

# Pulmonary Recruitment Strategy in Preterm Neonates < 29 Weeks of Gestational Age to Reduce the Need for Intubation in the Delivery Room

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## Abstract

**Background** The application of noninvasive ventilation (NIV) modalities from birth in the delivery room (DR) during fetal–neonatal transition reduces the need for invasive mechanical ventilation, mortality, and bronchopulmonary dysplasia (BPD). The use of a RAM nasal cannula (RAM NC) in the DR for resuscitation results in less need for intubation, chest compressions, and epinephrine administration when compared with using a face mask for PPV in the DR.

**Objective** To evaluate the need for endotracheal intubation in the DR among extremely low gestational age neonates treated at birth with sustained inflation (SI) followed by a nasal continuous positive airway pressure (NCPAP) (range: 6–8 cm of H<sub>2</sub>O) delivered through the RAM NC.

**Study Design** A retrospective study was conducted to compare the use of NIV techniques in the DR and the need for intubation in the DR in premature infants 23 to 28 weeks' gestational age from December 2016 to July 2018 (group A). These data were compared with those of premature inborn infants with similar GA born between April 2015 and November 2016 (group B). In the DR, immediately after birth, neonates in group A received SI through RAM NC followed by CPAP ranging from 6 to 8 cm H<sub>2</sub>O, whereas the neonates in group B were treated in the DR with SI administered through a face mask followed by the application of CPAP of 5 cm H<sub>2</sub>O delivered through a nasopharyngeal tube.

**Results** A total of 65 preterm infants 23 to 28 weeks of gestational age, 31 in group A and 34 in group B, were included in the study. The percentage of neonates intubated in the DR was significantly lower in group A ( $p < 0.008$ ). In both groups, no neonates died in the DR, and no one required epinephrine and/or chest compressions. For those neonates who did not require intubation in the DR, there was no significant difference in the average FiO<sub>2</sub> on arrival in the neonatal intensive care unit, rate of intubation

## Keywords

- ▶ neonatal noninvasive ventilation
- ▶ RAM nasal cannula
- ▶ pulmonary recruitment
- ▶ incremental PEEP in DR

within 24 hours, and use of surfactant. The incidence of BPD was similar in the two groups. Only one infant in group A developed moderate BPD, and no one needed oxygen and/or ventilatory assistance at discharge. Mortality was similar in the two groups, with a slight prevalence in group B (27.7 vs. 19.2%).

**Conclusion** SI with RAM NC followed by NCPAP ranging from 6 to 8 cm H<sub>2</sub>O, administered with RAM NC resulted in a significant reduction of intubation in the DR.

Respiratory distress syndrome (RDS) is the most frequent cause of respiratory failure in preterm infants. Incidence of RDS is inversely related to gestational age, with the highest incidence in preterm infants < 29 weeks of gestational age (GA). In the extremely low birth weight infants (<1,000 g), the need for invasive mechanical ventilation (MV) is also high. Avoiding early invasive MV results in a decrease in ventilator-associated lung injury and ventilator-associated brain injury.<sup>1,2</sup>

A recent systematic review and meta-analysis of a population of preterm infants < 32 weeks of GA reported that application of noninvasive ventilation (NIV) modes from birth results in less need for invasive MV and less bronchopulmonary dysplasia (BPD).<sup>3</sup> The fetal-neonatal transition represents a crucial moment of rapid physiological changes in respiratory function and hemodynamics, and a protocol that provides NIV support in the delivery room (DR) reduces mortality, BPD, and severe intraventricular hemorrhage.<sup>4,5</sup> Achieving and maintaining functional residual capacity (FRC) through pulmonary recruitment strategies is the main goal of the neonatologists in the DR.<sup>6</sup>

Several patient nasal interfaces such as binasal prongs, nasal mask, and a modified nasal cannula ([NC] RAM NC, Neotech RAM Cannula, Neotech Products, Valencia, CA) have been used in the DR during resuscitation. The use of RAM NC in the DR for resuscitation from a tertiary level neonatal center in the United States has been recently reported.<sup>7</sup> Interestingly, authors also used nasal intermittent positive pressure ventilation (NIPPV) as the mode of NIV, with a T-piece and RAM NC as the patient-nasal interface. In this retrospective study of very low birth weight infants, they showed that positive pressure ventilation (PPV) use in DR using RAM NC resulted in less need for intubation, chest compressions, and epinephrine administration when compared with a face mask for PPV in the DR.<sup>8</sup> Other pulmonary recruitment strategies in the DR, such as the use of sustained inflation (SI) and caffeine in the DR, are currently being evaluated.<sup>9,10</sup>

Since November 2016, as part of an ongoing trial named IN-REC-SUR-E (INtubate-REcruit-SURfactant-Extubate),<sup>11</sup> our group has standardized the approach to extremely low GA neonates (ELGANs) in the DR with the use of a protocol that includes SI<sup>9</sup> followed by a nasal continuous positive airway pressure (NCPAP) (range: 6–8 cm of H<sub>2</sub>O) delivered through RAM NC. Prior to this time period, these infants were resuscitated with SI using face mask followed by the application of CPAP of 5 cm H<sub>2</sub>O with a nasopharyngeal tube.

In this study, we evaluated the rate of intubation in the DR in premature infants 23 to 28 weeks of GA before and after the implementation of a standardized approach to ELGANs in the DR. Short-term outcomes were also compared between the two groups.

## Materials and Methods

A retrospective study was conducted to compare the use of NIV techniques in the DR and the need for intubation in the DR in premature infants 23 to 28 weeks' GA from December 2016 to July 2018 (group A). These data were compared with those of premature inborn infants with similar GA born between April 2015 and November 2016 (group B). Neonates with congenital malformations were excluded from the study.

In the DR, immediately after birth, neonates in group A received SI through RAM NC followed by CPAP ranging from 6 to 8 cm H<sub>2</sub>O, whereas the neonates in group B were treated in the DR with SI administered through a face mask followed by the application of CPAP of 5 cm H<sub>2</sub>O delivered through the nasopharyngeal tube. The decision to use the RAM NC in the DR was started in December 2015 when the use of this interface for NIV in neonatal intensive care unit (NICU) was successful even in extremely premature infants in our center. The goal was to avoid the nasal injuries, to improve patient and care provider comfort, and to reduce pulmonary derecruitment by using the same NC in the DR and in the NICU for ongoing respiratory support. The SI in group A was provided by placing the NC into both nostrils, holding the NC with the index finger and closing the mouth with the third to fifth fingers.<sup>8</sup> Subsequently, CPAP of 6 cm H<sub>2</sub>O was applied. The increase in CPAP up to 7 or 8 cm H<sub>2</sub>O was used to reach the oxygen saturation pulse oximeter (SpO<sub>2</sub>) target, as recommended by the European consensus guidelines for RDS management.<sup>12</sup> To avoid intubation, NIPPV was started (with peak inspiratory pressure [PIP] = 25, respiratory rate [RR] = 40, and FiO<sub>2</sub> > 40%), if necessary, to stabilize the neonate through the RAM NC.

Infants failing the aforementioned NIV strategies or infants with apnea or severe RDS with no improvement in heart rate or SpO<sub>2</sub> (refer to Wyllie et al<sup>13</sup>) were intubated. The NIPPV through RAM NC was continued during the process of intubation to provide oxygenation. Infants were transferred to NICU once stabilized on NIV with RAM NC or MV with an endotracheal tube (ETT). Also in group A, to reduce as much as possible the risk of pulmonary derecruitment during transport from the DR to NICU, CPAP or NIPPV

was provided using the transport ventilator, and after arrival in the NICU, patients were immediately placed on the ventilator using the same modality. Extensive training was provided to all staff in our NICU prior to implementing this strategy. In the neonates from group B, SI was applied with a face mask. Subsequently, CPAP of 5 cm of H<sub>2</sub>O was applied through the nasopharyngeal tube. NIPPV started to stabilize in those neonates who failed to improve at CPAP of 5 at the discretion of the care provider. Intubation criteria were similar to group A. Infants were transferred using CPAP or NIV through the nasopharyngeal tube or MV with ETT.

The rate of intubation in the DR was compared in both groups A and B. Infants not intubated in the DR were compared for the following: (1) intubation within the first 24 hours of life, (2) the incidence of pneumothorax (PNX) in the first 72 hours of life, (3) surfactant use, (4) the incidence of intraventricular hemorrhage (IVH), (5) the incidence of blood transfusions, (6) the incidence of BPD, (7) and the incidence of death.

### Statistical Analysis

The data are presented as median with interquartile range for dispersion for normally distributed continuous variables. Categorical variables are expressed as numbers and percentages. The clinical characteristics and outcome parameters were compared using Wilcoxon's rank-sum test for continuous variables, and chi-square test and Fisher's test (in case of expected frequency of less than 5) for categorical variables. A *p*-value of <0.05 was considered statistically significant.

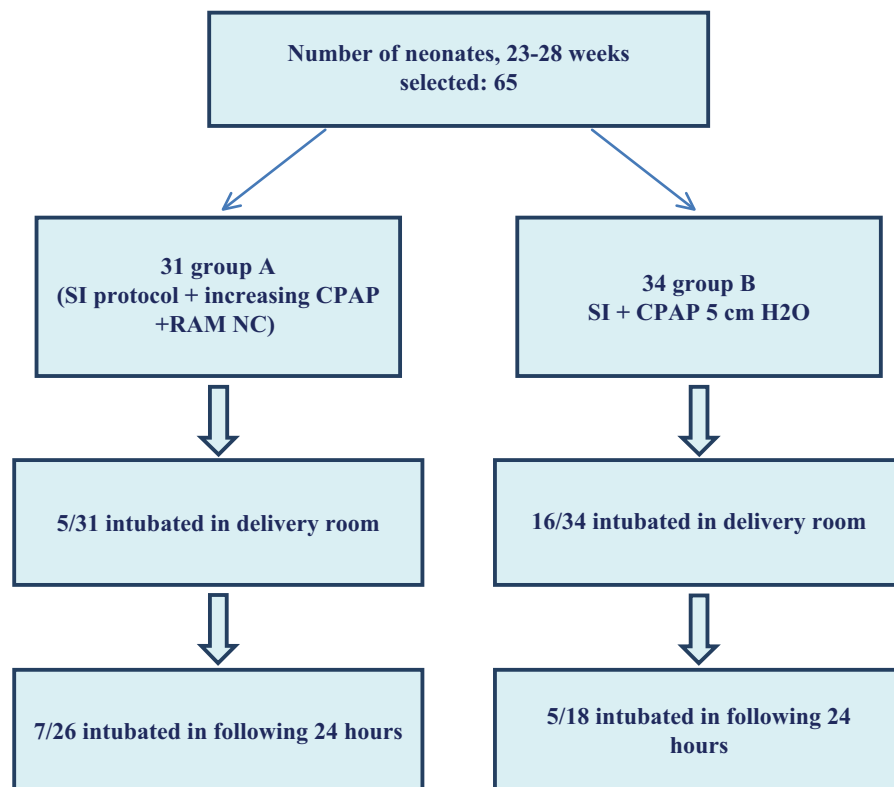
### Results

A total of 66 preterm infants 23 to 28 weeks of GA were born during these two time periods. There were 31 preterm neonates in group A and 34 neonates in group B. One infant was excluded from group A due to congenital heart disease (►Fig. 1).

►Table 1 compares the demographic data of the neonates in the two groups. Average birth weight and GA were similar, as well as the distribution of gender. Most mothers received at least one dose of corticosteroids before delivery; in group A, there was a significantly higher rate of mothers who received complete prophylaxis (two doses of corticosteroids) compared with group B (*p* = 0.01). There were no statistically significant differences between the two groups regarding the incidence of maternal complications, such as pregnancy-induced hypertension and preterm premature rupture of membranes, and mode of delivery.

The percentage of neonates intubated in the DR was significantly lower in group A (*p* < 0.008). In both groups, no neonates died in the DR, and no one required epinephrine and/or chest compressions. For those neonates who did not require intubation in the DR, there was no significant difference in the average FiO<sub>2</sub> on arrival in NICU, rate of intubation within 24 hours, and use of surfactant. No infants developed PNX in the first 72 hours of postnatal life (►Table 2).

Among the other data collected, for the infants of the two nonintubated groups in the DR, there was evidence in group A of a nonsignificant reduction in the incidence of grades III and IV IVH. The use of packed red blood cell transfusions was



**Fig. 1** Study flowchart. CPAP, continuous positive airway pressure; RAM NC, RAM nasal cannula; SI, sustained inflation.

**Table 1** Maternal and infants' characteristics

	Group A (n = 31)	Group B (n = 34)	p-Value
Birth weight, median (SD), grams	980 (375)	860 (275)	0,23
Gestational age, median (SD), weeks	27.6 (1,9)	27 (2.9)	0,23
Male, n (%)	16 (51,6)	22 (64,7)	0,28
Caesarean section, n (%)	22 (70,9)	23 (67,6)	0,8
Prenatal steroids, n (%)			
Any	3 (9.6)	8 (23.5)	0,19
Incomplete	5 (16.1)	11 (32.3)	0,27
Complete	23 (74.1)	15 (44.1)	0,01
Maternal preeclampsia	5 (16.1)	6 (17.6)	0,9
Premature rupture of membranes > 18 h	10 (32)	14 (41.1)	0,5
Apgar score at 5 min, median (IQR), %	9 (1)	9 (2)	0,45
Delivery room intubation, n (%)	5 (16.1)	16 (47)	0.008

Abbreviations: IQR, interquartile range; SD, standard deviation.

reduced in group A but was not statistically significant. Regarding the patent ductus arteriosus (PDA), the treatment with ibuprofen was necessary in 12.9% of the infants in group A and 27.7% of the infants in group B but was not statistically significant. In the latter, around 25% required surgical ligation. No patients required surgical ligation in group A.

**Table 2** Neonatal outcomes of the nonintubated in delivery room study groups

	Group A (n = 26)	Group B (n = 18)	p-Value
Respiratory outcomes in NICU			
FiO <sub>2</sub> In NICU, median (IQR)	0,25 (0,09)	0,25 (0,09)	0,49
Intubated in the following 24 h, n (%)	7 (26,9)	5 (27,7)	1
Surfactant, n (%)	15 (48.4)	10 (55.6)	0.63
Others outcomes			
PDA	4 (12.9)	5 (27.7)	0.44
Severe IVH, n (%)	1 (3,8)	3 (16,6)	0,3
RBC transfusions, n (%)	10 (38,4)	11 (61,6)	0,13
BPD, n (%)	2 (7,6)	1 (5,5)	1
Death, n (%)	5 (19,2)	5 (27,7)	0,7

Abbreviations: BPD, bronchopulmonary dysplasia; IQR, interquartile range; IVH, intraventricular hemorrhage; NICU, neonatal intensive care unit; PDA, patent ductus arteriosus; RBC, red blood cell; SD, standard deviation.

The incidence of BPD was similar in the two groups. Only one infant in group A developed moderate BPD, and no one needed oxygen and/or ventilatory assistance at discharge.

Mortality was similar in the two groups, with a slight prevalence in group B (27.7 vs. 19.2%).

## Discussion

The protocol adopted for group A: SI with RAM NC followed by NCPAP ranging from 6 to 8 cm, H<sub>2</sub>O administered with RAM NC, resulted in a significant reduction of intubation in the DR.

The SI was also a part of the protocol, although the efficacy of this technique has to be confirmed by the ongoing SAIL (Sustained Aeration of Infant Lungs) trial, and it is used routinely in the DR in most of the centers that use exclusively NIV to assist the neonates. In contrast, SI was administered by face mask in group B. SI is a useful technique to promote drainage of the alveolar fluid. This fluid accumulates in the interstitium and is subsequently drained through the lymphatic and capillary vessels. CPAP should be used to counteract the fluid back to the alveoli and to maintain the previous effect of SI.<sup>14</sup>

In group A, the combination of the pulmonary recruitment protocol with CPAP ranging from 6 to 8 cm H<sub>2</sub>O with the use of RAM NC significantly affected our results.

To obtain satisfactory respiratory work and oxygen saturation values within the expected range for minutes of life and GA, Mehler et al suggest to gradually increase CPAP also beyond 8 cm H<sub>2</sub>O in combination with SI. This approach would allow less intubation.<sup>4,5</sup>

The use of higher CPAP in the DR in group A was not a risk factor for PNX evaluated at 72 hours of life.

The recent European Guidelines for the management of the RDS recommend the use of face masks or short NCs<sup>12</sup> for the neonatal assistance in the DR. Maintaining the same NC to practice NIV and also during the transportation of the neonate from the DR to the NICU allows avoiding hazardous pulmonary derecruitment. Indeed, recently published researches emphasize the importance of maintaining CPAP and early recruitment in the DR.<sup>6</sup>

Reaching and maintaining an optimal FRC requires the ventilation with devices that allow maintaining an effective CPAP, avoiding pulmonary derecruitment. Therefore, it is extremely important to choose the short NC rather than the face mask to be positioned at birth and maintained for the subsequent NIV support.

The use of the face mask for SI and subsequent resuscitation is burdened by the consequences of both inadequate seal and obstruction of the airways related to poor positioning of the mask.<sup>15</sup> Some studies report that inadequate seal due to poor positioning of the mask can reach up to 75% leaks<sup>16</sup> in the first 2 minutes of life. The mask may require repeated readjustments to ensure good ventilation, causing a delay in achieving adequate ventilation. Furthermore, the use of the mask implies a transition to a different interface to allow the subsequent stabilization and the transport of the neonate to the NICU.

Thus, the short NC is a valid alternative to the mask to start and optimize the assistance in the DR. Paz et al and Capasso et al have shown how the use of NCs in the DR reduces the rates of intubation.<sup>7,17</sup> Moreover, the short NC, positioned immediately after birth, provides oxygenation even if the intubation becomes necessary.

We speculate that the lower incidence of IVH, transfusion, and treatment of PDA in group A, although not statistically significant, could be related to a lower recourse to intubation in the DR and in the following 24 hours of life.

We also speculate that the higher number of mothers of neonates in group A treated with complete steroid prophylaxis could have influenced the positive results of our protocol. That is why it is important to include steroid use in the model.

According to the most recent literature, this study shows how the adoption of a protocol aimed to recruit the lung (and keeping it well recruited) reduces the rate of intubation among those neonates 23 to 28 weeks of GA.<sup>4,5</sup>

Considering that it is a retrospective study and there are biases related to the small sample size, it would be necessary to promote a multicenter trial to evaluate the efficacy of the protocol and techniques performed in our study.

#### Conflict of Interest

None declared.

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