusion

In our setting, combining two individualized LR manoeuvres at birth showed significant benefits, on short- and mid-term pulmonary outcomes without increasing morbidity or mortality. These results may open the door to a randomized controlled trial.