Comparative evaluation of the effects of BLES and Survanta on treatment of respiratory distress syndrome in newborns

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Abstract

Background and Objectives: Symptoms of respiratory distress syndrome (RDS), which is inverse correlation with gestational age and birth weight, occur in premature infants and newborns. The main objective of the study is comparative evaluation of the effects of BLES and Survanta on treatment of RDS in newborns. Materials and Methods: In all, 100 patients were randomly divided into two groups of 50 subjects in this study. While the group receiving BLES included 32 (64%) male and 18 (36%) female infants, there were 29 (58%) male and 51 (52%) female infants in the other group which received Survanta. Results: Although the results of this study showed improvement in respiratory status based on Downes scoring system in both groups after receiving surfactant, there was no significant difference in terms of short-term respiratory enhancement based on Downes scoring system among two groups. Pulmonary hemorrhage was the most frequent complication, with five cases (10%), among infants in BLES group; with five cases, pneumonia was the most observed complication in the group receiving Survanta. No significant difference in terms of complication was observed between two groups (P = 0.438); there was no significant difference in terms of mortality among two groups (P = 0.828). Conclusion: Both groups experienced respiratory status enhancement after receiving surfactant and the results of arterial blood gas (ABG) showed positive effects and efficiency of both drugs. Lack of significant difference in the effects of two mentioned drugs, BLES and Survanta, can be the main cause behind the absence of significant difference between two groups in terms of changes in respiratory status or ABG in newborns. No significant difference was observed in terms of complication between two groups, indicating lack of difference in the effects of medicines injected for infants suffering from RDS.

Keywords: BLES, newborn, respiratory distress syndrome, Survanta

Introduction

The risk of respiratory distress syndrome (RDS) is reduced in three situations: pregnant mothers taking heroine, prolonged membrane rupture, and receiving prophylactic corticosteroids. The use of corticosteroids in preterm deliveries reduces respiratory complications by 50% and mortality rate by 40%. Glucocorticoids reduce the incidence and severity of neonatal respiratory distress and health costs through producing surfactant proteins and increasing phospholipid synthesis. Surfactant deficiency, reduction in either production or secretion, is the major cause behind the emergence of RDS. Dipolyymytol phosphotidylcholine (lectin), phosphatidyglycerol, apolipoprotein, and cholesterol are the main components of surfactant; though surfactant appears in fetal lungs 20 weeks after pregnancy, it does not come to alveolar surface for a long time. Surfactant appears in amniotic fluid between 28 and 32 weeks of pregnancy, but its mature

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pulmonary level appears normally 35 weeks after pregnancy. Although rare, genetic abnormalities may cause respiratory distress. Disorders in B and C protein genes, which are the main surfactant transition factors through membrane, often cause severe and fatal familial respiratory distress. The main factors which necessitate treatments of RDS are inadequate exchange of carbon dioxide and oxygen, metabolic acidosis, and inadequate blood circulation. Mortality of this disease is 10% which occurs mostly due to hemorrhage, lung infections, and treatment complications. Inflammatory response of the lungs caused by complications of treatment through oxygen and mechanical ventilation is the main cause behind the emergence of the most fatal complications of this disease, broncho-pulmonary dysplasia (chronic lung disease).

For the first time in 1980, Fujiwara explained surfactant replacement therapy for the treatment of neonatal RDS. The immediate effects of surfactant therapy include improved alveolar-arterial gradient of oxygen, decreased respiratory support, increased lung compliance, and improved appearance of chest radiography. Treatment starts as soon as possible in the first hours after birth. Dose is repeated every 6–12 h for 2–4 days through endotracheal intubation. Survanta is derived from bovine lung extract fat and synthetic fats and it was registered by Food and Drug Administration in July 1991. Survanta is a non-pyrogenic suspension which is obtained from bovine lung and is used for endotracheal intubation; it contains palmitate, palmitic acid, and tripalmytin to standardize the composition and mimic particular qualities of natural human surfactant to reduce surface tension. The resulting mixture contained 25 mg/mL of phospholipid per 0.5–1.75 mg/mL of triglycerides, 1.4–3.5 mg/mL of free fatty acids, and less than 1 mg/mL of protein.

First research projects on BLES were carried out by Dr. Fred Possmayer and his colleagues at the University of Ohio and the first treatment with this drug was done on a group of newborns in 1983. It was approved by Canadian Pharmaceutical Organization in 2002 and it was first sold on February 5th in the same year; it was imported to Iran and India in 2006.

Considering the importance and frequent confrontation with the mentioned disease and since Martyr Motahari Hospital is the main medical center for patients with RDS, this study was carried out to investigate the effect of two mentioned drugs on neonatal RDS to improve treatment, reduce complications, and mediate patient treatment and care costs.

The main objective of the study is comparative evaluation of the effects of BLES and Survanta on treatment of RDS in newborns, and the research hypotheses are as follows:

1. There is no difference between BLES and Survanta in terms of recovery time for preterm infants who receive these drugs
2. There is no difference between BLES and Survanta in terms of complications for preterm infants who receive these drugs
3. There is no difference between BLES and Survanta in terms of mortality rate for preterm infants who receive these drugs
4. There is no difference between BLES and Survanta in terms of treatment outcome for preterm infants who receive these drugs

Materials and Methods

The research community included infants with RDS hospitalized in Martyr Motahari Hospital. Samples were selected out of the available hospitalized patients and divided randomly into two groups. According to Lam’s systematic review, two-tailed test with a sample size of 97 was used to measure complications, outcomes, and recovery time of both drugs; a total of 100 patients were studied. Necessary data were collected through clinical examinations and checklists provided for data collection and tracking. The present randomized clinical trial study was conducted to evaluate comparative efficiency, complications, and mortality rate of patients with RDS in Martyr Motahari Hospital in Urmia from February 2013 to August 2014. Surfactant with a dosage of 100 mg/mL was the prescribed medication. Appropriate time for receiving surfactant was recorded in hours after birth; if necessary, a second injection was administered. Other common treatments which were conducted equally among all infants during hospitalization included serum glucose, antibiotics, and oxygen. Short-term effect was recorded based on Downes scoring system, necessity to readminister the injection, recovery time, continuation of mechanical ventilation, arterial blood gas (ABG), the start of the feeding, and infant death during hospitalization. The most common complications during pregnancy were pneumothorax, pneumonia, sepsis, bleeding lungs, disseminated intravascular coagulation (DIC), and intraventricular hemorrhage. All collected data were put into SPSS software and presented in frequency graphs and tables. P value of less than 0.05 was considered significant in determining descriptive features.

Results

This study included 100 patients with RDS who were randomly divided into two groups of 50 members; for the first group, BLES and for the second group Survanta was prescribed. Basic information such as age, gender, gestational age, birth weight, interval between birth and surfactant reception, and clinical signs were recorded for the patients and Downes scoring system was used for grading. While the group receiving BLES included 32 (64%) male and 18 (36%) female infants, there were 29 (58%) male and 51 (52%) female infants in the other group which received Survanta and no significant difference was observed between two groups (P = 0.682) [Table 1].

The mean of gestational age of patients was 30.95 ± 3.18 weeks, 31.04 ± 3.59 weeks for the group which received BLES and 30.68 ± 2.14 weeks for the receivers of Survanta. The highest and lowest gestational age was 40 and 27 weeks in order, and there was no significant difference between two groups in this regard (P = 0.779).
The mean ± standard deviation of birth weight of the infants was 598.9 ± 1536 g, 656.6 ± 1609 g for the group which received BLES and 531.6 ± 1463 g for the group of Survanta. The highest and lowest birth weight was 3270 and 550 g in order, and there was no significant difference between two groups in this regard (P = 0.225).

The mean of recovery time was 7.67 ± 10.42, 7.66 ± 10.06 for the receivers of BLES and 7.40 ± 10.78 for the group which received Survanta. Log-rank test showed no significant difference between two groups in terms of hospitalization period (P = 0.583).

Downes scoring system was used to determine the severity of RDS, the mean of which was 1.21 ± 4.28 among infant patients. This amount was 1.30 ± 4.38 for the group which received BLES and 1.11 ± 4.18 for the receivers of Survanta; there was no significant difference between two groups in terms of Downes scoring system (P = 0.413).

The mean ± standard deviation of birth up to surfactant reception interval of under-study patients was 19.13 ± 16.67, 19.6 ± 16.93 for BLES group and 18.84 ± 16.29 for the group which received Survanta (P = 0.868). In terms of type of delivery, there were 34 cases (68%) of caesarean section and 16 cases (32%) of natural delivery in the group which received BLES; 38 cases (76%) of caesarean section and 12 cases (24%) of natural delivery were reported in the receivers of Survanta group. There was no significant difference in terms of delivery type between two under-study groups (P = 0.828).

In terms of pregnancy type, there were 31 cases (62%) of singleton pregnancy, 14 cases (34%) of twins, and 2 cases (4%) of triplets in the group which received Survanta; the group which was injected with Survanta included 34 cases (68%) of singleton, 15 cases (30%) of twins, and 1 case (2%) of triple pregnancy. There was no significant difference between two groups in terms of pregnancy type (P = 0.445).

According to carried out ABGs, the mean ± standard deviation of ABGs and PH factor of patients before receiving surfactant is as given in Table 2. The mean ± standard deviation of PH factor in carried out ABG for under-study patients was 0.12 ± 7.27, 0.12 ± 7.28 for the group which received BLES and 0.13 ± 7.28 for the receivers of Survanta; no significant difference was observed between two groups in this regard (P = 0.389). The mean ± standard deviation of PO₂ for under-study patient infants was 53.66 ± 85.76; this amount was 24.54 ± 50.02 for PCO₂ and 3.61 ± 20.15 for HCO₃; no significant difference was observed between two groups in terms of PO₂ (P = 0.973), PCO₂ (P = 0.069), and HCO₃ (P = 0.882).

After the initial surfactant dose, if necessary, the dose was administered again. The frequency of the administered dose in

| Type of delivery frequency, n (%) | BLES n (%) | Survanta n (%) |
|----------------------------------|------------|----------------|
| Caesarean section                | 34 (68)    | 18 (72)        |
| Natural delivery                 | 16 (32)    | 14 (28)        |

| Type of pregnancy frequency, n (%) | BLES n (%) | Survanta n (%) |
|-----------------------------------|------------|----------------|
| Singleton                         | 31 (62)    | 34 (68)        |
| Twin                              | 17 (34)    | 15 (30)        |
| Triple                            | 2 (4)      | 1 (2)          |

Table 1: Comparative evaluation of two groups in terms of age, gender, type of pregnancy, gestational age, and type of delivery

| Mean±SD  | BLES       | Survanta   |
|----------|------------|------------|
| PH       | 7.28±0.12  | 7.26±0.13  | 0.389 |
| PO₂      | 82.76 ±54.66 | 82.42±47.63 | 0.973 |
| PCO₂     | 46.57±16.86 | 55.24±28.75 | 0.069 |
| HCO₃     | 20.62±3.84  | 20.51±3.40  | 0.882 |

Table 2: Comparative investigation of the results of arterial blood gas for infants in two groups before surfactant reception

| Frequency (%) | BLES n (%) | Survanta n (%) | P     |
|---------------|------------|----------------|-------|
| 1 day         | 33 (66)    | 34 (68)        | 0.834 |
| 2 days        | 17 (34)    | 16 (32)        |       |

Table 3: Comparison of the number of and the need to repeat doses in both groups

| Ventilation type | Frequency (%) | BLES n (%) | Survanta n (%) | P     |
|------------------|---------------|------------|----------------|-------|
| CPAP             | 21 (38)       | 23 (46)    | 0.486           |
| Ventilator       | 18 (36)       | 23 (46)    |                 |       |
| Hood             | 3 (6)         | 2 (4)      |                 |       |

CPAP: Continous positive airway pressure.
received surfactant are given in Table 4. As shown in Table 4, there was no significant difference in terms of mechanical ventilation continuity between two groups which received surfactant ($P = 0.486$).

The analysis of the frequency of common complications in under-study infant patients in two groups is as shown in Table 5. According to Table 5, the total number of complications in under-study groups was equal in both groups receiving surfactant; pulmonary hemorrhage had highest complication frequency, five cases (38.4%), in the group which received BLES; pulmonary hemorrhage with DIC had highest complication frequency, with four cases (30.8%), among subjects who were injected with Survanta; there was no significant difference between two groups in terms of disease complication ($P = 0.438$).

The results of disease outcome analysis are listed in Table 6. According to Table 6, the frequency of mortality rate in the group which received BLES was 16 cases (32%) and 14 cases (28%) in Survanta group; no significant difference was observed between two groups in terms of mortality rate ($P = 0.828$).

More ABG was carried out to evaluate changes and patients’ status after receiving surfactant, and the results are shown in Table 7.

According to carried out ABG, there was no significant difference between two groups in terms of changes after receiving surfactant; that is, PH ($P = 0.657$), $\text{PO}_2$ ($P = 0.905$), $\text{PCO}_2$ ($P = 0.279$), and $\text{HCO}_3$ ($P = 0.135$). However, the results of ABG showed significant difference in terms of PH ($P = 0.003$); there was no significant difference in terms of $\text{PO}_2$ ($P = 0.0001$), $\text{PCO}_2$ ($P < 0.001$), and $\text{HCO}_3$ ($P = 0.002$).

The mean ± standard deviation of respiratory status of patient infants was $15.28 \pm 1.60$, $14.31 \pm 59.34$ for the group which received BLES and $16.30 \pm 60.86$ for the receivers of Survanta, and there was no significant difference between two groups in this regard ($P = 0.621$). The respiratory status of the newborns was reexamined after receiving surfactant and the mean ± standard deviation was $15.96 \pm 49.20$ breaths/min, $16.58 \pm 51.68$ for receivers of BLES and $15.09 \pm 56.88$ for the group which received Survanta; no significant difference was observed in terms of respiratory status of patients after receiving surfactant ($P = 0.133$). However, the analysis of the number of breaths before and after surfactant injection showed significant difference ($P < 0.001$) [Table 8].

Whereas Downes scoring system yields no significant difference between two groups in terms of short-term effects of drugs ($P = 0.635$), it showed significant difference before and after surfactant injection ($P < 0.001$).

### Discussion

The study by Clark et al., which investigated mortality rate of Survanta and Inasurf, showed no significant difference between groups in terms of mortality; Lam et al., as well, did not report any complications for different objections of examined medicines, showing the consistency of the results with the findings of other previous studies.

According to the study by Barouti et al., which examined the impact of Survanta in comparison to other synthetic surfactants, there was no significant difference between this range of drugs in terms of recovery time which is also consistent with the findings of this study.

Considering that according to this study, there was no significant difference between two groups in terms of dose readministration need, it can be implied that BLES and Survanta are equally effective in improving respiratory status of the infant patients. The need
for dose readministration can be attributed to deterioration of respiratory status of the infant or failure to respond properly to surfactant rather than inefficiency of medicines.

This study investigated comparative efficiency of two surfactants, BLES and Survanta, administered for RDS newborns in terms of recovery time, complications, and mortality rate. Downes scoring system was applied to measure the efficiency of BLES and Survanta in improving respiratory status. Although this was consistent with the findings of the study by Lam et al., BLES had higher efficiency in comparison to Survanta in their study. The main cause of difference in the findings of these studies is using different factors for investigating the improvement of respiratory status of newborns in these two studies. This study used Downes scoring system which is a more precise factor to check respiratory status in comparison to Lam et al.'s oxygenation index.

The results of this study indicated improved respiratory status after receiving surfactant and the results of ABGs showed positive effect and efficiency of both drugs. Lack of significant difference between two groups in terms of changes in the number of breaths or ABG results administered for newborns can be due to similar effect of the drugs.

Despite difference in the type of complication which had highest frequency between two groups, there was no difference in terms of post-injection complication, which shows the similarity of both drugs in terms of post-injection complication in RDS infant patients.

An overall view of the results of this study and comparing them with the findings of previous researches shows lack of clear distinction between the efficiency of two administered surfactants. Given that this study used Downes scoring system, which is a scientifically more precise criterion to evaluate short-term effects of the drugs, the resulting differences with previously carried out studies are trivial and can be safely ignored.

**Conclusion**

Since all stage of study, including injection, evaluation, and data recording, was conducted under and confirmed by the supervision of neonatologist, we can also assure the accuracy and precision of the results. Finally, it is suggested that considering the results of the present and previous similar studies which showed the similarity of both administered drugs and that the present study was conducted under the supervision of professional specialist in an academic environment and the results have been far from financial or advertising bias, the decision to prescribe administered surfactants, proving the availability and chip price, is safe and scientifically supported. It is, also, suggested that future studies focus on factors effective in the treatment of this disease. It is recommended that future studies with larger sample size investigate the effect of maternal disease during pregnancy on the number of Surfactant doses that must be administered for RDS newborn patients. Both groups experienced respiratory status enhancement after receiving surfactant and the results of ABG showed the positive effects and efficiency of both drugs. Lack of significant difference in the effects of two mentioned drugs, BLES and Survanta, can be the main cause behind the absence of significant difference between two groups in terms of changes of respiratory status or arterial blood gas in newborns. No significant difference was observed in terms of complication between two groups, indicating lack of difference in the effects of medicines injected for infants suffering from RDS.

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**Conflicts of interest**

There are no conflicts of interest.

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