

Indications for Surfactant Therapy—The aAPo₂ Coming of Age

ABSTRACT. Indications for administration of surfactant to infants with established respiratory distress syndrome (RDS; rescue therapy) remains an area of continued investigation. Current recommendations vary from use in infants who are intubated and have an aAPo₂ <0.22 to use in infants receiving ≥40% oxygen administered in a hood when the PaO₂ is <80 TORR (aAPo₂ approximately <0.36).

This commentary is written in response to the article by Verder et al, in this issue of *Pediatrics*, who evaluated early versus late treatment of RDS in 60 preterm infants <30 weeks' gestation receiving nasal continuous positive airway pressure (CPAP). Early-treated infants (aAPo₂, 0.22 to 0.35; mean, 0.26) had a lower incidence of mechanical ventilation or death (21%) than did late-treated infants (63%), who did not receive surfactant treatment until the aAPo₂ was <0.22 (0.15 to 0.21; mean, 0.16). The authors conclude that although approximately half of infants <30 weeks' gestation with RDS can be treated with nasal CPAP alone, early treatment with surfactant when the aAPo₂ is 0.22 to 0.36 reduced significantly the need for mechanical ventilation.

Limitations of applicability of the study to widespread use include determination of Po₂ values from transcutaneous measurements, which may vary from those obtained from arterial samples and affect significantly aAPo₂ ratios. Likewise, use of nasal CPAP significantly affects oxygenation, and interpretation of results cannot be extrapolated to intubated infants or those receiving oxygen delivered under a hood. Nonetheless, the use of the aAPo₂ ratio and early administration of surfactant are supported by this study. *Pediatrics* 1999;103(2). URL: <http://www.pediatrics.org/cgi/content/full/103/2/e25>; arterial to alveolar oxygen tension ratio, nasal continuous positive airway pressure, respiratory distress syndrome, surfactant, transcutaneous O₂ determinations, very low birth weight.

ABBREVIATIONS. CPAP, nasal continuous positive airway pressure; aAPo₂, arterial to alveolar oxygen tension ratio; RDS, respiratory distress syndrome; FiO₂, fraction of inspired oxygen.

The laboratory and clinical investigation of endogenous pulmonary surfactant therapy for respiratory distress syndrome (RDS) in preterm infants is one of the most comprehensive therapeutic adventures in neonatal medicine of this decade. Mortality in the very low birth weight infant with RDS clearly has improved along with a reduction in the incidence of pulmonary interstitial emphysema, pneumothorax, and bronchopulmonary dysplasia.

One issue that remains unresolved is the use of surfactant as prophylaxis versus rescue therapy in infants with established disease. Installation before

or at the initiation of respiration is no longer believed to be essential for successful intrapulmonary distribution or clinical response; however, early treatment of infants with RDS may be beneficial.

Clearly, gestational age and birth weight are directly related to endogenous surfactant production. However, multiple variables including maternal steroid administration, duration of ruptured membranes, amniotic fluid volume, intrauterine growth, infection, and other forms of intrauterine stress make the decision to treat a clinical one rather than a decision based on gestational age and birth weight alone. Unfortunately, no rapid test for identification of surfactant deficiency has emerged, and clinical features of grunting, nasal flaring, and retracting, plus radiographic features and oxygen needs remain the mainstay for evaluation of disease severity.

In this issue of *Pediatrics electronic pages*, Verder and colleagues¹ extend their observations on the early use of surfactant for the treatment of established RDS. This group demonstrated previously that surfactant therapy given to infants with moderate to severe RDS receiving nasal continuous positive airway pressure (CPAP) reduced the need for mechanical ventilation.² The current study extends and confirms those observations in infants <30 weeks' gestation.

The measure of disease severity in both studies was the arterial to alveolar O₂ oxygen tension ratio (aAPo₂). The earlier study group² had an aAPo₂ of 0.17 at randomization, with a rise to 0.37 ± 0.15 in the surfactant-treated group 6 hours after therapy, compared with 0.25 ± 0.10 in untreated control subjects. Subsequent mechanical ventilation was required in 43% (15/35) and 85% (28/33), respectively (*P* = .003). In the current study, the aAPo₂ was 0.26 ± 0.06 at the time of surfactant therapy in the early-treated group and 0.16 ± 0.04 in the late-treated group (*P* = .0001). The 6-hour aAPo₂ response was greater in the early-treated group, 0.48 ± 0.18 versus 0.36 ± 0.18 in the late-treated group (*P* = .02). Fewer early-treated infants required mechanical ventilation or died within 7 days of age, 21% (7/33) versus 63% (17/27) (*P* = .0013). The authors conclude from the current study that although approximately half of infants <30 weeks' gestational age with RDS can be treated with nasal CPAP alone, early treatment with surfactant when the aAPo₂ is 0.22 to 0.36 reduced significantly the need for mechanical ventilation.

The use of the aAPo₂ as an estimate of gas exchange and severity of pulmonary disease is an old technique³ with a relatively newer variation; ie, the estimate of PaO₂ with a transcutaneous monitor. A major variable in the reports of the Danish collaborative studies is the use of transcutaneous Po₂ measurements as estimates of PaO₂. No data are provided

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TABLE 1. aA_{o2} Ratios at Varying F_{io2} and P_{aO2} Values

P _{aO2}	F _{io2}			F _{io2} P _{aO2}
	0.3	0.4	0.5	
	157	226	295	
50	0.32	0.22	0.17	
60	0.38	0.27	0.20	
70	0.45	0.31	0.24	
80	0.51	0.35	0.27	
90	0.57	0.40	0.31	

aA_{o2} ratios assuming BP-47 = 690, P_{co2} ÷ 0.8 = 50.

to compare these measurements because P_{aO2} was not measured routinely. However, other reports^{4,5} indicate at least a 10 TORR standard deviation in transcutaneous measurements, suggesting that absolute values of aA ratios may vary considerably from those determined by arterial samples. The effect of nasal CPAP on arterial oxygenation also is uncertain and, therefore, the applicability of specific aA ratios in the Danish studies to values obtained from arterial samples in infants receiving oxygen delivered within a hood is unknown.

Almost all modern blood gas machines now use co-oximetry with measurement (rather than estimation) of hemoglobin and oxygen saturation in addition to pH, P_{co2}, and P_{o2}. Providing F_{io2}, therefore, allows calculation of the aA ratio, AaDo₂, and oxygen content, which are available as reported values.

The magnitude of the effect of measurement of P_{o2} on aA ratios at inspired O₂ concentrations from 0.3 to 0.5 is shown in Table 1. The Verder et al data suggest that all infants <30 weeks' gestation with RDS requiring an F_{io2} ≥0.5 would benefit from surfactant. However, there may be considerable variation among infants qualifying to receive surfactant whose F_{io2} is 0.3 to 0.5. Therefore, the precision of the measurement may affect the number of infants receiving early surfactant treatment.

The variations in transcutaneous o₂ determinations likely affected infants similarly in early- and

late-treated patients in the current study and do not detract from the value of the results. Early treatment is better than late treatment. Unfortunately, both studies fell short of the projected number of subjects planned. Additional data involving patients with and without nasal CPAP, ie, those receiving hood o₂ and correlation of transcutaneous with arterial P_{o2}, would be helpful. In the meantime, data are mounting that spontaneously breathing, very low birth weight infants with RDS will benefit from surfactant therapy when the aA_{o2} is <0.36 corresponding to F_{io2} <0.5. The observation supplements existing recommendations that infants with RDS requiring mechanical ventilation receive surfactant when the aA_{o2} is <0.22.

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REFERENCES

1. Verder H, Albertsen P, Ebbesen F, et al. Nasal continuous positive airway pressure and early surfactant therapy for respiratory distress syndrome in newborns of less than 30 weeks' gestation. *Pediatrics*. 1999;103(2). URL: <http://www.pediatrics.org/cgi/content/full/103/2/e24>
2. Verder H, Robertson B, Greisen G, et al. Surfactant therapy and nasal continuous positive airway pressure for newborns with respiratory distress syndrome. *N Engl J Med*. 1994;331:1051-1055
3. Gilbert R, Keighley J. The arterial/alveolar oxygen tension ratio. An index of gas exchange applicable to varying inspired oxygen concentrations. *Am Rev Respir Dis*. 1974;109:142-145
4. Krauss A, Waldman S, Frayer W, Auld PAM. Noninvasive estimation of arterial oxygenation in newborn infants. *J Pediatr*. 1978;93:275-278
5. le Souef P, Morgan A, Soutter L, Reynolds EOR, Parker D. Comparison of transcutaneous oxygen tension with arterial oxygen tension in newborn infants with severe respiratory illnesses. *Pediatrics*. 1978;62:692-697
6. Rooth G, Huch A, Huch R. Transcutaneous oxygen monitors are reliable indicators of arterial oxygen tension (if used correctly). *Pediatrics*. 1987;79:283-286

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