

Assessment of bronchodilator response by forced oscillation technique in preterm infants with evolving bronchopulmonary dysplasia

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Abstract

Inhaled bronchodilators are often given in preterm infants with evolving or established bronchopulmonary dysplasia. However, it is unclear which patients may benefit from it and when it is the best time to start treatment. The forced oscillation technique (FOT) is a noninvasive method for assessing lung mechanics that proved sensitive to airway obstruction reversibility in children and adults. FOT does not need patient cooperation, which is ideal for infants. Bedside tools for applying FOT in infants during spontaneous breathing and different respiratory support modes are becoming available. This case report illustrates for the first time that FOT has potential value in assessing airway obstruction reversibility in preterm infants, informing which infants may manifest a clinical benefit from the treatment with bronchodilators.

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Running head : Functional response to bronchodilators in infants

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Abstract

Inhaled bronchodilators are often given in preterm infants with evolving or established bronchopulmonary dysplasia. However, it is unclear which patients may benefit from it and when it is the best time to start treatment. The forced oscillation technique (FOT) is a noninvasive method for assessing lung mechanics that proved sensitive to airway obstruction reversibility in children and adults. FOT does not need patient cooperation, which is ideal for infants. Bedside tools for applying FOT in infants during spontaneous breathing and different respiratory support modes are becoming available. This case report illustrates for the first time that FOT has potential value in assessing airway obstruction reversibility in preterm infants, informing which infants may manifest a clinical benefit from the treatment with bronchodilators.

Introduction

Preterm infants with evolving or established bronchopulmonary dysplasia (BPD) are predisposed to reactive airway obstruction¹. In these patients, inhaled bronchodilators are used to treat acute events and improve respiratory outcomes. On average, bronchodilators improve short-term lung mechanics and reduce the work of breathing².

Not all infants manifest a positive response to bronchodilators³. Moreover, within the same patient, the response may change over time. The lack of suitable tools for measuring lung function in this population prevents the possibility of assessing airway obstruction reversibility. Clinically, infants get treated with bronchodilators if they manifest a positive response to a short trial. In this way, some infants receive a drug they do not need, while others who would manifest a delayed benefit may not receive it.

The forced oscillation technique (FOT) is a noninvasive method for assessing lung function that proved sensitive to bronchodilators response in adults and children⁴. FOT applies small amplitude pressure oscillations to the respiratory system and measures its mechanical response in terms of resistance (R_{RS}) and reactance (X_{RS} , proxy of lung compliance). FOT is ideal to be used in infants because it does not need patient cooperation. Novel devices for the application of FOT at the bedside are becoming available. In this article, we report preliminary data suggesting that FOT has potential value to assess the responsiveness to bronchodilators in preterm infants.

Methods

This preliminary study has been conducted in the Neonatal Intensive Care Unit of Fondazione Monza e Brianza per il Bambino e la sua Mamma. Written informed consent was obtained from both parents for publication of this case report. In our unit, we perform FOT measurements routinely to optimize the respiratory support strategy and evaluate the response to pharmacological treatments. We perform measurements at the bedside during natural sleep using a mechanical ventilator (Fabian HFOi, Vyairé) that superimposes pressure oscillations (amplitude 5 cmH₂O, frequency 10 Hz) during different respiratory support modes. Inhaled bronchodilators are used in patients with an intensive or prolonged need for respiratory support if they manifest a positive response to a short therapy trial.

This paper reports preliminary data of a male infant born at 29+2 weeks with a birth weight of 990 grams. He received a prolonged period of respiratory support, including 31 days of invasive ventilation, 20 days of nCPAP and 69 days of high flow nasal cannula (HFNC), and was discharged home at 46 weeks' postmenstrual

age (PMA) on HFNC in room air. We performed trials with bronchodilators on postnatal days 7 and 14 when he was intubated with high oxygen requirement (43% and 35%, respectively), and at 40 weeks' PMA when he was on HFNC with a persistent need for $\text{FiO}_2 > 30\%$.

For each trial, we assessed lung mechanics by FOT before and 15 minutes after administering 200 mcg/kg of nebulized salbutamol. Differences between before and after administering bronchodilators were compared with the measurements' short-term repeatability, defined as the 95% limits of agreement between duplicate measurements performed in 23 preterm infants.

Results

The measurements' short-term repeatability was ± 7.7 and ± 5.2 $\text{cmH}_2\text{O}^*\text{s}/\text{L}$ for R_{RS} and X_{RS} , respectively. At 7 and 14 postnatal days, the differences between before and after bronchodilators were 1.1 $\text{cmH}_2\text{O}^*\text{s}/\text{L}$ (2.8 %) and -0.1 $\text{cmH}_2\text{O}^*\text{s}/\text{L}$ (0.1 %), respectively, for R_{RS} and 0.2 cmH_2O (-0.5 %) and -0.4 $\text{cmH}_2\text{O}^*\text{s}/\text{L}$ (0.4 %) for X_{RS} . Such differences were within the limits of agreement. We did not repeat the treatment on these occasions because we did not observe any improvement in terms of FiO_2 , ventilation parameters, respiratory distress, auscultatory signs, and lung function. At 40 weeks' postmenstrual age (PMA), R_{RS} decreased by 19.1 $\text{cmH}_2\text{O}^*\text{s}/\text{L}$ (48 %), and X_{RS} increased by 19.5 $\text{cmH}_2\text{O}^*\text{s}/\text{L}$ (69 %) after bronchodilators, the changes being larger than the limits of agreement (Fig.1, left). On this occasion, we started therapy with 200 mcg/kg of nebulized salbutamol every 8 hours with the rationale to reduce the infant's work of breathing, even if we did not observe any improvement in other clinical parameters. The oxygen requirement markedly decreased after a couple of days. After ten days, bronchodilators were given every 12 hours for the following four days, and oxygen requirement reached 21% at the end of the 2-week treatment (Fig. 1, right).

Discussion

To our knowledge, this is the first report describing the use of FOT to assess bronchodilators responsiveness in preterm infants. This case illustrates that FOT can be used in preterm newborns to detect lung function response to inhaled bronchodilators and inform an appropriate and personalized therapy.

Bronchodilators are used in infants with evolving or established BPD⁵, but there are no clear indications on who may benefit from them. In some cases, the patient does not manifest a positive clinical response after a single administration but after a few days of treatment. Consequently, some infants may receive a treatment they do not need, being exposed to potential side effects like tachycardia or hyperglycemia, and others do not receive a treatment they may benefit from. We speculate that in chronic patients with peripheral airways obstruction, the improvement in gas exchange may not be evident after a single administration but after a few days of treatment.

The standard way to test airway obstruction reversibility is by spirometry, which is not feasible in infants. Several studies demonstrated an improvement in R_{RS} and X_{RS} and investigated the thresholds for bronchodilator responsiveness bronchodilators in adults and children⁴. However, FOT has never been used to test airway obstruction reversibility in infants, and the threshold for bronchodilator response has never been studied.

Conclusion

Bronchodilators can help reduce the respiratory support requirement in infants with BPD. However, not all infants respond, and, within the same patient, the response may change over time. FOT is a noninvasive bedside tool that may assess airway obstruction reversibility and allow for a more appropriate and personalized administration of bronchodilators.

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Figure Legend

Fig. 1. Lung mechanics (left) and clinical (right) response to bronchodilator at 40 weeks' postmenstrual age. BD: bronchodilators. PNA: postnatal age. R_{RS} and X_{RS} : respiratory system resistance and reactance. FiO_2 : fraction of inspired oxygen. Closed circles: R_{RS} , open symbols: X_{RS} . Dashes lines: limits of agreement.

