NEURODEVELOPMENTAL OUTCOME ONE YEAR AFTER EARLY VERSUS LATE SELECTIVE SURFACTANT TREATMENT

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SUMMARY: To investigate whether neurodevelopmental outcome at age one year might be different after early versus late rescue surfactant treatment in preterm infants.

In 54 preterm infants, having gestational age between 25-30 weeks who were enrolled in a controlled trial of early versus late selective surfactant treatment (45 vs.70 min respectively), a standardized follow up of medical history, neurodevelopmental outcome using the Bayley Scales of Infant and Toddler Development, Second Edition at 9-12 months corrected age.scales were carried out.

Median Mental developmental index (MDI) score was 107 for early group and 111 for late group. Median Psychomotor developmental index (PDI) score was 82 for early group and 93 for late group. Although median MDI and PDI scores were slightly higher in late poractant treatment group and neurodevelopmental impairment was higher in early rescue group than the late rescue group, this was not statistically significant.

Our results demostrated that both early and late poractant treatment had similiar effects on the neurodevelopmental outcomes of preterm infants with RDS. In terms of neurodevelopmental outcomes there is no obvious advantage of an immediate surfactant administration in preterm infants according to our results.

Key words: preterm, surfactant, neurodevelopmental outcome

INTRODUCTION

Perinatal care has changed over the past 20 years. During this time, new treatment strategies including antenatal steroid therapy and surfactant administration have contributed to improved survival of preterm infants (1). While short-term effectiveness of surfactant treatment is well established, data on long-term outcome in terms of developmental outcomes remain scarce, but this issue is gaining increasing interest (2).

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We followed up infants from our previous surfactant study who had received either early or late surfactant treatment up to an age of about 9-12 months. The aim of the study was to investigate whether early surfactant treatment might result in improved developmental outcome at this age.

MATERIALS AND METHODS

Subjects

Originally enrolled in this study were preterm infants of 25-30 completed weeks of gestation who were randomly assigned to early or late surfactant treatment.

Patients in the early selective group (ES) were stabilized with nCPAP. Intubation was performed for the sole purpose of surfactant (with poractant alfa (Curosurf©) with a dose 200

Table 1: Guide for postnatal days of obtaining cranial ultrasounds according to birthweight.

Randomized to:	Early selective N=33	Late selective N=21	p
Gestational age (weeks)	29.1 (26-30)	29.7 (26-30)	0.56
Birth weight (grams)	1130 (770-1630)	1155 (710-1560)	0.66
Apgar score 1.'	6 (2-8)	6 (3-8)	0.35
Apgar score 5.'	8 (4-9)	8 (6-9)	0.44
Initial venous pH	7.29 (7.14-7.43)	7.28 (7.22-7.50)	0.96

mg/kg) administration in the first hour of life and infants were extubated and their treatments were continued with nCPAP. In the NICU, infants who were randomly assigned to ES group were intubated if they met any of the following criteria: FiO_2 greater than 0.60 required maintaining an indicated SpO_2 at or above 88% after the 1 hour of surfactant treatment or need $FiO_2 \geq 0.45$ last 12 hours.

Patients in the late selective group (LS), after admission to NICU, were stabilized with nCPAP. Diagnosis of RDS was established with clinical signs (tachypnea, cyanosis, groaning, intercostal retraction) and radiological findings (reticulo-nodular opacities, lung areolisation, air-bronchograms). Infants who diagnosed with RDS and their reqiurement of $FiO_2 > 0.4$ and MAP > 8 cmH_2O between 1 and 6 hours they were treated with poractant alfa (Curosurf©) with a dose 200 mg/kg.

After the first administration of surfactant, second dose surfactant was administered if they met any of the following criteria: a fraction of inspired oxygen (FiO_2) greater than 0.40 required maintaining an indicated saturation of peripheral oxygen (SpO_2) at or above 85% between 6 and 24 hours of the surfactant administration. The maximum total dose of surfactant were 400 mg/kg (Maximum two doses were administered).

Basic data of the study infants as enrolled in the original surfactant trial are given in Table 1.

In addition to these data, the following patient characteristics (gender, rate of multiple gestation, prenatal corticosteroid administration), the following outcome variables (mortality rate, duration of neonatal intensive care, time on mechanical ventilation) and complications (grade III or IV intraventricular hemorrhage, necrotizing enterocolitis, nasocomial infections, bronchopulmonary dysplasia) were not significantly differ between groups.

Table 2: The neurodevelopmental outcomes of the groups at 9-12 months corrected age.

	Early Rescue	Late Rescue	p
n	33	21	-
Median MDI (min-max)			
Median PDI (min-max)			
MDI Group			
<70	1 (3.0%)	1 (4.8%)	
70-85	1 (3.0%)	1 (4.8%)	0.70
85-110	18 (54,5%)	8 (38,1%)	
>110	13 (39,4%)	11 (52,4%)	
PDI Group			
<70	11 (33,3%)	2 (9,5%)	
70-85	6 (18,2%)	6 (28,6%)	0.24
85-110	13 (39,4%)	11 (52,4%)	
>110	3 (9.1%)	2 (9.5%)	

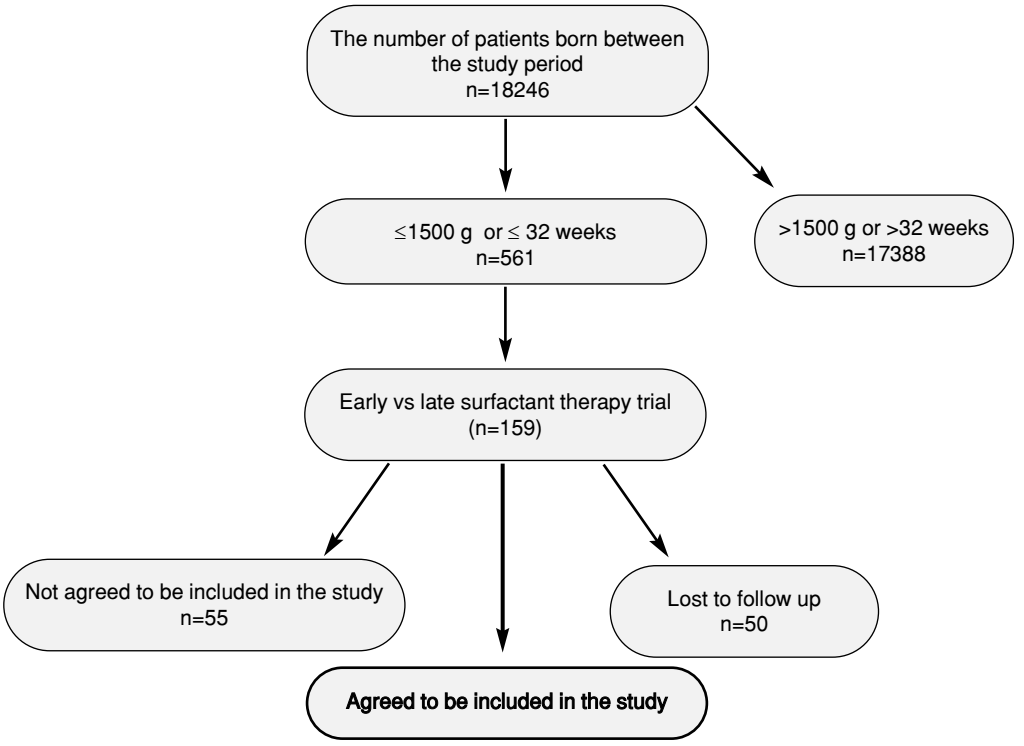

Figure 1: The flowchart of the study group.

Instruments and procedures

This follow-up study was conducted at developmental pediatrics unit in Zekai Tahir Burak Maternity Hospital for approximately one year. Follow-up was done by a developmental pediatrician and child developmental specialist. Evaluation was done by another child developmental specialist who was specially trained in the test applied in this study at 9-12 months corrected age.

Mental and psychomotor evaluations were performed using the Bayley Scales of Infant and Toddler Development Second Edition (BSID-II) (3,4). All tests were performed in the presence of the infant's parents. The examiner was blinded to both groups. For analysis of developmental performance, the infant's postnatal age was corrected by the degree of prematurely before term (40 weeks).

The study was approved by the local ethics committee at Zekai Tahir Burak maternity Hospital.

Statistical analysis

The data were analyzed with SPSS statistics version 17.0.0. Chi square test and Mann-Whitney U test were used to compare the groups. A P value of <.05 was considered significant.

RESULTS

Of 159 preterm infants, having gestational age between 25-30 weeks, evaluated in the previous controlled trial of early versus late surfactant treatment, 33 (61.1%) in early group and 21 preterm infants (38.9%) in late group were assessed at 9-12 months corrected age. Figure 1 shows the flowchart of the groups.

Median MDI score was 107 for early group and 111 for late group. Median MDI score was not statistically different in both groups (p=0.79).

Median PDI score was 82 for early group and 93 for late group. Although median MDI and PDI score was slightly higher in late poractant treatment group, this was not statistically significant between groups (p= 0.22).

Cerebral palsy, blindness and deafness was not detected.

Neurodevelopmental impairment was higher in early rescue group than the late rescue group but this was not statistically significant (33.6% vs 9.5%; p=0.057).

DISCUSSION

We reported early neurodevelopmental outcome related to early versus late surfactant administration. Our results showed that there were no statistically significant difference between groups among neurodevelopmental outcomes.

A significant number of studies have established that surfactant treatment of RDS in preterm infants reduces mortality and morbidity. Early studies have compared surfactant treatment versus placebo, but later on, different modes of surfactant administration were studied against each other (5,6).

In a recent study, comparing neurodevelopmental outcomes through 1 year corrected age of preterm infants who received lucinactant and other surfactants (Safety and Effectiveness of Lucinactant Versus Exosurf in a Clinical Trial) and STAR (Surfaxin Therapy Against RDS) trials, there was no significant difference in neurologic outcomes between groups (7).

Nonetheless, published follow-up data from studies that compared various surfactants with placebo demonstrate that the improved survival observed resulting from surfactant treatment is not associated with increased subsequent morbidity (8).

A strength of our study is the attainment of close to %100 follow-up, eliminating possible bias of outcome interpretation by the high risk for neurodevelopmental morbidity among those lost to follow-up. The other strength is the time of the evaluation. To provide a more complete picture of neurodevelopmental outcome of this cohort, we plan to follow and repeat the evaluation at 24 months age.

One limitation of this follow-up study is the high dropout rate. Only 33 of 79 patients in the early selective treatment group and 21 of 80 patients in the late selective treatment group, respectively, remained in the statistical analysis after restriction to the predetermined narrow timeframe for follow-up. Most often parents had moved to an unknown new address or changed their telephone number. In only a few cases parents had refused to have their infant examined, but we have no indication that parents whose infants were presumably handicapped were more likely to decline the examination or be lost to follow-up for other reasons.

CONCLUSION

Our results demostrated that both early and late poractant treatment had similiar effects on the neurodevelopmental outcomes of preterm infants with RDS. In terms of neurodevelopmental outcomes there is no obvious advantage of an immediate surfactant administration in preterm infants according to our results.

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