Editorial

Neonatal acute respiratory distress syndrome—is the Montreux definition useful?

Vineet Bhandari

Section of Neonatology, Department of Pediatrics, St. Christopher's Hospital for Children, Drexel University College of Medicine, Philadelphia, PA, USA
Correspondence to: Vineet Bhandari, MD, DM. Drexel University College of Medicine, St. Christopher's Hospital for Children, 160 Erie Avenue, Philadelphia, PA 19134, USA. Email: vineet.bhandari@drexel.edu.

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A recent publication has attempted to define neonatal acute respiratory distress syndrome (ARDS), using a consensus conference of the opinion of 13 experts from Europe, USA and Australia (1). RDS is a well-defined entity in neonates characterized by the presence of clinical features (evidence of respiratory distress as manifested by tachypnea, sub-costal and inter-costal retractions, use of accessory muscles of respiration, and grunting) at birth or within the first 6 hours of life, in a preterm neonate, along with a characteristic radiograph (diffuse reticulo-granular opacification with air bronchograms and decreased lung volumes) suggesting a primary surfactant deficiency. The terminology of "adult" RDS was subsequently used to designate the presence of symptomatology of surfactant deficiency in adult patients and referred to as ARDS. However, since secondary surfactant deficiency can occur in children, too, the "A" in ARDS was changed to "acute" to be inclusive.

While definitions of pediatric ARDS exist (1), the attempt in the consensus ("Montreux") definition of neonatal ARDS is to delineate this condition from RDS or primary surfactant deficiency due to immaturity of the lung. Limitations of the approach being used have been delineated in the manuscript; specifically, strong opinions could sway the discussion in the absence of supportive objective data. However, the authors put forth convincing arguments for the need for a neonatal, as opposed to, pediatric ARDS. These include the presence of developmental properties of the lung and chest wall, specific neonatal disorders [for e.g., meconium aspiration syndrome (MAS)] as well as differences in management styles in neonatal intensive care units (NICUs) *vs.* pediatric ICUs (PICUs), to name three.

Among the fairly non-controversial strengths of the definition are the following parameters:

(I) The definition is applicable from birth to 44 weeks post-menstrual age or until 4 weeks of post-natal age for a term infant;
(II) Excluding well-defined entities such as RDS, transient tachypnea of the newborn (TTN), congenital anomalies and genetic disorders of the surfactant system;
(III) Excluding the origin of pulmonary edema to be congenital heart disease including the presence of a patent ductus arteriosus (PDA), confirmed by echocardiography;
(IV) Including neonates being managed by invasive or non-invasive modalities of respiratory support;
(V) Classification of the severity of neonatal ARDS based on the oxygenation index (OI) using PaO_2, rather than SpO_2, values.

However, difficulties do arise [since all five criteria listed in Table 2 of the article (1) need to be fulfilled] with the following suggested inclusions:

(I) The time frame is suggested to be "acute onset (i.e., within 1 week) from a known or suspected clinical insult". This may potentially be problematic as 7 days is a fairly long time-frame to link an

associated presumably inciting factor;

(II) While MAS is a fairly well-defined entity, and known to be associated with secondary surfactant deficiency (2), the chest radiograph of MAS may show "diffuse, bilateral, and irregular opacities, or complete opacification", or the disease may be localized. In the latter scenario, would MAS be considered a stand-alone condition, and only be classified as neonatal ARDS if the process has initial or progresses to diffuse involvement?

(III) How is systemic sepsis going to be defined as an inciting factor? Since blood cultures are not always positive, will a set of hematological criteria and/or biomarkers be considered as appropriate surrogates (3-6)? This is a critical point as epidemiological data needs to be able to isolate a definitive predisposing factor for ARDS. While full-blown neonatal ARDS, regardless of etiology/inciting factors, shares similar pathophysiological appearances and can be managed by common supportive therapy (for e.g., exogenous surfactant), prevention of this condition from reaching a higher level of severity would require definitive identification/isolation of the inciting event to target it for specific intervention in the future;

(IV) The diagnosis of neonatal pneumonia has been controversial (7), and would require invasive diagnostic criteria to be fulfilled (8,9) to be included as a definitive predisposing criterion;

(V) In terms of radiographic imaging criteria, the differential diagnosis of "atelectasis" may be challenging. While chest X-rays are easily available, interpretation of the findings may not always be definitive. Additional imaging modalities for e.g., ultrasonography (10) and/or quantitative magnetic resonance imaging (MRI) availability (11) in the NICU environment may be useful adjuncts.

Given the varied pathological conditions that may give rise to neonatal ARDS, along with the variable degrees of pulmonary functional impact, it is not surprising that an umbrella definition is going to be challenging. While a consensus of expert opinions is a useful beginning, the validity of such a definition will only be borne out by prospective collection of data and detailed analysis of the same. The prospective multicenter international study envisaged in the paper will hopefully sort out some of the troublesome issues as they crop up. The definition of neonatal ARDS is an important step in the right direction to understand the pathology of diverse inciting/etiological factors that lead to a common pathophysiological picture. This will pave the way for clinical trials for directed surfactant replacement and/or anti-inflammatory therapeutic approaches for such neonates. Identification of predisposing factors to ARDS could be useful in recognizing the specific inciting agent and/or the high-risk neonate for targeting potential preventive management strategies. Furthermore, categorization of a neonate with a diagnosis of neonatal ARDS may also lead to long-term follow-up studies in terms of increased risk of pulmonary disorders during childhood, adolescence and adult stages of life as developmental disorders are well-known to have lifelong consequences (12,13).

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None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

References

1. De Luca D, van Kaam AH, Tingay DG, et al. The Montreux definition of neonatal ARDS: biological and clinical background behind the description of a new entity. Lancet Respir Med 2017;5:657-66.
2. Keiser A, Bhandari V. The Role of Surfactant Therapy in Nonrespiratory Distress Syndrome Conditions in Neonates. Am J Perinatol 2016;33:1-8.
3. Gonzalez BE, Mercado CK, Johnson L, et al. Early markers of late-onset sepsis in premature neonates: clinical, hematological and cytokine profile. J Perinat Med 2003;31:60-8.
4. Wang K, Bhandari V, Chepustanova S, et al. Which biomarkers reveal neonatal sepsis? PLoS One 2013;8:e82700.
5. Bhandari V. Effective Biomarkers for Diagnosis of Neonatal Sepsis. J Pediatric Infect Dis Soc 2014;3:234-45.
6. Gilfillan M, Bhandari V. Biomarkers for the diagnosis of neonatal sepsis and necrotizing enterocolitis: Clinical practice guidelines. Early Hum Dev 2017;105:25-33.
7. Baltimore RS. The difficulty of diagnosing ventilator-associated pneumonia. Pediatrics 2003;112:1420-1.
8. Cernada M, Aguar M, Brugada M, et al. Ventilator-associated pneumonia in newborn infants diagnosed with

an invasive bronchoalveolar lavage technique: a prospective observational study. Pediatr Crit Care Med 2013;14:55-61.
9. Lee PL, Lee WT, Chen HL. Ventilator-Associated Pneumonia in Low Birth Weight Neonates at a Neonatal Intensive Care Unit: A Retrospective Observational Study. Pediatr Neonatol 2017;58:16-21.
10. Liu J, Chen SW, Liu F, et al. The diagnosis of neonatal pulmonary atelectasis using lung ultrasonography. Chest 2015;147:1013-9.
11. Walkup LL, Tkach JA, Higano NS, et al. Quantitative Magnetic Resonance Imaging of Bronchopulmonary Dysplasia in the Neonatal Intensive Care Unit Environment. Am J Respir Crit Care Med 2015;192:1215-22.
12. Bhandari A, Carroll C, Bhandari V. BPD Following Preterm Birth: A Model for Chronic Lung Disease and a Substrate for ARDS in Childhood. Front Pediatr 2016;4:60.
13. Raju TN, Buist AS, Blaisdell CJ, et al. Adults born preterm: a review of general health and system-specific outcomes. Acta Paediatr 2017;106:1409-37.

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