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Case Report

Endotracheal N-acetylcysteine for Atelectasis in Neonatal Pneumonia

Mustafa Dilek, Halil İbrahim Atasoy, Seher Açar

Bolu Abant İzzet Baysal University Faculty of Medicine, Department of Pediatrics, Bolu, Turkey

ABSTRACT

Although there is no gold standard therapy in the treatment of atelectasis in newborns, surfactant therapy, inhaled mucolytic agents, recombinant human deoxyribonuclease, positive pressure mechanical ventilation, postural changes and drainage can be used. However, N-acetylcysteine (NAC), via endo-bronchoscopy, is rarely used to break the disulfide bonds in the mucus. It is a cheap and readily available treatment to apply. Here, we present a newborn with neonatal pneumonia to whom we instilled NAC thorough an endotracheal tube to resolve right lung total atelectasis. The atelectasis responded to instillation quickly and successfully. We are presenting this case in order to suggest a novel effective treatment modality for already intubated newborns with atelectasis. This case also represents the first successful treatment case in the newborn period.

Keywords: Atelectasis, N-acetylcysteine lavage, newborn

Introduction

Inflammatory response in the airway causes necrosis and loss of the respiratory epithelium. The result of tissue edema and mucus production with the addition of air causes thick mucus plugs. This can disrupt the normal function of the airways. Full mucus plug blockages lead to atelectasis, whereas partial blockage causes air trapping. In neonatal intensive care, there are limited treatment options for atelectasis. This lack of options in resistant atelectasis has led to the search for safe and effective novel treatment modalities. Here, we report an atelectasis which occurred in a premature neonate which resolved quickly after N-acetylcysteine (NAC) instillation through an endotracheal tube. We report the case and similar literature findings since this treatment modality might be a novel treatment for neonatal atelectasis in intensive care units.

Case Report

A premature baby was born after 34 weeks of gestation. He weighed 1.785 kg and was born to a non-consanguineous marriage. The antenatal follow-up was normal. A history of cystic fibrosis was not obtained. Physical examination revealed respiratory distress. He was hospitalized in the neonatal intensive care unit. During the next 48 hours, chest retractions and oxygen demand increased despite nasal positive pressure support. We started ampicillin with sulbactam and amikacin for the treatment of neonatal pneumonia and early onset sepsis. However, the patient developed hypercapnia and required endotracheal intubation. During mechanical ventilation, C-reactive protein increased and antibacterial therapy was substituted for teicoplanin and meropenem. Intravenous immunoglobulin was given for sepsis. On postnatal day 9,

Address for Correspondence
Mustafa Dilek MD, Bolu Abant İzzet Baysal University Faculty of Medicine, Department of Pediatrics, Bolu, Turkey
Phone: +90 505 377 95 09 E-mail: mustafadilek@gmail.com ORCID: orcid.org/0000-0002-3802-0336
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we observed increased respiratory effort and substantial retractions. Chest examination showed decreased respiratory sounds over the right lung. Radiography demonstrated total loss of volume in the relevant lung with the trachea and heart displaced to the right (Figure 1). The patient needed postural drainage for the atelectasis. The mediastinal shift to the right did not respond to effective chest therapy. After parental consent, we tried NAC (Asist® for parenteral use) 200 mg-1 mL mixed with 3 mL of 0.9% saline (1). One mL of a total of 4 mL was introduced each time through a tracheal tube and the patient was aerated and oxygenated via bag and mask ventilation for 1 minute. We positioned the patient's head to the left, aiming the solution to the right main bronchus. The patient was also positioned to the right lateral side during the instillation. After four 4-hour-apart instillations, we observed increased sounds over the right lung. The need for oxygen also decreased. At the end of 12 hours from the first instillation, near total resolution of the atelectasis was seen in chest X-ray (Figure 2).

The patient was extubated 24 hours following the procedure. Antibacterial treatment was completed in 14 days. He was discharged on postnatal day 30. The repeat sweat test was negative.

Discussion

Pulmonary atelectasis is defined as a partial or total collapse or incomplete expansion of the alveolar spaces. One factor leading to atelectasis results from an obstruction of the airways by an abundant, thick and sticky mucus (2). Mucus is a non-homogeneous, viscoelastic fluid and is composed of glycoproteins predominantly linked by disulfide bonds, proteins, lipids and water. Another factor for atelectasis is the poor clearance of inflammatory debris that occludes the lumen of the airways. Edema of the bronchial wall and smooth muscle constriction are additive factors leading to complete obstruction. A third factor for atelectasis is surfactant deficiency or dysfunction, which causes increased alveolar surface tension with subsequent diffuse atelectasis.

Atelectasis is a severe problem in many newborn babies with pulmonary infections, surfactant insufficiencies or ventilator support (3). The most common cause during the neonatal period is hyaline membrane disease. Pneumonia or pulmonary edema by way of secondary surfactant insufficiency are the other causes (4).

Treatment options for atelectasis such as chest physiotherapy, inhaled bronchodilators, steroids, nebulized

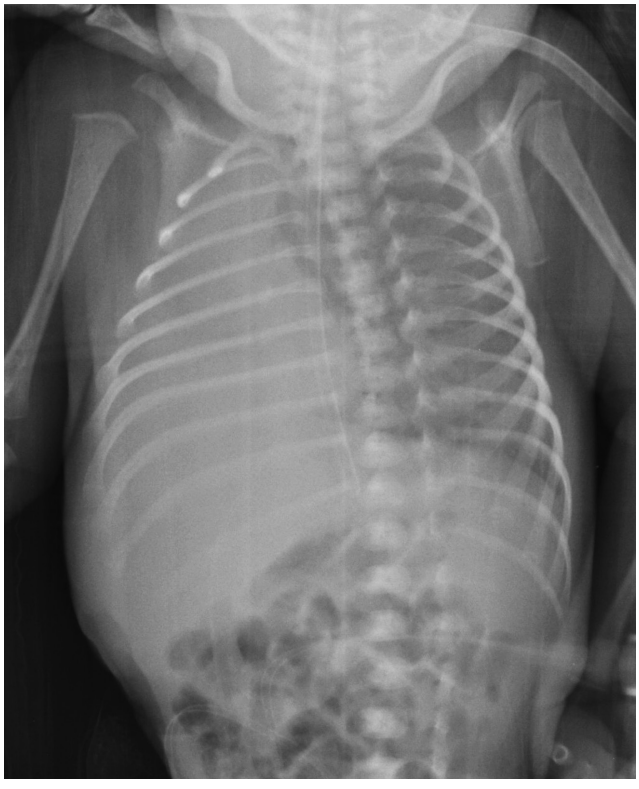

Figure 1. Chest X-ray before N-acetylcysteine instillation. Note the collapse of the right lung with right mediastinal shift

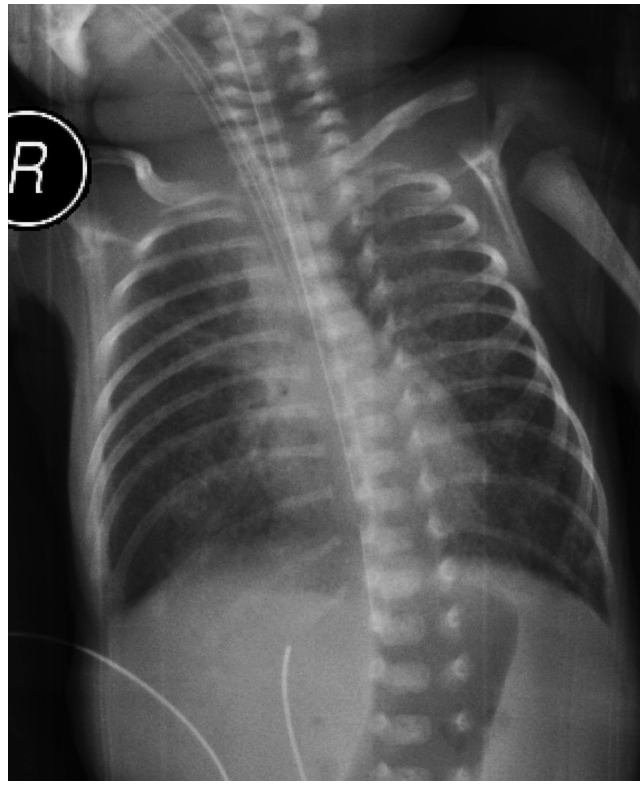

Figure 2. Chest X-ray after 12 hours of N-acetylcysteine instillation. Near-total resolution or expansion of the right lung was observed

sodium chloride (NaCl 0.9%) and recombinant human deoxyribonuclease (DNase) have been developed but their efficiency has not been proven in the neonatal period. The treatment objective in atelectasis is mainly focused on eliminating the viscoelastic plugs within the airways (2).

Mucolysis can be achieved either through physical intervention, such as high frequency oscillation, or by biochemical or pharmacologic agents, such as NAC or DNase (5,6). Mucolytic agent NAC with inherent anti-inflammatory properties in experimental models reduces the mucus viscosity and elasticity by breaking disulfide bonds (7,8).

Human DNase has also been used to reduce the viscosity of secretions in acute and chronic respiratory conditions. DNase application via bronchoscopy for mucolysis in the treatment of atelectasis in preterm and term neonates has been reported (2,3,9,10). We preferred NAC as the mucolytic agent in our patient for several reasons. The first factor is that its use is feasible. Another factor is that it is easily affordable. To our knowledge, there are no studies comparing the efficacy of NAC to DNase or saline but our research has shown that it has great potential in the treatment of newborns. The drug was applied to a newborn who had already been intubated with a tracheal tube, so no further invasive measures were needed for this alternative treatment.

In animal models, NAC improved oxygenation, reduced lung edema, decreased polymorphonuclear leukocytes in bronchoalveolar lavage fluid, diminished peroxidation and meconium-induced airway reactivity compared with untreated animals (11).

In accordance with our observation, a previous case study also observed a successful expansion of an atelectatic lung in a 35-year-old women with pneumonia in whom NAC in 3 ml of physiologic saline was instilled through an endotracheal tube (12). In another case report, a 2-month-old male infant presenting with atelectasis, severe respiratory failure and pulmonary hypertension, and requiring extracorporeal membrane oxygenation responded well to repeated NAC instillations with bronchoscopy (9). Our newborn patient, the youngest reported in English literature, had a near total collapse or atelectasis in the right lung. After one hour of instillation through an endotracheal tube, clinical improvement occurred. There was near-complete resolution of the right lung on chest X-ray after 12 hours of instillation.

Bibi et al. (13) previously reported such side effects as bradycardia, cyanosis and increased airway resistance in preterm babies who had received intratracheal 5% NAC every 4 hours. The findings of the authors did not support the use of NAC as mucolytic for extremely preterm neonates with chronic pulmonary disease. The absence of the desired effects of NAC in that study conducted in preterm infants with chronic pathology characterized by alveolar and vascular insufficiency in addition to fibrosis as opposed to our case which was an acute pathology with neonatal pneumonia in a late preterm infant is an important difference.

On these grounds, we suggest that NAC instillation through tracheal tube for already intubated newborns can be considered as an effective, easy and novel treatment modality for atelectasis. This case is unique since there are no similar reports in the literature for this particular age group. Our case has demonstrated the need for further controlled studies in which similar implementations of NAC are used.

Ethics

Informed Consent: Permission and consent was obtained from parents.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.D., H.İ.A., S.A., Concept: M.D., H.İ.A., Design: M.D., H.İ.A., Data Collection or Processing: M.D., H.İ.A., S.A., Analysis or Interpretation: M.D., H.İ.A., S.A., Literature Search: M.D., H.İ.A., Writing: M.D., H.İ.A.

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References

1. Shafiq M, Khan RA, Iqbal M, Khan H. Bronchopulmonary lavage and re-expansion of the atelectatic lung without bronchoscopy. Anaesthesia, Pain & Intensive 2011;15:173-5.
2. Altunhan H, Annagür A, Pekcan S, Ors R, Koç H. Comparing the efficacy of nebulizer recombinant human DNase and hypertonic saline as monotherapy and combined treatment in the treatment of persistent atelectasis in mechanically ventilated newborns. Pediatr Int 2012;54:131-6.
3. Hendriks T, de Hoog M, Lequin MH, Devos AS, Merkus PJFM. DNase and atelectasis in non-cystic fibrosis pediatric patients. Crit Care 2005;9:R351-6.
4. Peroni DG, Boner AL. Atelectasis: mechanisms, diagnosis and management. Paediatr Respir Rev 2000;1:274-8.
5. King M, Rubin BK. Pharmacological approaches to discovery and development of new mucolytic agents. Advanced drug delivery reviews 2002;54:1475-90.

6. Dasgupta B, Tomkiewicz RP, Boyd WA, Brown NE, King M. Effects of combined treatment with rhDNase and airflow oscillations on spinnability of cystic fibrosis sputum in vitro. Pediatr Pulmonol 1995;20:78-82.

7. Sheffner AL. The reduction in vitro in viscosity of mucoprotein solutions by a new mucolytic agent, N-acetyl-L-cysteine. Ann N Y Acad Sci 1963;106:298-310.

8. Sheffner AL, Medler EM, Jacobs LW, Sarett HP. The in vitro reduction in viscosity of human tracheobronchial secretions by acetylcysteine Am Rev Respir Dis 1964;90:721-9.

9. Mata AF, Sarnaik AA. Bronchoscopy with N-acetylcysteine lavage in severe respiratory failure from pertussis infection. Pediatrics 2013;132:1418-23.

10. Merkus PJ, de Hoog M, van Gent R, de Jongste JC. DNase treatment for atelectasis in infants with severe respiratory syncytial virus bronchiolitis. Eur Respir J 2001;18:734-7.

11. Mokra D, Drgova A, Petras M, Mokry J, Antosova M, Calkovska A. N-acetylcysteine Alleviates the Meconium-Induced Acute Lung Injury. Adv Exp Med Biol 2015;832:59-67.

12. Shafiq M KR, Iqbal M, Khan H. Bronchopulmonary lavage and re-expansion of the atelectatic lung without bronchoscopy. Anaesth Pain & Intensive Care 2011;15:173-5.

13. Bibi H, Seifert B, Oullette M, Belik J. Intratracheal N-acetylcysteine use in infants with chronic lung disease. Acta Paediatr 1992;81:335-9.