



Effectiveness of surfactant treatment and retreatment in moderately preterm infants

Carlo Dani^{1,2}, Simone Pratesi^{1,2}, Giulia Inguscio¹, Alessia Bonetti¹, Lara Devilli¹, Alessia Rizzello¹, Ginevra Prelazzi¹, Greta Mariani¹, Iuri Corsini^{1,2}

¹Department of Neurosciences, Psychology, Drug Research and Child Health, University of Florence, Florence, Italy; ²Division of Neonatology, Careggi University Hospital of Florence, Florence, Italy

Contributions: (I) Conception and design: C Dani, S Pratesi, I Corsini; (II) Administrative support: None; (III) Provision of study materials or patients: G Inguscio, A Bonetti, L Devilli, A Rizzello, G Prelazzi, G Mariani; (IV) Collection and assembly of data: G Inguscio, A Bonetti, L Devilli, A Rizzello, G Prelazzi, G Mariani; (V) Data analysis and interpretation: C Dani, S Pratesi, I Corsini; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Carlo Dani, MD. Department of Neurosciences, Psychology, Drug Research and Child Health, University of Florence, Florence, Italy; Division of Neonatology, Careggi University Hospital of Florence, Largo Brambilla 3, 50134 Florence, Italy. Email: carlo.dani@unifi.it.

Background: Respiratory distress syndrome (RDS) is commonly treated in preterm infants with surfactant and artificial respiratory support. However, their effects have been demonstrated in infants born before 30 weeks of gestational age, while there are no data on the efficacy of surfactant treatment and retreatment in the subgroup of moderately preterm infants (MPIs). We aimed to assess changes in oxygenation indices and RDS severity after surfactant administration in MPIs and to identify possible risk factors for the need for multiple doses of surfactant in these patients.

Methods: We conducted a retrospective study on 60 MPIs born between 30⁺⁰ and 33⁺⁶ weeks of gestational age who were affected by RDS and required surfactant treatment. Peripheral oxygen saturation (SpO₂)/fraction of inspired oxygen (FiO₂) ratio and arterial/alveolar partial pressure of oxygen (a/APO₂) ratio before and after the administration of the first and second surfactant doses were calculated. Clinical characteristics of infants who required one or more doses of surfactant were compared.

Results: A total of 48 infants (80%) received a single dose of surfactant, while 12 infants (20%) received multiple doses. Both the SpO₂/FiO₂ ratio and the a/APO₂ ratio significantly increased after the first and second doses of surfactant. However, we did not identify any clinical predictors for the need of surfactant retreatment in this population. Receiver operating characteristic (ROC) analysis indicated that the SpO₂/FiO₂ ratio measured 1 h after administration of the first dose is a significant predictor of the need for additional doses.

Conclusions: The first and second doses of surfactant improved the oxygenation indices and reduced the severity of RDS in MPIs. The post-surfactant SpO₂/FiO₂ ratio can be a useful adjunct in determining the need for additional doses of surfactant. These findings help further our understanding of the effects of surfactant treatment in MPIs.

Keywords: Surfactant; multiple doses; respiratory distress syndrome (RDS); preterm infant

Submitted Jul 24, 2025. Accepted for publication Sep 24, 2025. Published online Nov 25, 2025.

doi: 10.21037/tp-2025-501

View this article at: <https://dx.doi.org/10.21037/tp-2025-501>

Introduction

Respiratory distress syndrome (RDS) is commonly treated in preterm infants with surfactant and artificial respiratory support. Surfactant therapy has been found to decrease mortality and the risk of air-leak (1), while early nasal continuous positive airway pressure (NCPAP) (2) combined with surfactant treatment (3) has been shown to decrease the requirement of mechanical ventilation (MV) and the frequency of bronchopulmonary dysplasia (BPD) (4-6).

However, these effects have been demonstrated in infants born before 30 weeks of gestational age, whereas they are not in moderately preterm infants (MPIs; infants born between 30 and 33 weeks of gestational age). Indeed, the effectiveness of surfactant therapy in MPIs is more difficult to demonstrate because they are treated less frequently and have a lower incidence of mortality and BPD than more immature infants. The Neobs study prospectively analyzed the clinical course and management of 279 MPIs born in France in 2018 (7). RDS was diagnosed in 49% of cases, and 57% were treated with surfactant, while 5% received more than two doses (7). Similar data were reported by Walsh *et al.*, who found that 23% of MPIs required surfactant treatment (8), and by Raimondi *et al.*, who reported that 23% of 99 infants born between 31 and 33 weeks of gestation received one dose of surfactant and 3% >2 doses (9). In these studies, no cases of BPD (7-9) and a mortality of 0.7% (7) in MPIs were reported.

There are no specific recommendations for surfactant treatment in MPIs with RDS. A fraction of inspired oxygen (FiO₂) threshold of 0.30 has been shown to have a sensitivity in predicting the first surfactant administration

that is inversely proportional to gestational age (10). Conversely, lung ultrasound score has been shown to be a reliable criterion for administering the first dose of surfactant regardless of gestational age (9). Furthermore, its association with the peripheral oxygen saturation (SpO₂)/FiO₂ ratio further improved its predictive power for the need for surfactant (9).

Indications for surfactant retreatment have been very poorly studied. Previous studies have reported that hypertension during pregnancy (11,12), low birth weight for gestational age (11-13), low birth weight (14), severe RDS (13,14), a first dose of surfactant of 100 mg/kg (14), and lack of antenatal steroids (13) are significant predictors of the need for two or more doses of surfactant in very preterm infants. However, it is unknown whether these conditions are also risk factors for the need for two or more doses of surfactant in MPIs.

Based on these considerations, our aim was to assess the effectiveness of surfactant treatment and retreatment in MPIs with RDS. Furthermore, we sought to recognize possible risk factors for the need of retreatment with surfactant in MPIs. To achieve these objectives, we evaluated changes of indices of oxygenation and RDS severity after surfactant treatment and retreatment, while clinical characteristics of infants who had received one or more doses of surfactant were compared. We present this article in accordance with the STROBE reporting checklist (available at <https://tp.amegroups.com/article/view/10.21037/tp-2025-501/rc>).

Methods

We retrospectively studied preterm infants born from January 2020 to June 2024 in the third-level neonatal intensive care unit (NICU) of the Careggi University Hospital of Florence. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the “National Ethics Committee for Clinical Trials in Pediatrics of the Italian Medicines Agency” (ID 0024705-25/02/2025). Informed consent was waived in this retrospective study.

Patients

Inclusion criteria were a gestational age of 30⁺⁰–33⁺⁶ weeks and a diagnosis of RDS requiring respiratory support and surfactant treatment. The diagnosis of RDS was made in the presence of respiratory distress, oxygen requirement

Highlight box

Key findings

- The first and second doses of surfactant improve oxygenation indices in moderately preterm infants (MPIs) with respiratory distress syndrome.

What is known and what is new?

- The effectiveness of surfactant is proven in very preterm infants.
- We assessed for the first time the effectiveness of single and multiple doses of surfactant in MPIs.

What is the implication, and what should change now?

- Our findings support the utility of treating with one or more doses of surfactant a population in which the importance of this therapy is often underestimated, probably due to lower mortality and morbidity compared to very preterm infants.

during the first hours of life, chest radiograph showing reduced lung air content, reticulogranular appearance, and air bronchograms, without other causes of respiratory failure (15). Patients with severe congenital malformations, genetic disorders, and inherited metabolic diseases were excluded.

Respiratory management

Resuscitation in the delivery room was provided following American Academy of Pediatrics (AAP) and the American Heart Association (AHA) guidelines (16,17). Noninvasive respiratory support was performed in the NICU using NCPAP, bi-level NCPAP, or nasal intermittent positive pressure ventilation (NIPPV). As for local protocol, MV (patient triggered ventilation with or without volume guarantee or high frequency ventilation) was started when infants' pH was <7.20 with partial pressure of arterial carbon dioxide (PaCO_2) >65 mmHg, or partial pressure of arterial oxygen (PaO_2) <50 mmHg with $\text{FiO}_2 \geq 0.50$, after surfactant treatment, or if they had more than four episodes of apnea in 1 h, or more than two episodes requiring bag-and-mask ventilation despite proper oxygenation and NCPAP and oxygenation. The goal of respiratory support was to maintain a PaCO_2 of 55–65 mmHg and a 90–95% SpO_2 .

The indication for the administration of 200 mg/kg of surfactant (Curosurf®, Chiesi Farmaceutici Spa, Parma, Italy) was the need for MV or an $\text{FiO}_2 > 0.30$ (18). Further surfactant doses of 100 mg/kg were given following the same indications, without a pre-established time interval. Surfactant was administered to non-intubated patients using the less invasive surfactant administration (LISA) or Intubation-SURfactant-Extubation (InSURE) procedure.

Collected data

Patient medical records were reviewed for the following variables: gestational age, birth weight, sex, antenatal steroids, mode of delivery, clinical chorioamnionitis, Apgar score at 5 min, need and duration of noninvasive and invasive ventilation, occurrence of sepsis, BPD, intraventricular hemorrhage (IVH), retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC) >2 grade, duration of hospitalization, and death.

$\text{SpO}_2/\text{FiO}_2$ ratio 1 h before (T_0) and 1 (T_1), 3 (T_3), 6 (T_6), and 12 h (T_{12}) after the 1st and 2nd dose of surfactant were recorded. Arterial/alveolar partial pressure of oxygen (a/APO₂) ratio 1.5 h before (T_0') and 1.5 h after (T_1') the

1st and 2nd dose of surfactant were also calculated with the following formula: $[\text{PaO}_2/(\text{FiO}_2 \times 713) - 1.25 \times \text{PaCO}_2]$. The a/APO₂ ratio was no longer calculated due to the lack of subsequent serial blood gas analyses. Blood gas analyses were performed on post-ductal samples.

Sepsis diagnosis was based on clinical and laboratory data (total neutrophil count, C-reactive protein, procalcitonin), confirmed by the presence of at least one positive blood or liquor culture. BPD, IVH, NEC, and ROP were diagnosed according to Ehrenkranz *et al.* (19), Papile *et al.* (20), Bell *et al.* (21), and the International Classification (22), respectively.

Collected maternal variables were antenatal steroid treatment, type of delivery, placental abruption, hypertensive disorders, prolonged premature rupture of membranes (pPROMs) >18 h, and clinical chorioamnionitis.

Primary and secondary endpoint

The primary endpoint was the evaluation of changes of the $\text{SpO}_2/\text{FiO}_2$ ratio after the administration of the 1st dose of surfactant as an index of oxygenation and RDS severity. Secondary endpoints were changes of a/APO₂ after the 1st dose of surfactant and changes of $\text{SpO}_2/\text{FiO}_2$ and a/APO₂ ratios after the 2nd dose of surfactant.

Statistical analysis

Demographics of infants were reported as mean and standard deviation, rate and percentage, or median and range. Missing data (less than 2% of the total data) were replaced with an estimated value based on available information by mean imputation without affecting the distributions or relationships between variables. Patients were stratified into subgroups of infants requiring one or more doses of surfactant. To analyze the data, the Student *t*-test was used for normally distributed numeric variables, the Wilcoxon two-sample rank sum test for non-normally distributed numeric variables, and the χ^2 test for qualitative variables. Repeated-measures analysis of variance (ANOVA) was used to compare changes of SpO_2 . A $P < 0.05$ was considered statistically significant.

Logistic regression analyses were used to assess possible independent risk factors for the need for multiple doses of surfactant in MPIs. We evaluated the possible correlation between variables that at univariate analysis were different between the groups ($P < 0.20$) and the risk for requiring multiple doses of surfactant. Variables which were found to

be collinear by calculating variance inflation factors (VIFs) were excluded. Thus, the effect of Apgar score at 5 min, age at 1st dose of surfactant, need for MV, cesarean section, and SpO₂/FiO₂ ratio at T₁ after the 1st dose of surfactant on the risk for multiple doses of surfactant was evaluated by logistic regression analysis.

To analyze the predictive value of SpO₂/FiO₂ ratio at T₁ on the need for multiple doses of surfactant, receiver operating characteristic (ROC) curve analysis was performed. The area under the ROC curve (AUC) represented the ability of the test to classify patients as requiring or not requiring multiple doses of surfactant.

Results

During the study period 291 MPIs were born in our center and 60 (21%) were treated with surfactant. Forty-eight patients (80%) were treated with one dose of surfactant, while 12 (20%) received multiple doses. Clinical characteristics of infants who received single or multiple doses of surfactant were similar, except for the need for MV (15% *vs.* 42%, *P*=0.050) which was lower in the first group, and SpO₂/FiO₂ (362±97 *vs.* 282±95, *P*=0.03) and a/ApO₂ (0.59±0.23 *vs.* 0.44±0.14, *P*=0.04) ratios after the first dose which were higher (Table 1).

The first dose of surfactant was given at 13±12 h of life and the second at 22±22 h, when FiO₂ was 0.33±0.23 and 0.48±0.24 (*P*=0.049), respectively (Table 2). SpO₂/FiO₂ and a/ApO₂ ratios significantly increased after both the first and second doses of surfactant, but their values were lower after the second dose (Table 2, Figure 1).

Logistic regression analysis showed no effect of the studied variables on the risk of multiple doses of surfactant (Table 3). In ROC analysis, SpO₂/FiO₂ ratio at T₁ significantly predicted (*P*=0.01) the need for additional doses of surfactant with an AUC of 0.741 [95% confidence interval (CI): 0.599–0.881], showing the best prognostic threshold at SpO₂/FiO₂ ratio <378, with a sensitivity of 62% and specificity of 45% (Figure 2).

Discussion

In this study, we aimed for the first time to evaluate the effectiveness of both the first and second doses of surfactant in MPIs with RDS. We found that both SpO₂/FiO₂ and a/ApO₂ significantly increased after surfactant treatment. These results confirm previous finding of Raimondi *et al.*, who studied 99 infants born at 31–33 weeks of gestational

age and found that SpO₂/FiO₂ ratio increased within 24 h from administration of the first dose of surfactant in a cohort (9).

The increase of SpO₂/FiO₂ ratio indicates the reduction of patients' oxygen dependence and confirms that surfactant treatment is effective in improving respiratory failure in MPIs. As expected, exogenous surfactant can correct the deficiency caused by preterm birth and improve respiratory function by allowing alveolar recruitment and increasing the surface area available for gas exchange. The concomitant increase in the a/APO₂ ratio is important since this biomarker depends on the ventilation/perfusion balance, and its improvement suggests better lung perfusion (23). In fact, this biomarker is of particular interest in cases of severe RDS when persistently high vascular resistance can induce a ventilation/perfusion mismatch.

We provide the first evidence that administering a second dose of surfactant leads to an increase in the SpO₂/FiO₂ and a/APO₂ ratios in MPI. The sequential improvement in the oxygenation indices after the second dose suggests that some MPIs may continue to experience surfactant deficiency despite receiving one dose of surfactant therapy. These findings contrast with previous studies that reported that premature infants with RDS have a surfactant pool size of 1–15 mg/kg with slow kinetics and prolonged half-life (47–106 h) (24), and which support the idea that a dose of 100 or 200 mg/kg of surfactant should be adequate in these patients. However, it is possible that the subgroup of infants requiring repeated doses of surfactant and larger than expected amounts of exogenous surfactant to correct their deficit may have had an uneven distribution of the surfactant, or its inactivation due to inflammatory factors or a delayed synthesis.

We did not identify clinical predictors for the need for surfactant retreatment in MPIs. This is contrast with previous studies in very preterm infants, which found that infants whose mothers had hypertensive disorders of pregnancy (11,12), who are small for gestational age (11–13), had low birth weight (14) or severe RDS (13,14), a reduced first dose of surfactant (14), or a lack of antenatal steroids (13) were at increased risk of requiring multiple doses of surfactant. However, it is possible that the small size of our population and/or the limited surfactant deficiency in MPIs reduced the possibility of highlighting this finding in our population. However, ROC analysis showed that SpO₂/FiO₂ ratio at T₁ significantly predicted the need for additional doses of surfactant with the best cut-off point at 378, although with a sub-optimal sensitivity

Table 1 Baseline clinical characteristics of the infants and their mothers who received single or multiple doses of surfactant

Characteristics	Single dose (n=48)	Multiple doses (n=12)	P
Infants			
Gestational age (weeks)	31.4±1.1	31.7±1.2	0.41
30	13 [27]	3 [25]	<0.99
31	10 [21]	2 [17]	0.72
32	16 [33]	3 [25]	0.74
33	9 [19]	4 [33]	0.27
Birth weight (g)	1,666±377	1,655±394	0.93
<10 th percentile	3 [6]	2 [17]	0.29
Apgar score			
1° min	7 [2–9]	7 [2–9]	0.37
5° min	8 [4–9]	8 [5–9]	0.13
Noninvasive ventilation	48 [100]	12 [100]	<0.99
MV	7 [15]	5 [42]	0.050
SpO₂/FiO₂			
SpO ₂ /FiO ₂ before the first dose of surfactant	240±76	214±77	0.30
SpO ₂ /FiO ₂ after the first dose of surfactant	362±97	282±95	0.01
P (before vs. after)	<0.001	0.01	
a/ApO₂			
a/ApO ₂ before the first dose of surfactant	0.37±0.15	0.32±0.12	0.29
a/ApO ₂ after the first dose of surfactant	0.59±0.23	0.44±0.14	0.04
P (before vs. after)	<0.001	<0.01	
Sepsis	1 [2]	1 [8]	0.36
BPD	1 [2]	2 [17]	0.10
Death	0	1 [8]	0.20
Duration of hospital stay (days)	37±20	50±30	0.08
Mothers			
Antenatal steroids	38 [79]	8 [67]	0.45
Cesarean section	42 [88]	8 [67]	0.10
Gestational diabetes	17 [35]	2 [17]	0.31
Hypertensive disorders of pregnancy	7 [15]	0	0.33
pPROM	0	0	N/A
Chorioamnionitis	0	0	N/A

Data are presented as mean ± SD, n [%], or median [range]. a/ApO₂, arterial/alveolar partial pressure of oxygen; BPD, bronchopulmonary dysplasia; FiO₂, fraction of inspired oxygen; MV, mechanical ventilation; N/A, not available; pPROM, prolonged premature rupture of membrane; SD, standard deviation; SpO₂, peripheral oxygen saturation.

Table 2 Changes of SpO₂/FiO₂ and a/ApO₂ before and after the first and second doses of surfactant

Variables	1 st dose of surfactant (n=60)	2 nd dose of surfactant (n=12)	P
Age at surfactant (h)	13±12	22±22	0.058
FiO ₂ before surfactant	0.33±0.23	0.48±0.24	0.049
SpO ₂ /FiO ₂			
SpO ₂ /FiO ₂ before surfactant	240±76	198±74	0.09
SpO ₂ /FiO ₂ after 1 h from surfactant	362±97	287±110	0.03
SpO ₂ /FiO ₂ after 3 h from surfactant	372±87	338±137	0.29
SpO ₂ /FiO ₂ after 6 h from surfactant	414±70	371±102	0.09
SpO ₂ /FiO ₂ after 12 h from surfactant	422±63	375±92	0.04
P (before vs. after)	<0.001	<0.001	
a/ApO ₂			
a/ApO ₂ before surfactant	0.42±0.19	0.31±0.15	0.07
a/ApO ₂ after 1 h from surfactant	0.65±0.20	0.44±0.27	<0.01
P (before vs. after)	<0.001	0.02	

Data are presented as mean ± SD. a/ApO₂, arterial/alveolar partial pressure of oxygen; FiO₂, fraction of inspired oxygen; SD, standard deviation; SpO₂, peripheral oxygen saturation.

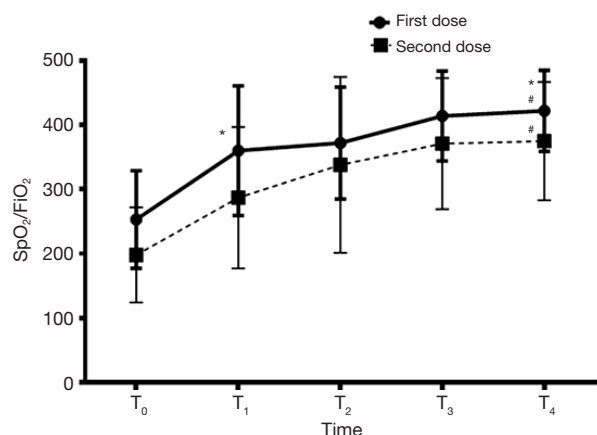


Figure 1 Changes of SpO₂/FiO₂ ratio before and after the first and second doses of surfactant (mean ± SD). *, P<0.05 first vs. second dose; #, P<0.001 vs. baseline. FiO₂, fraction of inspired oxygen; SD, standard deviation; SpO₂, peripheral oxygen saturation.

(62%) and specificity (45%). Thus, as expected, the more severe the RDS, the more doses of surfactant were required. However, the limited success in identifying clinical predictors for novel surfactant treatment in MPIs and the suboptimal sensitivity and specificity of the SpO₂/FiO₂ ratio at T₁ as a predictor suggest that larger prospective studies and more robust predictive markers are needed to

complement our findings.

Our study presents some limitations, such as its retrospective design and the population size, which limited the possibility of performing a more rigorous analysis of risk factors for the need for multiple doses of surfactant. On the other hand, the strength of this study lies in its originality, as no data on the efficacy of surfactant in MPIs, particularly about the second dose, have been reported in the literature to date. This is very important because we believe our results can be generalized to other NICUs and can contribute to the discussion on the appropriateness of treating the understudied MPI population with multiple doses of surfactant. Furthermore, our findings could enable further refinement of clinical practice and ensure that every newborn receives the most appropriate and timely surfactant treatment.

Conclusions

We demonstrated that both the first and second doses of surfactant improved oxygenation indices and RDS severity in MPIs. We did not identify risk factors for the need for multiple doses of surfactant, but we demonstrated that SpO₂/FiO₂ ratio calculated 1 h after the first dose of surfactant can help predict the need for retreatment. These data contribute to quantifying the efficacy of surfactant in

Table 3 Logistic regression analysis to evaluate possible clinical predictors of the need for multiple doses of surfactant in MPI

Variables	Odds ratio	95% CI	P
Cesarean section	1.176	0.211–6.148	0.85
Apgar score at 5 min	0.889	0.451–1.753	0.73
Age at surfactant treatment	0.999	0.997–1.000	0.25
SpO ₂ /FiO ₂ ratio after the 1 st dose of surfactant	0.994	0.986–1.001	0.10
MV	1.749	0.328–9.317	0.51

CI, confidence interval; FiO₂, fraction of inspired oxygen; MPI, moderately preterm infant; MV, mechanical ventilation; SpO₂, peripheral oxygen saturation.

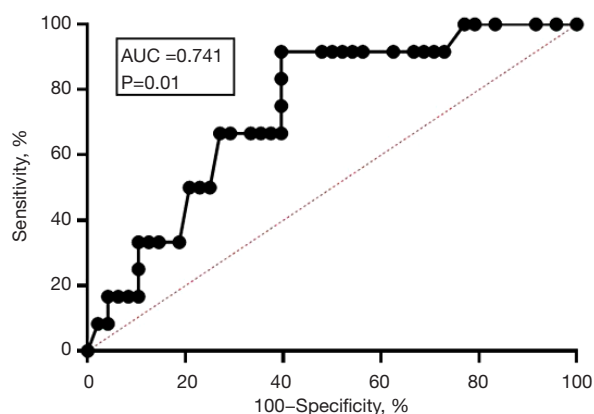


Figure 2 ROC curve for SpO₂/FiO₂ ratio after the first dose of surfactant and need for multiple doses of surfactant. The AUC is 0.741 (95% CI: 0.599–0.881), with 378 as the best prognostic cut-off with a sensitivity of 62% and specificity of 45%. T₀, 1 h before; T₁, 1 h after; T₃, 3 h after; T₆, 6 h after; T₁₂, 12 h after. AUC, area under the ROC curve; CI, confidence interval; FiO₂, fraction of inspired oxygen; ROC, receiver operating characteristic; SpO₂, peripheral oxygen saturation.

MPIs with RDS and support the utility of treating with one or more doses of surfactant a population in which the importance of this therapy is often underestimated probably due to lower mortality and morbidity compared to very preterm infants.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://tp.amegroups.com/article/view/10.21037/tp-2025-501/rc>

tp.amegroups.com/article/view/10.21037/tp-2025-501/rc

Data Sharing Statement: Available at <https://tp.amegroups.com/article/view/10.21037/tp-2025-501/dss>

Peer Review File: Available at <https://tp.amegroups.com/article/view/10.21037/tp-2025-501/prf>

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tp.amegroups.com/article/view/10.21037/tp-2025-501/coif>). C.D. reports receiving consulting fees from Chiesi Farmaceutici SpA, and honoraria from Accurate Srl, and Sanofi Italia. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the “National Ethics Committee for Clinical Trials in Pediatrics of the Italian Medicines Agency” (ID 0024705-25/02/2025). Informed consent was waived in this retrospective study.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license).

See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Seger N, Soll R. Animal derived surfactant extract for treatment of respiratory distress syndrome. *Cochrane Database Syst Rev* 2009;2009:CD007836.
2. Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. *Cochrane Database Syst Rev* 2002;2002:CD002975.
3. Stevens TP, Harrington EW, Blennow M, et al. Early surfactant administration with brief ventilation vs. selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. *Cochrane Database Syst Rev* 2007;2007:CD003063.
4. De Klerk AM, De Klerk RK. Nasal continuous positive airway pressure and outcomes of preterm infants. *J Paediatr Child Health* 2001;37:161-7.
5. Gittermann MK, Fusch C, Gittermann AR, et al. Early nasal continuous positive airway pressure treatment reduces the need for intubation in very low birth weight infants. *Eur J Pediatr* 1997;156:384-8.
6. Polin RA, Sahni R. Newer experience with CPAP. *Semin Neonatol* 2002;7:379-89.
7. Guellec I, Debillon T, Flamant C, et al. Management of respiratory distress in moderate and late preterm infants: clinical trajectories in the Neobs study. *Eur J Pediatr* 2023;182:5661-72.
8. Walsh MC, Bell EF, Kandefer S, et al. Neonatal outcomes of moderately preterm infants compared to extremely preterm infants. *Pediatr Res* 2017;82:297-304.
9. Raimondi F, Migliaro F, Corsini I, et al. Neonatal Lung Ultrasound and Surfactant Administration: A Pragmatic, Multicenter Study. *Chest* 2021;160:2178-86.
10. Raimondi F, Dolce Veropalumbo C, et al. Inspired oxygen fraction thresholds to accurately predict surfactant administration in neonatal RDS is gestational age strata: A pragmatic, multi-center study. *Pediatr Pulmonol* 2024;59:1638-44.
11. Lanciotti L, Pasqualini M, Correani A, et al. Who Needs a Second Dose of Exogenous Surfactant? *J Pediatr* 2023;261:113535.
12. Coshall H, Mukerji A, Lemyre B, et al. Characteristics and outcomes of preterm neonates according to number of doses of surfactant received. *J Perinatol* 2021;41:39-46.
13. Greiner E, Wittwer A, Albuissou E, et al. Outcome of Very Premature Newborn Receiving an Early Second Dose of Surfactant for Persistent Respiratory Distress Syndrome. *Front Pediatr* 2021;9:663697.
14. Cogo PE, Facco M, Simonato M, et al. Pharmacokinetics and clinical predictors of surfactant redosing in respiratory distress syndrome. *Intensive Care Med* 2011;37:510-7.
15. Dani C, Mosca F, Vento G, et al. Effects of surfactant treatment in late preterm infants with respiratory distress syndrome. *J Matern Fetal Neonatal Med* 2018;31:1259-66.
16. Wyckoff MH, Aziz K, Escobedo MB, et al. Part 13: Neonatal Resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care (Reprint). *Pediatrics* 2015;136 Suppl 2:S196-218.
17. Aziz K, Lee CHC, Escobedo MB, et al. Part 5: Neonatal Resuscitation 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Pediatrics* 2021;147:e2020038505E.
18. Sweet DG, Carnielli VP, Greisen G, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update. *Neonatology* 2023;120:3-23.
19. Ehrenkranz RA, Walsh MC, Vohr BR, et al. Validation of the National Institutes of Health consensus definition of bronchopulmonary dysplasia. *Pediatrics* 2005;116:1353-60.
20. Papile LA, Burstein J, Burstein R, et al. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. *J Pediatr* 1978;92:529-34.
21. Bell MJ, Ternberg JL, Feigin RD, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. *Ann Surg* 1978;187:1-7.
22. The International Classification of Retinopathy of Prematurity revisited. *Arch Ophthalmol* 2005;123:991-9.
23. Hsu JT, Chu CM, Chang ST, et al. Prognostic value of arterial/alveolar oxygen tension ratio (a/APO2) in acute pulmonary embolism. *Circ J* 2007;71:1560-6.
24. Carnielli VP, Zimmermann LJ, Hamvas A, et al. Pulmonary surfactant kinetics of the newborn infant: novel insights from studies with stable isotopes. *J Perinatol* 2009;29 Suppl 2:S29-37.

Cite this article as: Dani C, Pratesi S, Inguscio G, Bonetti A, Devilli L, Rizzello A, Prelazzi G, Mariani G, Corsini I. Effectiveness of surfactant treatment and retreatment in moderately preterm infants. *Transl Pediatr* 2025;14(11):3045-3052. doi: 10.21037/tp-2025-501