



The importance of administration of early surfactant and nasal continuous positive airway pressure in newborns with respiratory distress syndrome

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Abstract

Aim: Mechanical ventilation is an invasive method and causes to important problems in the respiratory tract and lung parenchyma. The objective of our study was to investigate if administration of early surfactant and nasal continuous positive airway pressure (nCPAP) was superior to delayed surfactant administration and mechanical ventilation.

Material and Methods: The study was conducted in the Van 100th Year University, Medical Faculty Hospital, Neonatal Intensive Care Unit. One hundred and nine infants with respiratory distress syndrome (RDS) with a gestational age of 32 weeks and/or below were included in the study. Surfactant was given to 61 infants in the delivery room or intensive care unit and subsequently nCPAP was administered. Surfactant was administered in 48 infants in the control group and mechanical ventilation was initiated subsequently. Informed consent was obtained from the relatives of all patients and ethics committee approval was also obtained (Approval number: 03.02.2011/15).

Results: There was no statistically significant difference between the two groups in terms of gestational age, birth weight, gender, height and head circumference measurements ($p>0.05$). The mean hospitalization time in the patients in the study group was 24.4 ± 17.8 days, whereas the mean time of nCPAP was 28.4 (4-120) hours. In the study group, intracranial hemorrhage was found with a rate of 27.85%, bronchopulmonary dysplasia was found with a rate of 4.91%, pneumothorax was found with a rate of 3.27%, necrotizing enterocolitis was found with a rate of 3.27%, patent ductus arteriosus was found with a rate of 16.39%, sepsis was found with a rate of 22.95% and retinopathy of prematurity was found with a rate of 1.63%. No statistically significant difference was found between the study and control groups in terms of the rates of complications. During the follow-up period, 17 (27.86%) patients were lost. The length of stay on mechanical ventilation in the study group was found to be statistically significantly shorter compared to the control group ($p<0.05$).

Conclusions: In our study, it was observed that administration of early surfactant and nCPAP in treatment of preterm newborns with a diagnosis of RDS markedly decreased the length of stay on mechanical ventilation, but had no significant impact on morbidity and mortality.

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Key words: Preterm baby, mechanical ventilation, nasal continuous positive airway pressure, respiratory distress syndrome, surfactant

Introduction

Respiratory distress syndrome (RDS) is the most important cause of morbidity and mortality in preterm babies. The cornerstones in treatment of respiratory distress syndrome include respiratory support and surfactant treatment. In treatment of respiratory distress syndrome, mechanical ventilation (MV) and nasal continuous positive airway pressure (nCPAP) are the most widely known and used respiratory support techniques. nCPAP prevents alveolar collapse and pulmonary shunts by preserving functional residual capacity (FRC). It decreases obstructive apnea attacks and respiratory work load by stabilizing large and small airways and prevents surfactant destruction (1). Early nCPAP and surfactant administration decreases requirement for MV and related side effects (2-4). Unfortunately, this approach is generally ignored in neonatal intensive care units. Mechanical ventilation is initially used widely after administration of surfactant. It should be noted that respiratory support can

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be made only with nCPAP after administration of surfactant in babies with spontaneous respiration (5-7).

In this study, it was aimed to investigate if early surfactant and nCPAP administration was superior to later surfactant and MV in preterm babies (<32 weeks). Secondly, it was aimed to compare morbidity and mortality rates between these two approaches.

Material and Methods

Our study was conducted in Van Yüzüncü Yıl University, Medical Faculty Hospital between 2009 and 2011. The preterm newborn babies included in the study were divided into two groups. Sixty-one newborns who were examined prospectively, who had a gestational age below 32 weeks, who were found to have RDS, who received early surfactant and who were followed up with nCPAP were included in the first group. The second group constituted the control group. This group included the newborns who had similar gestational age and antropometric measurements, but who were examined retrospectively and who were followed up with "Synchronised Intermittent Mandatory (SIMV)" after surfactant treatment (8). The subjects who had hypocalcemia, hypoglycemia, convulsion, meconium aspiration and congenital malformation and the ones who had a suspicion of chromosomal or genetic disease were excluded from the study.

The gestational age, mode of delivery (cesarean/vaginal), birth weight, height and head circumference, gender, if resuscitation was performed at birth, if steroid was given to the mother before delivery, the type and amount of surfactant administered, if a second dose of surfactant was administered, the time of respiratory support given, hospitalization time, presence of complications including bronchopulmonary dysplasia (BPD) and necrotizing enterocolitis and blood gases values measured at 6-hour intervals in the first 24 hours in the babies in the study group were recorded. The data of the control group were obtained from the files. Birth weight standards prepared from our community were considered for evaluation of weight according to gestational age. Accordingly, the babies who were born below the 10th percentile were considered small for gestational age (SGA), the babies who were born between the 10th and 90th percentile were considered appropriate for gestational age (AGA) and the babies who were born above the 90th percentile were considered large for gestational age (LGA) (9).

Survanta® (Abbott®) 100 mg/kg or Curosurf® (Chiesi®) 200 mg/kg was given to the patients in the study group in the neonatal intensive care unit in the first two hours after delivery (early rescue treatment). Clinical evaluation was performed, lung graphy was obtained and blood gases were measured

4-6 hours after surfactant treatment and a second dose of surfactant was administered, if necessary. The patients were extubated after surfactant administration and were followed up with nCPAP. INCA set which was available in our hospital was used for this. The treatment was started with a pressure of 6 cm H₂O and the pressure was increased to 10 cm H₂O, when necessary. Surfactant (Survanta or Curosurf) was also administered to the patients in the control group in the delivery room. Afterwards, the patients were taken to the neonatal intensive care unit and followed up with MV (PCV and/or SIMV+PC). CPAP was discontinued according to the clinical state and blood gases values. Afterwards, respiratory support was discontinued, when it was found that there was no requirement for respiratory support. Lung graphies were taken before and after surfactant administration. nCPAP was discontinued in the babies whose clinical states and blood gases improved in the follow-up.

Disease variables found in the subjects were evaluated using the current diagnostic criteria. The diagnosis of bronchopulmonary dysplasia was evaluated according to the criteria and classification of the American National Health Institute (NIH) (10). The diagnosis of patent ductus arteriosus was made by a pediatric cardiologist on the 2-7th days after delivery with the finding of a ductal patency of >1.4 mm and/or a left atrium/aortic arcus diameter ratio of (LA/AO) >1.4 on echocardiography (11). Intracranial bleeding was defined based on Papille classification on transfontanel ultrasonography performed by neonatologists experienced in the area of transfontanel ultrasonography on the postnatal second day. Retinopathy of prematurity screening was performed by experienced ophthalmologists in the postnatal 4-6th weeks using the "International Committee for Classification". The diagnosis of necrotizing enterocolitis was made considering direct abdominal X-ray taken in standing position together with findings including abdominal distension, feeding intolerance, gastric residue and presence of evident or occult blood in the feces. Informed consent was obtained from the relatives of all patients and ethics committee approval was obtained (approval number:03.02.2011/15).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median (the lowest-the highest) values in this study. Categorical variables were given as frequency and related percentage values. Inter-group analyses of continuous variables were made using t test or Mann-Whitney U test for independent pair samples. Inter-group comparisons of categorical variables were made using chi-square test. The analyses of the study was performed using (Statistical Package for the Social Sciences, Chicago, IL, USA) 15th version and a p value of <0.05 was considered significant.

Results

The demographic properties of the study and control groups are shown in Table 1. There was no statistically significant difference between the groups in terms of gestational age, birth weight, gender and height and head circumference measurements ($p>0.05$ for all) (Table 1). The height, weight and head circumference measurements by gestational age in the patients in both groups were in the normal percentiles. As a result of evaluation of weight for gestational age, 52 of 61 subjects in the study group were considered AGA, 6 were considered SGA and the remaining three subjects were considered LGA. 44 of the subjects in the control group were considered AGA, two were considered SGA and the remaining two were considered LGA. No statistically significant difference was found between the two groups in terms of weight for gestational age.

While there was a significant difference between the study group and control group in terms of use of surfactant (Survanta, Curosurf) and time on MV ($p<0.05$), no significant difference was found in terms of steroid usage, requirement for a second surfactant dose and hospitalization time ($p>0.05$) (Table 2). None of the babies of the mothers who received prenatal steroid required a second surfactant dose. MV time was observed to be shorter in these babies compared to the ones whose mothers did not receive steroid. In 25% of the patients in the study group, MV was required for a mean period of 28 hours (4-120) because of nCPAP failure. A second dose of surfactant was administered to 15 subjects who were given MV support, since nasal CPAP support was insufficient. It was found that prenatal steroid was not given in any of these cases with a gestational age below 27 weeks. The mean time on MV in the subjects in the control group in which all subjects were given MV support was 77.3 (8-240) hours and afterwards nCPAP was started. A statistically significant difference was found between the study and control groups in terms of usage of Curosurf and Survanta ($p=0.013$). Proctant alfa (Curosurf®) was administered to 36 of the subjects in the

study group. We observed that the time of respiratory support was shorter, extubation occurred earlier and MV requirement was less in these subjects. No statistically significant difference was found between the study and control groups in terms of complication rates (Table 3).

Discussion

Currently, respiratory distress syndrome itself and its complications which occur during the follow-up are the most important causes of morbidity and mortality in preterm babies. Early treatment is important in terms of hospitalization time and problems. Therefore, different studies related with surfactant which is used in treatment have been performed (12-14). Adequate oxygenation and ventilation treatment are very important in treatment of respiratory distress syndrome.

Table 2. Steroid usage, mechanical ventilation and hospitalization times in the study and control groups

Clinical property	Study group n=61	Control group n=48	p
Steroid usage after birth	26 (42.62)	18 (37.50)	0.730
Curosurf	36 (59.01)	16 (33.33)	0.013
Survanta	25 (40.98)	32 (66.66)	0.013
Need for a second surfactant	18 (29.50)	14 (29.16)	1
MV time (h)	28.4 (4-120)	77.3 (8-240)	0.001
Hospitalization time (days)	24.99 (1-60)	25.15 (0.5-79)	0.964
NSVD	19 (31.1)	18 (37.5)	0.54
Cesarean section	42 (68.9)	30 (62.5)	0.54

MV: mechanical ventilation; NSVD: normal spontaneous vaginal delivery

Table 3. Complications in the study and control groups

Complication	Study group n=61	Control group n=48	p
Intracranial bleeding	17 (27.86)	15 (31.25)	0.863
BPD	3 (4.91)	5 (10.41)	0.297
Pneumothorax	2 (3.27)	2 (4.16)	1
Necrotizing enterocolitis	2 (3.27)	2 (4.16)	1
Patent ductus arteriosus	10 (16.39)	8 (16.66)	1
Sepsis	14 (22.95)	5 (8.19)	0.145
Pulmonary hemorrhage	0	3 (6.25)	0.082
Retinopathy of prematurity	1 (1.63)	0	1
Exitus	17 (27.86)	16 (33.33)	0.684

BPD: bronchopulmonary dysplasia

Table 1. Demographic properties of the study and control groups

Demographic property	Study group n=61	Control group n=48	p
Gestational age (week)	29.4±1.8	29.3±1.9	0.658
Birth weight (g)	1368±323	1338±347	0.583
Male	42 (68.85)	30 (62.50)	0.526
Female	19 (31.14)	18 (37.50)	0.526
Height (cm)	39.7±2.4	39.7±3	0.913
Head circumference (cm)	28.5±1.8	28.9±2.2	0.351

Different forms of various ventilator types are used to increase efficiency of administration of MV which is an invasive method and to decrease adverse effects (15-17). CPAP was initially used in term newborns with respiratory distress and afterwards in preterm babies. In recent years, nCPAP has been widely used in preterm babies with RDS because of its convenient use, its efficiency and its lower rate of complications (18).

Dani et al. (19) compared 13 preterm babies in whom early surfactant and nCPAP was administered and 14 preterm babies in whom MV was administered. In the 13 preterm babies in the study group, the mean gestational age was 29 ± 2.2 weeks and the mean birth weight was 1078 ± 321 grams. The mean time on nasal CPAP was 3.2 ± 2.4 days and mean hospitalization time was 58.3 ± 21.5 days. While pneumothorax, necrotizing enterocolitis, periventricular leukomalacia was not observed in these patients, BPD was observed with a rate of 23%, intracranial hemorrhage was observed with a rate of 8%, patent ductus arteriosus was observed with a rate of 31% and retinopathy of prematurity was observed with a rate of 8%. The hospitalization time and the time on ventilation was shorter and the rates of BPD, pneumothorax, intracranial hemorrhage and sepsis were lower in the patients in whom nasal CPAP was administered compared to the patients in whom MV was administered. When our study was compared with the study of Dani et al. (19), it was found that the hospitalization time and the time on CPAP was shorter and the rates of BPD, patent ductus arteriosus and retinopathy of prematurity were lower in our study. This difference was attributed to the younger gestational age, lower birth weight and more severe RDS in the subjects included in the study of Dani et al. (19).

In the study of Kribs et al. (20) including 153 subjects, the rates of mortality and BPD were found to be lower in the nCPAP group compared to the MV group and the difference was statistically significant. It was observed that the hospitalization time and the time on MV was shorter in the nCPAP group compared to the MV group. In our study, it was found that the time on ventilation was shorter and the mortality rate was lower compared to the MV group, but the difference was not statistically significant.

In the study of Finner et al. (21), the rate of pneumothorax was found to be 7.4%, the rate of necrotizing enterocolitis was found to be 9.9%, the rate of grade 3-4 intracranial hemorrhage was found to be 11.5%, the mean time on mechanical ventilation was found to be 27 ± 1.1 days and the mortality rate was found to be 17.5% in preterm babies with RDS in whom surfactant and MV was administered. Postnatal steroid was given to 96% of the mothers of the babies included in the study. In the same study, postnatal steroid was given with a

rate of 97% to the mothers of the preterm babies in the other group in whom nCPAP was administered. In our study, it was observed that the mortality rate was 14.2%, the rate of pneumothorax was 6.8%, the rate of necrotizing colitis was 12.7% and the rate of grade 3-4 intracranial hemorrhage was 14.3% in the nCPAP group in whom the mean mechanical ventilation time was 24 ± 1 days. The rates of the complications of pneumothorax and necrotizing enterocolitis were found to be lower in our study compared to the study of Finner et al. (21). The higher mortality rate in our study was attributed to the fact that prenatal steroid was given to the mothers with a rate of 42.6% in the study group and with a rate of 37.5% in the control group.

In another study in which the gestational ages and birth weights were similar to our study group and which included 141 subjects (22), intracranial hemorrhage was observed with a rate of 1%, BPD was observed with a rate of 49%, pneumothorax was observed with a rate of 2% after administration of nCPAP and the mortality was found to be 9% and the mean time on nCPAP was found to be 4.6 ± 4.7 days. In this study, the rates of intracranial hemorrhage, mortality and pneumothorax were lower and the rate of BPD was higher compared to our study.

In the study of Dizdar et al. (23) in which proctant alpha was given to one group of patients with RDS and beractant was given to another group, it was found that the requirement for a second dose of surfactant was lower, extubation occurred earlier, oxygen requirement was lower, but the rate of BPD was higher in the proctant alpha (Curosurf®) group compared to the beractant (Survanta®) group and the morbidity and mortality rates were similar in both groups. In our study, we found that the time of respiratory support was shorter, extubation occurred earlier and MV requirement was lower in the study group in whom proctant alpha was administered with a rate of 59%. However, we found that the rate of BPD was higher in the control group in whom beractant (Survanta®) was used generally. Similar to the study of Dizdar et al. (23), the morbidity and mortality rates were similar in both groups in our study.

Administration of surfactant plus nCPAP and surfactant plus MV have been investigated in different centers in terms of various aspects. In these studies, time on MV, complications including pneumothorax, sepsis, necrotizing enterocolitis, intracranial hemorrhage and BPD and the mortality rate were investigated generally (24-26). The results of the studies are generally similar and it has been shown that these complications can be prevented with administration of surfactant and nCPAP. In the meta-analysis performed by Schmölzer et al. (27), it was found that MV support was given to 518 of 1296 subjects in whom treatment was initiated with nC-

PAP. Considering the fact that the rate of MV was 25% in our study which can be considered as failure, it is noted that the literature has reported more successful results. In addition, this rate of requirement (25%) for MV in our subjects may be attribute to insufficient maturation of the lung because of young gestational age and lack of prenatal steroid administration.

Conclusively, early surfactant and nCPAP administration in treatment of preterm babies diagnosed with RDS decreases the time on mechanical ventilation markedly compared to the subjects followed up with MV with intubation, but it does not lead to a significant difference in terms morbidity and mortality.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Yüzüncü Yıl University Faculty of Medicine (Approval number: 03.02.2011/15).

Informed Consent: Written informed consent was obtained from the parents of the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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