· Study on Neonatal Disease · Original Article ·

Evaluation of the effects of surfactant replacement therapy in neonatal respiratory distress syndrome

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Abstract: Objective Respiratory distress syndrome (RDS) is a major cause of morbidity and mortality in preterm neonates. Pulmonary surfactant deficiency is the primary cause of RDS. The purpose of this study was to determine the effect of surfactant therapy in reduction of the mortality rate in premature neonates with RDS and to assess the relationship between the efficacy of surfactant therapy and some risk factors associated with RDS. **Methods** This study comprised 89 premature neonates with signs of RDS. The neonates were selected by simple sampling from those admitted to the Neonatal Intensive Care Unit (NICU) of Shaheed Beheshti Hospital. The eligible neonates received surfactant replacement therapy (100 mg/kg) during 48 hours after birth. **Results** Overall, 34 (38.2%) out of 89 neonates who received surfactant survived. The higher efficacy of surfactant replacement therapy was observed in neonates with gestational age of more than 32 weeks (47.5%), in those who received the first dose of surfactant during the first 24 hours of life (43.3%), in those with an Apgar score of more than 7/10 at 1 and 5 min (48.1%), and in those with a birth weight of more than 1 500 g (52.5%). The neonates whose mother received steroid therapy before labor had higher reduction in mortality after surfactant therapy (41.7% with steroid vs 34.2% without steroid; $P < 0.05$). **Conclusions** Surfactant replacement therapy in neonatal RDS should be started as soon as possible after birth. It could reduce the mortality rate from RDS by 38.2%. The efficacy of surfactant therapy for neonatal RDS may be associated with gestational age, Apgar score, birth weight, starting time of surfactant therapy and maternal steroid therapy.

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Key words: Surfactant; Respiratory distress syndrome; Maternal steroid therapy; Mortality; Premature neonate

表面活性物质替代治疗新生儿呼吸窘迫综合征的疗效评估

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[**摘 要**] **目的** 呼吸窘迫综合征 (RDS) 是早产儿发病和死亡的重要原因。RDS 主要由肺表面活性物质缺乏所致。该研究调查了表面活性物质治疗在减少早产儿死亡率中的作用,并评估了表面活性物质疗效与一些 RDS 相关危险因素的关系。**方法** 通过简单抽样抽取符合入选要求的 89 例 RDS 早产儿,他们均来自于 Shaheed Beheshti 医院新生儿重症监护室。生后 48 h 内给予表面活性物质治疗(100 mg/kg)。**结果** 89 例得到表面活性物质治疗的 RDS 早产儿中,34 例(38.2%) 幸存, 55 例死亡。其中胎龄大于 32 周,表面活性物质治疗开始于生后 24 h 内,1,5 分钟 Apgar 评分大于 7/10 分,或出生体重大于 1 500 g 者治疗效果较好,存活率分别为 47.5%, 43.3%, 48.1%,52.5%。表面活性物质治疗后母亲孕前经过激素治疗的 RDS 早产儿的存活率(41.7%)显著高于那些母亲孕前未经激素治疗者(34.2%)($P<0.05$)。**结论** 表面活性物质替代治疗新生儿 RDS 应尽可能早地进行,能减少 38.2% 的死亡率。新生儿胎龄、出生体重、Apgar 评分、表面活性物质治疗开始时间及母亲孕期是否经激素治疗等均可影响表面活性物质替代治疗的疗效。

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[**关 键 词**] 表面活性物质; 呼吸窘迫综合征; 孕期激素治疗;死亡率; 早产儿

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Respiratory distress syndrome (RDS) occurs primarily in premature infants. Its incidence is inversely related to gestational age and birth weight. It occurs in 60%-80% of infants of less than 28 weeks, in 15%-

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30% of those between 32 and 36 weeks, and in about 5% beyond 37 week of gestational age[1, 2].

The risk of RDS increases with maternal diabetes, elective cesarean section delivery, asphyxia, multiple births and maternal bleeding [1-5]. The incidence is higher in some genetic backgrounds such as white race, history of RDS in siblings and in the male sex[3-6].

The primary cause of RDS is inadequate pulmonary surfactant secretion because of preterm birth [4-7]. RDS is a major cause of morbidity and mortality in preterm infants. Previous experience has indicated that about 30% of neonatal mortality is related to this disease and its complications[1]. As reported in some studies, surfactant therapy can reduce the mortality from RDS by approximately 40% [1-3].

The purpose of this study was to determine the prevalence rate of reducing mortality in neonates with RDS after surfactant therapy and to assess the relationship between the efficacy of surfactant therapy and some risk factors associated with RDS.

Subjects and methods

Subjects

In this study, the neonates with signs of RDS, who were admitted to the Neonatal Intensive Care Unit (NICU) during an 18-month-period (from March 2003 to August 2004) in Shaheed Beheshti Hospital Affiliated to Isfahan University of Medical Sciences, Isfaha, Iran, were evaluated. Eligibility criteria included: 1) preterm birth (before the 37th week of gestation); 2) having RDS as diagnosed according to clinical and radiographic features [1-3]. The neonates who had cyanotic heart diseases and those without a PaO_2 >60 mmHg in the hyperoxia test were excluded from this study. The neonates who had appropriate increase in PaO_2 in the hyperoxia test, but who were diagnosed with persistent pulmonary hypertension of the newborn by pre-ductal and post-ductal pulse oximetry, were also excluded.

A total of 89 eligible neonates were selected by simple sampling. Data were collected from the mothers and neonates hospital records and from a check list provided for this study that included information about neonatal sex, gestational age, Apgar score, route of delivery, birth weight, multiple birth, time of starting surfactant therapy and steroid administration to mother before labor.

Surfactant therapy

Eligible neonates received surfactant therapy by a dosage of 100 mg/kg of Survanta (Abbott Laboratories, a mixture of phospholipids and hydrophobic proteins). It is a natural bovine lung extract containing phospholipids, neutral lipids, fatty acids and surfactant associated proteins and it is made in USA).

Surfactant was administered within 2-24 hours of life. Based on RDS criteria [1-3] and the results of arterial blood gas, surfactant administration was repeated every 6 hours in neonates with severe RDS.

Statistical analysis

Data were stored in a computer database and were analyzed by SPSS software. Comparison of the frequency according to the study objectives was analyzed by Chi-square test. The significance level was set at $P<0.05$.

Results

Overall, 34 (38.2%) out of 89 neonates who received surfactant survived. The mortality rate was related to gestational age. The highest mortality rate was noted in neonates with gestational age of less than 28 weeks (Table 1).

Table 1 Reduction in mortality from RDS after surfactant therapy according to gestational age [n(%)]

Gestational age (weeks)	Number	Died	Survived
<28	24	20 (83.3)	4 (16.7)
28-32	25	14 (56.0)	11 (44.0)
32-37	40	21 (52.5)	19 (47.5)
P value		<0.05	<0.05

The effect of surfactant replacement therapy was higher in the affected female neonates than in affected male neonates (survial 42.0% vs 36.2%; $P<0.05$).

In the neonates who received the first dose of surfactant during the first 24 hours after birth, the efficacy of therapy was higher than in those receiving therapy after 24 hours (13 cases, 43.3% vs 6 cases, 30.0% survival; $P<0.05$).

In addition, the higher efficacy of surfactant therapy was found in neonates with an Apgar score of more than 7/10 at 1 and 5 min (survival in 25 cases 48.1% with an Apgar score > 7/10 vs 9 cases, 24.3% with an Apgar score <7/10; $P<0.05$).

After surfactant replacement therapy in single pregnancy, 28 cases (41.8%) survived, but only 5 cases (27.8%) survived in twin pregnancy ($P<0.05$).

The efficacy of surfactant therapy was also associated with the birth weight. The highest survival rate was found in neonates with a birth weight of more than

1 500 g (52.5%), followed by in neonates with a birth weight of between 1 000 g and 1 500 g (35.3%). Only one case (6.7%) survived in neonates with a birth weight of less than 1 000 g.

In this study, 48 neonates' mothers received up to two doses of 12 mg Betamethasone 48 to 72 hours before delivery. This group of neonates had a higher reduction in mortality rate (Table 2).

Table 2 Reduction in mortality from RDS after surfactant therapy according to maternal steroid therapy [n(%)]

Maternal steroid	Number	Died	Survived
Not received	41	27 (65.9)	14 (34.2)
Received	48	28 (58.3)	20 (41.7)[a]

a: $P<0.05$, vs the group without maternal steroid therapy.

The efficacy of surfactant replacement therapy in neonates born by cesarean section was higher than in those born by normal vaginal delivery (survival in 27 cases or 39.7% vs 6 cases or 28.6%; $P<0.05$).

Discussion

The present study demonstrated that surfactant replacement therapy within 2-24 hours of life had favorable impacts in reducing mortality from neonatal RDS. These findings are consistent with some previous studies showing a 40% reduction in mortality rate [1-3].

This study also indicated that early administration of surfactant as soon as possible after birth, i.e. up to 24 hours after birth, had the higher efficacy. This was in line with some previous studies [4-7].

The efficacy of surfactant replacement therapy had a direct relationship with birth weight and gestational age. This result was also confirmed by other studies [7-10].

Other risk factors were multiple pregnancy, Apgar score and administration of steroid to mother before labor. The efficacy of surfactant was higher in neonates with an Apgar score >7/10 at 1 and 5 min, in single pregnancy and in neonates whose mother received steroid therapy before delivery. These findings were in line with previous studies[10-14]. The present study demonstrated that the efficacy of surfactant therapy was higher in cesarean section delivery than in normal vaginal delivery, and this finding was contrary to some other studies [7-10]. It should be noted that in cesarean section delivery there were also some associated risk factors such as low Apgar score and low birth weight of less than 1 500 g.

In conclusion, this study demonstrated that surfactant replacement therapy in neonatal RDS should be started as soon as possible after birth. It could reduce the mortality rate by 38.2%. Surfactant therapy also had beneficial effects on some risk factors associated with RDS.

The main limitation of this study was that the sample size was not large enough to exclude all possible risk factors associated with RDS, so a large sample, multicenter study is needed.

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