Clinical Pearls from Management of RSV Bronchiolitis Using High-Frequency Jet Ventilation in a Preterm Infant

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Abstract

In a 22-day old preterm infant with severe nosocomial respiratory syncytial virus (RSV) bronchiolitis, we have achieved effective respiratory management with the use of high-frequency jet ventilation (HFJV) combined with optimal sedation, adequate alveolar recruitment, and efficient pulmonary toileting. Other therapies including surfactant, antiviral medication, and inhaled prostacyclin were not used. HFJV might be useful for cases of hypoxemic respiratory failure due to nosocomial bronchiolitis pneumonia in the preterm population, as described in this report.

Keywords: premature infants, high-frequency jet ventilation, Respiratory Syncytial Virus Infections, pneumonia, respiratory failure, nosocomial infection.

Introduction

Respiratory syncytial virus (RSV) bronchiolitis in infants is the most common lower respiratory tract infection with a high disease burden worldwide (1). The majority of infants who experience RSV bronchiolitis will do so in the first two years of life (2). A great deal of literature in the past has explored the severity of RSV disease in the population of ex-preterm infants. Our case report differs in that we describe acute management of nosocomial RSV bronchiolitis pneumonia with high-frequency jet ventilation (HFJV), in a preterm infant of 30+2 weeks' gestational age prior to discharge home from the NICU.

Case Report

An ex 30+2 weeks' gestation female infant, was transferred to our NICU at 22-days of life for management of apneic episodes. Her initial neonatal course was uneventful. Her mother received a complete course of betamethasone and erythromycin because of prolonged rupture of membranes prior to delivery. The baby was born vigorous; her birth weight was 1220 g. and Apgar 91-95. She was placed on nasal CPAP (nCPAP) for one day but required intubation with surfactant administration on the second day of life, followed by rapid extubation to nCPAP. She completed a 7-day course of ampicillin and tobramycin. She was started on caffeine for apnea of prematurity. The baby was weaned from nCPAP to room air for two weeks and tolerated full feeds. A head ultrasound on the tenth day of life showed a unilateral caudothalamic cyst and no intraventricular hemorrhage. On day of life 18 (corrected gestational age of 32+6 weeks), she began having apneic spells, and nCPAP was again initiated. She continued to have worsening apneic spells requiring intubation and mechanical ventilation on day of life 21. The patient was orally intubated with a size 2.5 endotracheal tube (ETT). Prior to the transfer, she received a 10cc/kg transfusion of packed red blood cells for hemoglobin of 84 g/L. Chest (CXR) and abdominal x- rays showed normal lung parenchyma and a questionable area of potential bowel wall thickening on the left hemi colon. Bilious aspirates were noted, feeds were held, and she underwent a full septic workup, including blood, urine, and cerebrospinal fluid cultures. Ampicillin, cefotaxime, cloxacillin, and acyclovir were started empirically for presumed sepsis.

Upon arrival to our neonatal unit, the patient was ventilated on conventional assist- control volume guarantee (AC VG) with the following settings: tidal volume of 4ml/kg, respiratory rate (RR) of 45 bpm, PEEP 6 cm H_2O, PIP (measured) 14 cm H_20, FiO_2 0.21. Initial arterial blood gas (ABG): 7.35/44/63/24/-1.1. When urine, blood, and CSF cultures were negative, antibiotics, and antiviral therapies were discontinued. Nasopharyngeal aspirates were positive for RSV, presumed to be nosocomial, and the baby was isolated.

Due to progressive airway instability, including excessive secretions and high airway pressure, possibly contributing to inadequate ventilation and excessive intrathoracic pressure with potential hemodynamic consequences, the small size oral ETT was electively changed to a nasally placed size 3.0 uncuffed, which optimized pulmonary toileting. There was additionally asynchrony with mechanical ventilation, and poor chest compliance felt to be due to patient agitation; therefore, a fentanyl infusion of 1mcg/kg/hour was initiated.

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Over the next 36 hours, conventional ventilation settings were gradually escalated due to increased oxygen requirements and sustained respiratory acidosis (ABG: 7.21/68/49/27/-1.3) with an OI = 12.9. Additionally, there were challenges as the patient's oxygen requirements increased significantly, requiring frequent endotracheal suctioning. Ventilation parameter settings were optimized. At this time, the fentanyl infusion was adjusted to allow the patient to remain comfortable. Follow-up capillary blood gas results showed no significant improvement (7.23/65/33/27/-1.8). A decision was made to trial high-frequency oscillatory ventilation (HFOV) using the VN500 Dräger ventilator (Drägerwerk AG & Co. Lübeck, Germany).

Initial parameters on HFOV were: frequency 12 Hz, amplitude (AMP) 26 cm H_2O, measured tidal volume 2.2 ml/kg, MAP 16 cm H_20, FiO2 0.45. Chest x-ray findings one hour after initiation of HFOV are shown in Figure 1. Over the next several hours, the patient displayed episodes of "poor chest wiggle" with handling.

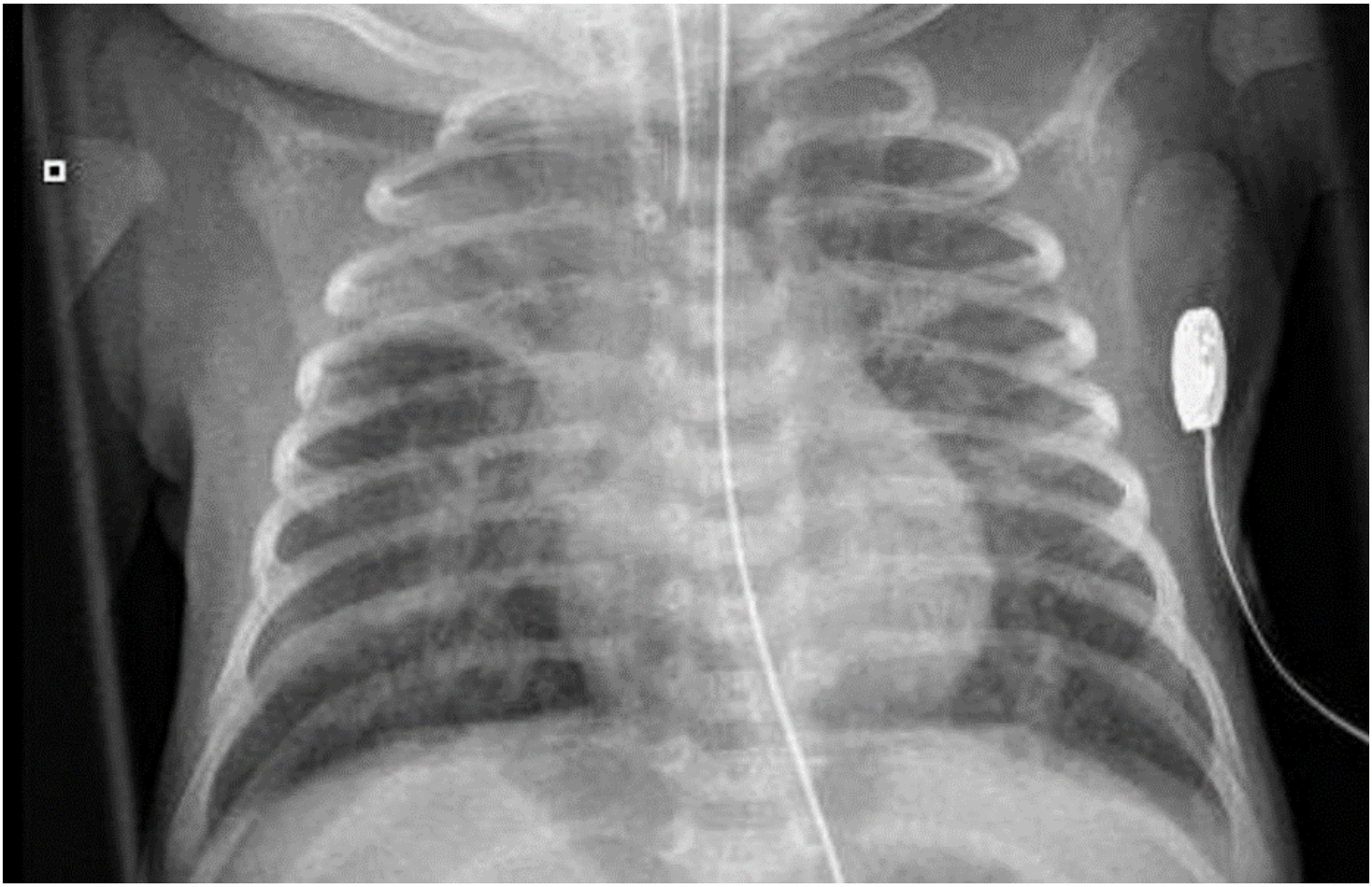

Figure 1. Endotracheal tube located at the T2 vertebra position, patchy opacities in the right lower lobe improved, denser opacities in the right upper lobe with volume lost, increased markings in the left perihilar and left lower lobe region, remainder of the lungs are clear.

The amplitude was increased to 30 cm H_2O with little benefit. The team recognized the need for a longer expiratory time, the urgency of enhancing secretion removal, and the need to reach an effective gas exchange at lower MAP due to lung hyperinflation. HFJV was indicated. The patient was switched to Life Pulse HFJV (Bunnell Inc, Salt Lake City, Utah) in tandem with Babylog 8000 plus (Drägerwerk AG & Co. Lübeck, Germany) with FiO_2 1.0. Initial parameters on HFJV: RR 240 /min, PIP 40 cm H_2O, PEEP (set/measured) 9/11.4 cm H_2O, MAP 14 cm H_2O, Ti 0.020, FiO_2 0.50, and no sigh breaths were initially used. Sedation needs were reevaluated, hydration readjusted, and frequent ETT suctioning continued. Within an hour of HFJV and effective sedation, the ABG showed: 7.34/46/58/25/-1.0, with a calculated OI value of 12.1.

After 15 hours of ventilation using HFJV, a CXR was done (Figure 2), which showed findings of hyperinflation and concurrent subsegmental atelectasis. Another CXR was repeated on the third day of therapy with HFJV and showed improvement in overall aeration with no obvious areas of consolidation, uneven residual hyperinflation, or persistent bilateral perihilar peribronchial thickening in keeping with RSV bronchiolitis.

Throughout the 6-day period of HFJV support, minimal changes were made to the original ventilation parameters and the patient remained hemodynamically stable with no need for inotropic support. During her hospitalization, we noticed that her heart rate was persistently greater than 180 bpm. Caffeine had been discontinued at the time of her transfer, and her heart rate did not decrease with adequate sedation. An electrocardiogram and echocardiogram excluded RSV myocarditis. Furthermore, her volume status was not consistent with dehydration as her total fluid intake and urinary output remained appropriate for gestational age. A repeat CBC showed anemia, therefore she received a second transfusion of packed red blood cells but her tachycardia persisted. Recurrent transient hypoxemia episodes lead to fluctuations in the patient's oxygen requirements (FiO_2 0.31-1.0). The PaO_2 ranged from 35 to 84 mmHg.

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Calculated OI ranged from 1.8 to 15.7, and there were no significant improvements associated with changing modes of ventilation or ventilator settings. Rather a gradual improvement with time was noted, which is in keeping with the natural history of RSV bronchi-

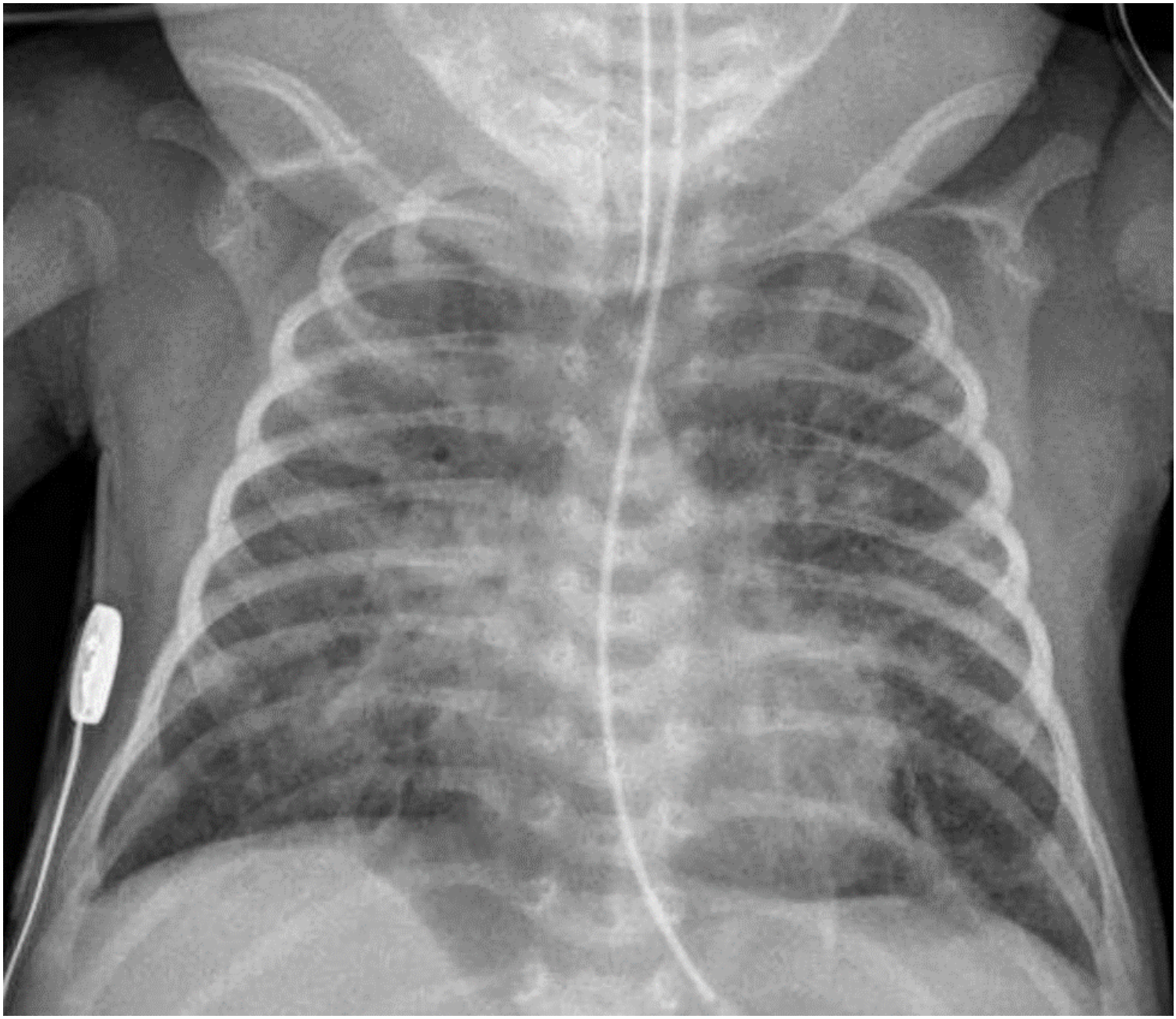

Figure 2. Reported CXR findings after 15 hours on HFJV: persistent bilateral peri-hilar bronchial thickening with uneven hyperinflation were seen in both lungs and are in keeping with known RSV bronchiolitis. There are persistent streaky linear opacities representing sub-segmental atelectasis, and a new area of atelectasis seen in the right upper lobe. Endotracheal tube position was unchanged.

olitis pneumonia. The measured PEEP values on the HFJV were always 2-3 cm H_2O higher than the set PEEP displayed on the Babylog 8000 plus, which was suggestive of air trapping.

By day 3 of HFJV, sedation was transitioned from fentanyl to morphine infusion, as it was felt the patient had developed tolerance to fentanyl. The intent was to improve patient comfort and relaxation on the ventilator. By day 6 of HFJV, the patient was successfully transitioned to conventional ventilation settings: AC VG (4.5 ml/kg), RR 55, Peep 8 cm H_2O, PIP 18 cm H_2O, FiO_2 0.25, $ETCO_2$ 51 mmHg. Conventional ventilation parameters were further weaned over the next 3 days as was sedation, and she was successfully extubated to nCPAP, followed by low flow oxygen and finally room air.

The baby was transferred to the Pediatric ward for convalescence at 43 days of life.

Discussion

A review of the literature at the time of this admission to our NICU revealed a significant gap in addressing the needs of premature infants in the context of nosocomial RSV. The majority of previously published literature addressed different management of RSV in ex-premature populations following discharge home from the NICU rather than during the initial course of admission (3). Although there have been a few case reports of surfactant, inhaled nitric oxide, and ribavirin as possible therapeutic avenues, none of these were part of the standard of recommended care, therefore inapplicable to our patient (4).

RSV bronchiolitis is characterized by obstruction and collapse of

small airways during expiration (4). The airway narrowing is due to virus-induced necrosis of the bronchiolar epithelium, mucus hypersecretion, and submucosal edema (4). Preterm infants due to the small size of their bronchioles are at a greater disadvantage compared to term infants. In addition, preterm infants are more susceptible to RSV disease from an immunological perspective (1). The majority of protective IgG is transferred across the placenta in the last four weeks of pregnancy prior to delivery, and as such preterm infants do not receive these antibodies prior to their birth (5).

The natural history of RSV is that the illness tends to peak in severity sometime between day 3 to day 6. In our patient, we appreciated the same pattern in that she seemed to be the most ill, requiring maximal ventilator support, oxygen needs, increased levels of sedation, and frequent pulmonary toileting, on day six of illness. Subsequently, illness resolution took much longer than anticipated, likely due in part to prematurity and complications associated with impaired immune function and smaller airways prone to mucus plugging. Previous work (6) found that children with atelectasis on days 1 and 2 following intubation for RSV bronchiolitis were more likely to have a protracted clinical course and intubation for greater than eight days' duration; this was in keeping with our case.

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At the time of arrival to our NICU, the patient was not comfortable, and during the course of her admission, it became evident that optimal sedation was key to effective ventilation. Secretions were overwhelmingly excessive as we observed that despite frequent suctioning, the continuous overproduction of mucous, secondary to necrotizing bronchiolitis, contributed to the baby struggling. What proved to be a relevant factor for managing our patient, more so than changing modes of ventilation, was changing to a nasal ETT of the appropriate calculated size to weight ratio. This elective change allowed for optimal airway stability and improved pulmonary toileting.

Retrospectively, the respiratory therapy team felt that while on HFOV, optimal sedation had not yet been achieved. Nevertheless, the care team deemed necessary to sedate our patient until the problematic issue of overabundant secretions was under control. HFJV was chosen primarily to facilitate secretion clearance, and acknowledging that the performance of the HFJV is not influenced by the airway resistance nor lung compliance. Another unique feature of jet ventilation compared to HFOV is that HFJV has the ability to indicate the presence of air- trapping by showing that the measured PEEP on HFJV is greater than the set PEEP on the conventional ventilator. The passive exhalation phase on HFJV allowed for a greater I:E ratio of 1:12. This was beneficial in the context of air trapping compared to the I:E ratio of 1:2 delivered with HFOV. In fact, we know from experience that sick prematures with only 1:2 or 1:3 ratios are prone to gas trapping. While on HFJV, the respiratory therapy team utilized manual lung volume recruitment techniques to improve secretion clearance. Although not supported by strong evidence, this maneuver is empirically associated with benefit in ventilated pediatric patients with RSV.

Possible explanations for lability in the oxygen requirement include challenges in maintaining adequate sedation and airway obstruction. Needing frequent pulmonary toileting, we prone-positioned our patient every 12 hours and trialed neuromuscular blockade (Rocuronium), with no substantial change in oxygen requirements.

Despite the escalation of ventilation support and periods of 100% oxygen requirements, episodes of hypoxemia were still noted. An echocardiogram was done to rule out a potential intracardiac shunt contributing to persistent hypoxemia. This echocardiogram revealed a structurally normal heart with no evidence of a PDA, PFO, or elevated pulmonary pressures. The hypoxemia was presumed to be likely due to intrapulmonary shunting with $\dot{V}$ /$\dot{Q}$ mismatch, secondary to RSV disease that resolved with the resolution of the patient's bronchiolitis pneumonia.

Persistent sinus tachycardia was a prominent feature of our patient's disease. In our NICU, tachycardia has also been clinically observed with other preterm infants on HFJV with non-compliant lung issues. Ultimately tachycardia did not resolve until our patient was extubated and had recovered from the worst phase of her RSV illness by day 11 of her admission.

Conclusion

- More research is needed to guide the supportive management of nosocomial RSV bronchiolitis in the preterm NICU population while these infants are still hospitalized prior to discharge home.
- Switching to an appropriately sized and more secure airway is indispensable to achieve effective pulmonary toileting as secretions can be abundant and present early in the course of the disease in premature lungs and airways.
- Adequate sedation remains a critical element of management to help optimize chest compliance and, therefore, efficient ventilation and oxygenation.
- In the clinical context of RSV in premature lungs, HFJV should be used with the understanding and the caution that measured PEEP and chest expansion, without hemodynamic instability, does not necessarily need to be matched.
- The main variable of treating premature with RSV is gas trapping, which leads to hyperinflated lungs. HFJV with passive exhalation enabled us to deliver longer i:e ratios of 1:12 compared to 1:1 to 1:3 provided by HFO with an active exhalation phase.
- In our experience, HFJV was able to support the management of hypercapnia and hypoxemia during the worst period of the disease in a premature infant.
- The duration of the disease was much more prolonged than what we would usually see in term babies or ex-preterm infants at a later age affected by RSV bronchiolitis: 11 days compared to the described average of 6 days.
- During RSV season, nosocomial bronchiolitis should be part of the differential for any baby presenting with a 'rule out sepsis' picture, and appropriate viral studies should be ordered.

- NICU personnel must be accountable for staying home when feeling unwell, and NICU visitation policies must be reinforced to exclude ill persons, including parents and siblings, especially during the viral season.

References:

1. *Kliegman R, Stanton B, Geme J, Behrman R, Schor N. Nelson textbook of Pediatrics 19th Edition. Philadelphia, PA. Kliegman et al.; 2011.*
2. *Robinson JL. Preventing respiratory syncytial virus infections. Pediatrics and Child Health. 2011; 16(8): 488-90. doi:10.1093/pch/16.8.487.*
3. *Valentine KM, Sarnaik AA, Sandhu HS, Sarnaik AP. High Frequency Jet Ventilation in respiratory failure Secondary to respiratory Syncytial Virus infection: A case series. Front. Pediatr. 2016;4(92). doi:10.3389/fped.2016.00092.*
4. *Friedman J, Rieder M, Walton J. Bronchiolitis: recommendations for diagnosis, monitoring and management of children one to 24 months of age. Pediatrics and Child Health. 2014; 19(9). https://www.cps.ca/en/documents/position/bronchiolitis.*
5. *Palmeira P, Quinello C, Silveira-Lessa AL, Zago CA, Carneiro-Sampaio M. IgG placental transfer in healthy and pathological pregnancies. Clinical and Developmental Immunology. 2012; 2012. doi: 10.1155/2012/985646.*
6. *Prodhan P, Westra SJ, Lin J, Karni-Sharoor S, Regan S, Noviski N. Chest radiological patterns predict the duration of mechanical ventilation in children with RSV infection. Pediatric Radiology. 2009; 39(2). doi:10.1007/s00247-008-1042-3.*

Disclosure: The authors have no disclosures.

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