Open lung high frequency ventilation in preterm infants with respiratory distress syndrome: practical considerations and recommendations

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Chapter 6

Chest X-ray characteristics during oxygenation guided open lung ventilation in preterm infants with respiratory distress syndrome.

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Submitted

Abstract

Background: Neonatal respiratory distress syndrome (RDS) is characterized by a reduced lung inflation and an increased radiolucency score on the chest X-ray (CXR). These characteristics are based on CXRs from conventionally ventilated preterms and may be different during open lung high frequency ventilation (OL-HFV), which aims to recruit collapsed alveoli.

Objective: Evaluate CXR characteristics during oxygenation guided OL-HFV in preterm infants with RDS, before and after surfactant therapy.

Materials and methods: Two pediatric radiologists scored the severity of RDS and the presence of lung hyperinflation and/or air leaks in 69 infants. A second analysis was performed in 39 patients treated with surfactant.

Results: After lung recruitment, the median RDS score was 2, with 44 (64%) infants having a score ≤ 2. Mostly mild hyperinflation was seen in 13 (19%) infants, with no air leaks. After surfactant RDS score improved in 62% of 39 paired CXRs ($p < 0.001$). Mild hyperinflation was seen in 9 (24%) patients.

Conclusion: Individual, oxygenation guided OL-HFV in preterm infants results in a relatively low RDS score on the CXR which is even further improved by surfactant treatment. Radiological signs of hyperinflation are rare and often mild and do not result in air leaks.

Introduction

Respiratory distress syndrome (RDS) is one of the most common causes of respiratory failure in preterm infants. Its diagnosis is based on clinical signs, including cyanosis at room air and respiratory distress, and a chest X-ray (CXR) showing reduced lung inflation and an opacity that ranges from diffuse granularity to a ground glass appearance (1). In an attempt to capture the severity of RDS, several scoring systems have been described based on the radiolucency of the lungs at CXR, using the presence or absence of an air bronchogram and the cardiomediastinal and diaphragmatic contours (2-4). Several studies in conventionally ventilated preterm infants with RDS have shown that the majority of these infants have a high pre-surfactant severity score on the first CXR, which tends to improve after surfactant treatment (5-8).

High frequency ventilation (HFV) is a frequently used lung protective ventilation mode in preterm infants with RDS (9). HFV is often combined with a recruitment procedure aiming to reverse atelectasis and stabilize lung volume at functional residual capacity, i.e. the optimal lung volume or open lung ventilation strategy (10-12). In daily practice most clinicians use oxygenation as an indirect bedside tool to optimize lung inflation (13,14). To date, the effect of such an oxygenation guided open lung ventilation strategy on the pre-surfactant severity score of RDS or the level of lung inflation on the CXR has not been studied. This information is especially important in light off previous studies reporting an increased incidence of lung over inflation and air leak syndrome in patients on HFV (15).

Therefore, the aim of this study is to evaluate the CXR characteristics of preterm infants with RDS ventilated with primary oxygenation guided open lung HFV before and after surfactant therapy. We were especially interested in (1) the RDS severity score after lung volume optimization, (2) the effect of surfactant therapy on this severity score, and (3) the incidence of hyperinflation and air leak syndrome following oxygenation guided lung recruitment.

Methods

The study was approved by the institutional review board.

Patients

The study was performed in the neonatal intensive care unit of the Emma Children's Hospital, Academic Medical Center (Amsterdam, the Netherlands), where preterm infants (gestational age <37 weeks) with a suspected diagnosis of RDS and failing nasal continuous positive airway pressure (nCPAP) are treated with primary open lung HFV. A detailed description of this open lung procedure has been published previously (13;16).

Briefly, collapsed alveoli/sacculi are first recruited by stepwise increasing the continuous distending pressure (CDP), until the fraction of inspired oxygen (FIO_2) is weaned to 0.25 (opening pressure or CDP_O). The CDP is than stepwise decreased until oxygenation deteriorates, indicating alveolar/sacullar collapse (closing pressure or CDP_C). Following a brief increase to CDP_O, the pressure is then set at 2 cm H_2O above the closing pressure (optimal pressure or CDP_{OPT}). Next, the position of the endotracheal tube is checked on a CXR unless this information is already available (e.g. intubation in another hospital with CXR taken). Patients are then treated with 100-200 mg/kg exogenous surfactant (Curosurf, Chiesi Pharmaceutici, Parma, Italy) and the CDP_{OPT} is once more determined as described above. In some patients umbilical lines are placed and the position is checked with a second CXR.

Patients were included in the study if they were ventilated with open lung HFV for RDS and had a CXR taken within a predefined time frame of 2 hours after reaching CDP_{OPT}. Post surfactant analysis was performed if a second CXR, taken within 6 hours after reaching post surfactant CDP_{OPT}, was available.

CXR acquisition and analysis

Bedside digital antero-posterior CXRs were taken according to a standard clinical procedure. The infant was placed in supine position directly on the flat panel detector inside the incubator and the radiograph was taken through the incubator canopy. Date and time of the different stages of lung recruitment before and after surfactant were prospectively collected and linked to the date and time of the CXR. The images were extracted from the picture archiving and communication system (IMPAX v. 4.5, Agfa Healthcare, Mortsel, Belgium) and were reviewed after DICOM anonimization. Studies were viewed under normal clinical conditions on a diagnostic workstation with Barco Coronis 2MP grayscale diagnostic medical display monitors (Barco, Kortrijk, Belgium).

The anonimized CXRs were interpreted, in random order, by two pediatric radiologists (RR 9 years experience and ED 4 years experience) blinded for all information related to the patients. Lung volume was assessed by scoring radiolucency, lung inflation and the presence of air leaks. Radiolucency was graded as described by Giedion (3) and Thome (4): grade 0: normal radiolucent lung fields with sharp cardiac and diaphragmatic margins; grade 1: slightly reduced radiolucency with still sharp cardiac and diaphragmatic margins; grade 2: markedly reduced radiolucency with retained cardiac and diaphragmatic margins; grade 3: severely reduced radiolucency with airbronchograms and blurred cardiac and diaphragmatic margins; grade 4: almost completely white lung fields with or without airbronchograms and barely visible cardiac and diaphragmatic margins. Lung hyperinflation was estimated through an inverted diaphragm shape and/ or the diaphragm position visible at more than 9 posterior ribs and/or the presence of lung

bulging. Three grades of hyperinflation were identified being mild, moderate and severe, correlating with respectively 1, 2 or all 3 aforementioned positive signs. Air leaks were classified as pneumothorax, tension pneumothorax, pulmonary interstitial emphysema , pneumomediastinum, pneumopericardium and/or subcutaneous emphysema. Computer assisted measurement (planimetry) of the CXR lung area was performed to assess lung volume. The projected area of the lung was measured using standard AGFA DICOM tools along the following borders: (1) lateral: the inner side of the ribcage; (2) inferior: the diaphragm; (3) medial: the lateral border of the thoracic spine; and (4) superior: the apex of the lung. The total lung surface area was defined as the sum of both lungs normalized for body weight.
In case of disagreement the CXRs were reevaluated by both radiologists in an attempt to reach consensus. The left and right lung were scored separately and in case of differences between both lungs the highest score was used for analysis.

Clinical data

The following patient characteristics were retrieved from the patient charts: gestational age, birth weight, use of antenatal steroids, route of delivery, five minute Apgar score, gender, singleton birth, surfactant therapy and the presence of air leaks during the admission. Data on ventilation settings, including airway pressures and FIO_2, at the different stages of lung recruitment, were prospectively recorded for each patient.

Statistical analysis

Statistical analysis was performed using SPSS version 18 (SPSS, Chicago, IL). Data are presented as mean ± standard deviation (SD) or median and interquartile range [IQR] depending on their distribution. The difference in radiolucency and inflation before and after surfactant was analyzed by paired Wilcoxon rank Sum test. The relationship between the CDP and the normalized lung surface area was analyzed using linear regression.

Results

Between March 2004 and August 2005 a total of 69 consecutive patients were included in the study and the basic characteristics are presented in Table 1. The first CXR was made at a median of 3.5 [2 - 9.5] hours after birth and 13 [4 - 32] minutes after completing the presurfactant recruitment procedure. Surfactant was administered in 67 (97%) of the included patients, but in only 39 patients a second CXR was made at a median of 135 [82 - 201] minutes after completing the postsurfactant recruitment procedure. In 11 (10 %) of the CXRs scoring was based on consensus.

Table 1: Patient and clinical characteristics. Data are presented as mean ± standard deviation unless stated differently.

	n 69
Gestational age, weeks	29 ± 2.4
Birth weight, gram	1250 ± 474
< 1000 gram, n (%)	24 (33)
SGA, n (%)	2 (3)
Antenatal steroids, n (%)	54 (74)
Complete course, n (%)	26 (36)
Delivery by Caesarean Section, n (%)	32 (44)
Male gender, n (%)	45 (62)
Singleton, n (%)	61 (84)
Five minute Apgar score, median [IQR]	8 [7 - 9]
Air leak during neonatal period n (%)	4 (6)
pulmonary interstitial emphysema	2 (3)
pneumothorax	2 (3)
other	0
Surfactant n (%)	67 (97)
CDP at 1st CXR, cm H_2O	15 ± 4.7
CDP at 2nd CXR, cm H_2O (n = 39)	9 ± 2.4
FIO_2 at 1st CXR, median [IQR]	0.25 [0.21 - 0.28]
FIO_2 at 2nd CXR median [IQR] (n = 39)	0.21 [0.21 - 0.25]

SGA, small for gestational age (< p2.3); CDP, continuous distending pressure; CXR, chest X-ray; FIO_2, fraction of inspired oxygen.

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The presurfactant recruitment procedure resulted in a $FIO_2 \leq 0.25$ in 49 (71%) and ≤ 0.30 in 63 (91 %) patients. Assessment of the radiolucency showed that the majority of infants 44 (64%) had a RDS score ≤ 2 with a median (IQR) score of 2 (1,3). In addition, the recruitment procedure only resulted in mild and moderate signs of hyperinflation in respectively 8 (12%) and 5 (7%) patients. None of the CXRs showed signs of air leaks (Table 2).

Table 2: Frequency distribution in numbers (%) of radiolucency, hyperinflation and air leaks at first CXR (n=69) and second CXR, after surfactant (n=39).

	All children	After surfactant
	n 69	n 39
Lung radiolucency		
grade 0	5 (7)	7 (18)
grade 1	22 (32)	20 (51)
grade 2	17 (25)	8 (21)
grade 3	23 (33)	3 (7)
grade 4	2 (2)	1 (3)
Median (IQR)	2 (1)	1 (1)
Lung hyperinflation		
mild	8 (12)	8 (21)
moderate	5 (7)	1 (3)
Planimetry		
surface lung area (cm^2)	15.8 ± 2.6	15.8 ± 2.3
Air leak		
any	0	0

IQR: interquartile range

Following surfactant treatment, there was a clear shift to lower RDS scores, with a median (IQR) score of 1 [1,2] (Table 2). On an individual level, RDS score improved in 62% of the 39 paired CXRs ($p < 0.001$, Table 3). After surfactant therapy there was no changes in the hyperinflation score in 23 (59%) patients, in 7 (18%) patients the score increased to mild or moderate, and in the remaining 9 (23%) patients hyperinflation decreased or disappeared. Again, air leaks were not encountered.

The normalized lung surface area was similar both before and after surfactant treatment (Table 2) and no correlation was found with the CDP_{OPT}.

Table 3: Change in radiolucency grades before and after surfactant administration.

calculated difference of radiolucency grade	number (%)	N =39
-2	1 (2.6)	same or worse 15 (38%)
-1	4 (10.3)	
0	10 (25.6)	
1	14 (35.9)	improved 24 (62%)
2	8 (20.5)	
3	2 (5.1)	

Calculated difference of radiolucency grade obtained by subtracting radiolucency grade before surfactant therapy and radiolucency grade after surfactant therapy in 39 patients, with two available CXRs.

Discussion

To our knowledge this is the first study that describes the effect of an oxygenation guided lung recruitment procedure on the CXR characteristics of preterm infants with RDS. Our study shows that following presurfactant lung recruitment radiolucency is only mildly reduced in the majority of infants with RDS and surfactant treatment augments this finding. Furthermore, hyperinflation is uncommon and none of the infants showed signs of air leaks.

The severity score of RDS following lung recruitment is considerable lower than previously reported in conventionally ventilated preterm infants with RDS (5-8). There may be several reasons explaining this finding. First, and probably most important, the recruitment procedure used in our study resulted in opening and thus better aeration of collapsed alveoli/saculli which not only improved oxygenation (low FIO_2) but also radiolucency of the CXR. Such a recruitment procedure was not applied in previous studies including conventionally ventilated patients. Second, and in contrast to our study, infants in most of the previous studies did not receive antenatal steroids, which are known to reduce the severity of RDS (17). However, the fact that a more recent study in conventionally ventilated preterm infants with RDS also showed higher RDS scores, makes this a less likely explanation for the observed difference in lung aeration (6). Finally, other differences in patient characteristics between studies, such as gestational age, birth weight, and timing of the CXR, may also have affected the severity score of RDS. However, most of these differences were small and the impact on RDS score was probably limited as indicated by the comparable FIO_2 at the start of ventilation in this and other studies.

It was interesting to observe that in a minority of the cases RDS score was still severe (grade 3 and 4) despite the recruitment procedure. It is, however, important to realize that oxygenation is an indirect parameter of lung volume, highly dependent on changes in intrapulmonary right to left shunt. In case of extra pulmonary right to left shunt (pulmonary hypertension) or adequate hypoxic pulmonary vasoconstriction, oxygenation will fail as a reliable monitor for lung volume. Both these circumstances are sometimes encountered in preterm infants with RDS and may therefore explain the discrepancy between the recruitment procedure and the radiolucency of the CXR. In addition, diffuse haziness with decreased radiolucency on the CXR may also, in part, be explained by the presence of interstitial lung fluid which usually takes several hours to be cleared after birth (18;19).

Surfactant treatment resulted in a significant improvement in the RDS severity score, a finding consistent with previous studies in conventionally ventilated preterm infants with RDS (5-8). Based on the median RDS scores, this improvement is modest, a finding best explained by the fact that the lung was already recruited at the time of surfactant treatment. It is, however, important to realize that the postsurfactant RDS scores were obtained at much lower airway pressures than before surfactant treatment. This finding once again confirms the surface tension lowering properties of surfactant, allowing stabilization of lung volume at much lower airway pressures compared to the surfactant deficient lung (20).

Since its introduction in the early 90s, HFV has been associated with an increased risk of air leaks (15;21). Despite the fact that infants in this study were subjected to relatively high airway pressures during the recruitment procedure, the CXR only showed mild to moderate signs of hyperinflation in a small proportion of infants. Consistent with this finding, no air leaks were seen during or immediately after the recruitment procedure. Administering surfactant did not change these findings. To allow for a better comparison with previous studies on HFV, we also assessed the number of air leaks during the entire admission and found a relatively low incidence of 6% (22;23), confirming more recent studies showing no increased risk of air leaks during HFV in preterm infants with RDS (10;12).

We feel it is important to emphasize that the results reported in this study were obtained by using an individual approach during lung recruitment. By stepwise increasing and decreasing the airway pressures before and after surfactant treatment, we aimed to optimize lung volume for each individual patient with the lowest possible airway pressure, titrated for the individual severity of lung disease. The lack of a correlation between lung volumes measured by planimetry, a method know to correlate with functional residual capacity, and the optimal CDP before and after surfactant strongly suggests that we were successful in this approach (24-26).

To date only one study compared CXR characteristics in infants with RDS ventilated with either HFV or conventional ventilation (27). Helbich and colleagues reported a median RDS severity score of 4 on the first day of life, independent of the ventilation mode and after surfactant treatment. This RDS score in HFV infants is much higher than the median score of 1 in our study. This discrepancy is probably best explained by the fact that Helbich and colleagues used the CXR (inflation up to the dorsal part of the 9th rib) to monitor lung volume optimization and not oxygenation. A previous study showed that the correlation between lung inflation on the CXR and the functional residual capacity is probably poor (4). This line of reasoning is also supported by the large differences in median FIO_2 after lung recruitment and surfactant in our study (0.21) and the study of Helbich and colleagues (0.54).

This study has several limitations that need to be addressed. First, this study has no control group with patients on conventional ventilation, because all infants with RDS and failing nCPAP in our institution are treated with primary open lung HFV. For this reason we used the cohorts of conventionally ventilated patients with RDS described in previous studies to compare the CXR characteristics during open lung HFV. Although not ideal, we do feel such an indirect comparison provides valuable and valid information. Second, the timing of the CXR after lung recruitment and surfactant varied between patients, which may have caused some variation in the CXR characteristics. Finally, the fact that CXRs were only available in approximately half of the patients may have biased the results. The fact that we found an improvement in RDS score similar to previous studies in conventionally ventilated patients seems reassuring.

Conclusion

An individual oxygenation guided recruitment procedure during HFV in preterm infants with RDS improves radiolucency on the CXR and this is even further improved by surfactant treatment. Radiological signs of hyperinflation are rare and, when present, often mild and do not result in air leaks. These results indicate that RDS scoring systems cannot be used to compare severity of lung disease in preterm infants with RDS treated with different ventilation strategies and – more importantly - that from a radiological perspective open lung HFV is safe in preterm infants with RDS.

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