Türk Kadın Sağlığı ve Neonatoloji Dergisi

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Original Article

Surfactant treatment for neonatal respiratory disorders in late preterm and term infants

Geç preterm ve term bebeklerdeki neonatal respiratuvar bozukluklarda surfaktan tedavisi

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Abstract

Aim: Surfactant treatment was reported to be effective in improving gas exchange in late preterm and term infants with respiratory failure. However, guidelines recommending surfactant therapy in these newborns are not clear. We aimed to investigate the clinical features of late preterm and term infants who received surfactant treatment for respiratory failure in the neonatal intensive care unit.

Material and Method: This retrospective study included neonates with gestational age >34 weeks who treated with exogenous surfactant in the neonatal intensive care unit between 2011-2013.

Results: During the study period a total of 3212 infants with gestational age >34 weeks were hospitalized in the neonatal intensive care unit, among them 28 infants (16 male/12 female) received surfactant treatment because of respiratory failure. Mean birth weight and gestational age for the total cohort were 2907 ± 145 gr and 36.14 ± 0.52 weeks respectively. There were 16 infants with neonatal pneumonia, 6 infants with transient tachypnea of the newborn, 4 infants meconium aspiration syndrome (MAS) and 2 infants with pulmonary hypoplasia. The mean postnatal age of surfactant treatment was 1.85 ± 0.44 days.

Conclusion: Secondary surfactant deficiency may cause serious respiratory failure in late preterm and term infants. Surfactant replacement therapy can be useful as a supporting treatment in this population. However additional studies are needed to establish the value and limitations of surfactant therapy for secondary surfactant deficiency in late preterm and term infants.

Key words: Surfactant; late preterm; term infant

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Öz

Amaç: Surfaktan tedavisinin, solunum yetmezliği olan geç preterm ve term bebeklerde gaz değişimini iyileştirmede etkili olduğu gösterilmiştir. Ancak bu bebeklerde surfaktan uygulaması ile ilgili öneriler net değildir. Bu çalışmada, solunum yetmezliği nedeni ile surfaktan tedavisi uygulanan geç preterm ve term bebeklerin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: 2011-2013 yılları arasında, gestasyon yaşı 34 hafta ve üzerinde olan RDS dışı akciğer hastalığı nedeni ile surfaktan uygulanan hastalar retrospektif olarak incelendi.

Bulgular: Çalışma süresince gestasyon yaşı 34 haftanın üzerinde olan 3212 hasta yenidoğan yoğun bakım ünitesine yatırıldı. Bu hastaların 28'ine (16 erkek/12 kız) solunum yetmezliği nedeni ile surfaktan uygulandı. Hastaların ortalama doğum ağırlığı 2907±145 gr, ortalama doğum haftası 36.14 ± 0.52 hafta idi. Surfaktan uygulanan hastaların 16'sında (%57.2) neonatal pnömoni, 6'sında (%21.4) yenidoğanın geçici takipnesi, 4'ünde (%14.2) mekonyum aspirasyon sendromu (MAS), 2'sinde (%7.1) pulmoner hipoplazi saptandı. Surfaktan uygulanma zamanı ortalama 1.85 ± 0.44 gün saptandı.

Sonuç: Sekonder surfaktan eksikliği geç preterm ve term bebeklerde ciddi solunum yetmezliğine neden olabilir. Bu bebeklerde solunum destek tedavisinde surfaktan kullanılabilir. Ancak geç preterm ve term bebeklerde sekonder surfaktan eksikliğinde surfaktan kullanımı ile ilgili ek çalışmalar gerekmektedir.

Anahtar Kelimeler: Surfaktan; geç preterm; term bebek

Introduction

Surfactant replacement therapy has been proven beneficial in the prevention and treatment of neonatal respiratory distress syndrome (RDS) (1,2). RDS in premature infants is a result of surfactant deficiency because of pulmonary immaturity (3). Surfactant inactivation and secondary dysfunction may occur in a broad group of disorders and may contribute to respiratory failure in newborns other than preterm infants. Meconium aspiration syndrome (MAS), persistent pulmonary hypertension of the newborn, neonatal pneumonia, and pulmonary hemorrhage may be complicated by surfactant inactivation (4-6). Surfactant replacement therapy was reported to be effective in improving gas exchange in late preterm and term infants with respiratory failure (3,7). However, guidelines recommending surfactant therapy in neonates with secondary surfactant deficiency are not clear.

In this study, we retrospectively reviewed clinical features of late preterm and term infants who received surfactant treatment for respiratory failure in neonatal the intensive care unit.

Material and Method

a. Patients and methods

A retrospective trial was conducted in Etlik Zübeyde Hanım Women's Health Teaching and Research Hospital, Ankara, Turkey between January 2011 - December 2013. Neonates with gestational age >34 weeks who received surfactant treatment for respiratory failure were enrolled. Medical records of patients were evaluated retrospectively. Clinical data including gestational age, birth weight, gender, type of delivery, the duration of ventilatory support (days on mechanical ventilation, nasal continuous positive airway pressure, supplemental oxygen), postnatal age of surfactant treatment and death were recorded.

b. Management and treatment

Patients were evaluated with history, physical examination and laboratory tests (a complete blood count, C-reactive protein and blood cultures) upon admission. Neonates with respiratory failure were provided supplemental oxygen by a hood to maintain oxygen saturation above 90%. Nasal continuous positive pressure (nCPAP) was used, if the patient has increased work of breathing and patients were intubated with FiO2 requirement >0.6 on nCPAP. Exogenous surfactant at a dose of 100 mg/kg beractant was considered in those with FiO2>0.6 requirement on ventilatory support to maintain oxygen saturation between 90-95%.

c. Definitions

Pneumonia: The presence of clinical signs of respiratory distress, supplemental oxygen and/or positive pressure ventilation requirement, extra-pulmonary clinical signs of sepsis beginning from birth, and typical chest X-ray findings (8).

Transient tachypnea of the newborn (TTN): The criteria for the diagnosis of TTN were presence of respiratory distress

(tachypnea, retractions, grunting, nasal flaring, mild cyanosis), persistence of tachypnea for at least 12 h and chest X-ray consistent with TTN (perihilar striking, hyperinflated lungs, flattening of the diaphragm, and fluid in the fissures) (9).

Meconium aspiration syndrome (MAS): Respiratory distress in an infant born through meconium-stained amniotic fluid whose respiratory and radiological signs cannot be otherwise explained (10).

Pulmonary hypoplasia: Pulmonary hypoplasia is defined as a primary failure of normal lung development by intrinsic factors or secondary caused by multiple pathologic processes that interfere with normal lung development (11).

Results

During the study period, a total of 3212 infants with gestational age>34 weeks were hospitalized in the neonatal intensive care unit, among them 28 infants (16 male/12 female) received surfactant treatment because of respiratory failure. Mean birth weight and gestational age for the total cohort were 2907 ± 145 grand 36.14 ± 0.52 weeks respectively. There were 16 infants with neonatal pneumonia, 6 infants with transient tachypnea of the newborn, 4 infants meconium aspiration syndrome and 2 infants with pulmonary hypoplasia. The mortality rate was 7.1%. The mean duration of mechanical ventilation, nasal CPAP and supplemental oxygen was 2.39 ± 1.13 days, 2.07 ± 0.89 days, 5.35 ± 3.96 days respectively. The mean postnatal age of surfactant treatment was 1.85 ± 0.44 days (**Table 1**).

Table 1: Clinical characteristics of the patients (n=28)

Patients	
Gestational age (weeks)*	36.14 ± 0.52
Birth weight (gram)*	2907 ± 145
Gender(M/F)	16/12
Mode of delivery (SVD/C/D)	11/17
Duration of supplemental O2 (day)*	5.35 ± 3.96
Duration of nasal CPAP (day)*	2.07 ± 0.89
Duration of mechanical ventilation* (day)	2.39 ± 1.13
Timing of surfactant treatment*(day)	1.85 ± 0.44
Mortality, n (%)	2 (7.1)

*data presented as mean ± standard deviation
M: Male; F: Female; SVD: Spontaneous Vaginal Delivery;
CD: Cesarean Delivery; O2: Oxygen; CPAP: continuous positive pressure

Discussion

Respiratory failure secondary to surfactant deficiency is a major cause of morbidity and mortality in preterm infants. Surfactant replacement was established as an effective and safe therapy for immaturity-related surfactant deficiency (1,2). Surfactant activity may be altered in respiratory disorders other than RDS and secondary surfactant deficiency may also contribute to acute respiratory morbidity in late preterm and term neonates. Surfactant replacement may be beneficial for these infants (12,13). However, evidence-based guidelines are not established in this population. We retrospectively reviewed the clinical characteristics of newborns treated with surfactant for respiratory failure other than RDS.

Inflammatory mediators released in pulmonary infection were shown to damage type II pneumocytes and inactivate surfactant (14). Small clinical experiences have demonstrated the benefit of surfactant to infants with pneumonia/sepsis. Rescue surfactant treatment in newborns with pneumonia was demonstrated to improve gas exchange (4,13,15). Pneumonia was the leading cause of respiratory failure treated with surfactant in our study.

TTN is a common respiratory morbidity in term and late preterm neonates due to delayed resorption of fetal lung fluid after birth (16,17). Mild surfactant deficiency is another hypothesis in this respiratory failure. Term infants with TTN were demonstrated to have low lamellar body counts associated with decreased surfactant function (18). Administration of exogenous surfactant promotes a dramatic clinical response in infants with TTN requiring intubation (19). In our study, six newborns with TTN were treated with exogenous surfactant.

Meconium inhibits the surface tension-lowering properties of surfactant and meconium aspiration syndrome with severe respiratory failure may be complicated by surfactant inactivation (14). Investigations have postulated surfactant treatment may be beneficial in infants with MAS (4-6). Surfactant treatment either as a bolus treatment or surfactant lavage has been proposed in MAS. Surfactant lavage for meconium aspiration was evaluated in a small, randomized trial; a lower duration of ventilation and severity of illness were reported (20). In one meta-analysis, bolus surfactant treatment for MAS decreased the need for extracorporeal membrane oxygenation (ECMO) but had no statistically significant effect on mortality and pulmonary morbidities (14). Surfactant administration was suggested to reduce the severity of illness and decrease the number of infants with progressive respiratory failure requiring ECMO support (12).

Both congenital and acquired lung growth impairments result in a decrease in lung alveolarization, type II pneumocyte counts and surfactant production (21,22), suggesting a potential benefit from surfactant replacement therapy. Newborns with a congenital diaphragmatic hernia (CDH) display pulmonary hypoplasia resulting in a high incidence of respiratory morbidity

and mortality (4,5). Animal models of CDH have revealed a deficient surfactant system (23,24). Data from cohorts of newborns with a prenatal diagnosis of isolated CDH do not show any benefit associated with surfactant therapy (25). In this study, 2 infants with pulmonary hypoplasia were treated with surfactant but they died because of severe respiratory failure.

Major limitation of this study is its retrospective design with no control group. It is based on the requirement of surfactant treatment with respiratory failure. However, a controlled study including all late preterm and term infants requiring mechanical ventilation would be better to evaluate the results of surfactant treatment in this population.

The deficiency of surfactant or surfactant dysfunction may contribute to respiratory failure in a broad group of disorders other than RDS in term infants.

Patient population, entry criteria, surfactant dosage vary considerably in infants with secondary surfactant deficiency. Surfactant replacement for illnesses other than RDS needs additional studies.

Declaration of Interest

The authors report no conflicts of interest.

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