Predisposing factors, severity and clinical outcomes of pulmonary hemorrhage in preterm infants with respiratory distress syndrome: A Tertiary NICU Experience

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Background: Pulmonary hemorrhage (PH) is a life-threatening condition. Low gestational age, male sex, vaginal birth, presence of respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), sepsis, hypoxia, severe hypothermia and congenital heart disease are associated with many conditions. Mortality in PH is reported up to 60%.

Objective: To determine the predisposing factors, response to surfactant therapy and clinical outcomes in preterm infants diagnosed with pulmonary hemorrhage.

Methods: Medical records of preterm infants with respiratory distress syndrome who admitted to a tertiary NICU were retrospectively evaluated.

Pulmonary hemorrhage (PH) was defined as blood suctioned from the endotracheal tube and classified as mild, moderate or severe based on the change in fraction of inspired oxygen requirement. Poractant alfa surfactant (Curosurf, Chiesi, Parma, Italy) was administered following pulmonary hemorrhage by the decision of attending neonatologist. Neonatal morbidities and mortality were assessed.

Results: There were 56 (8.6%) infants in PH and 594 (91.4%) infants in no PH groups. The mean (SD) birthweights were 891 (228) g and 1070 (230) g; the mean (SD) gestational ages were 27.6 (1.1) and 28.1 (1.2) weeks, respectively. The birth weight and gestational week were significantly lower in the PK group (p <0.001 and p = 0.003, respectively) (Table 1).

PH was associated with higher rates of death or bronchopulmonary dysplasia (BPD) (OR:26.77, 95% CI, 11.24-63.75; p<0.0001) and severe intraventricular hemorrhage (IVH) (OR:2.96, 95% CI, 1.50-5.85; p=0.001) compared with no PH group (Table 2).

Predisposing factors for PH were; birthweight <1000 g, gestational age < 28 weeks, 5' Apgar score ≤ 5, surfactant therapy and early onset sepsis (Table 3).

PH was severe in 43 (76.8 %), moderate in 10 (17.9%) and mild in 3 (5.4 %) infants. Median age (IQR) at occurrence of PH was 46 (33.2-86) hours. Thirty infants received surfactant therapy following PH.

The overall mortality rate was 78.6% in PH group. There was no difference in mortality, BPD, death or BPD and severe IVH among infants treated or not treated with surfactant in the PH group.

TABLE 1. Characteristics of the patients

	Without PH Group (n=594)	PH Group (n=56)	p
Birth weight (g)*	1070±230	891±228	<0.001
Gestational age (week)*	28.3±1.2	27.6±1.1	0.003
SGA, n (%)	72 (12.1)	15 (26.8)	0.002
Male gender, n (%)	311 (52.4)	25 (44.6)	0.26
Caesarean delivery, n (%)	496 (83.5)	53 (94.6)	0.02
Antenatal steroids, n (%)	403 (67.8)	35 (62.5)	0.41
APGAR score at 5 min†	8 (7-8)	6 (5.2-7)	<0.001
Multiple births, n (%)	131 (22.1)	13 (23.2)	0.84
Preeclampsia, n (%)	115 (19.4)	17 (30.4)	0.05
Chorioamnionitis, n (%)	78 (13.1)	6 (10.7)	0.60

*mean±SD †median, interquartile range (IQR). SGA, Small for gestational age (below the 10th centile)

TABLE 2. Clinical outcomes of the groups.

	Without PH Group (n=594)	PH Group (n=56)	p
hsPDA, n (%)	283 (47.6)	29 (51.8)	0.55
IVH> grade II, n (%)	53 (8.9)	13 (23.2)	0.001
Early onset sepsis, n (%)	105 (17.7)	18 (32.1)	0.008
Proven late onset sepsis, n (%)	159 (26.8)	9 (16.1)	0.08
ROP that required laser treatment, n (%)	59 (9.9)	3 (5.4)	0.71
BPD, moderate-severe, n (%)	(n=528)	(n=10)	
	68 (12.9)	6 (37.5)	0.004
Mortality, n (%)	66 (11.1)	44 (78.6)	<0.001
Duration of hospitalisation, days *	60 (47-79)	57 (58-114)	0.02

*median, interquartile range (IQR). BPD, Bronchopulmonary dysplasia;IVH, Intraventricular haemorrhage; hsPDA, hemodynamically significant patent ductus arteriosus; ROP, Retinopathy of prematurity

TABLE 3. Predisposing Factors for Pulmonary Hemorrhage

Variable	Odds Ratio	95% Confidence Interval	p value
Birth weight <1000 g	4.45	2.41-8.23	<0.001
Gestational age < 28 weeks	2.95	1.67-5.23	<0.001
5' Apgar score ≤ 5	2.86	1.48-5.53	0.01
Surfactant therapy	6.22	2.45-15.82	<0.001
Early onset sepsis	2.21	1.21-4.02	0.008

Conclusions: PH was associated with higher rates of death or BPD. Surfactant therapy might not alter the outcomes of infants with PH. However, the adjunctive therapies for PH have to be further investigated with prospective randomized control trials.

References:

1. Ahmad KA,, Bennett MM, Ahmad SF, et al. Morbidity and mortality with early pulmonary haemorrhage in preterm neonates. Arch Dis Child Fetal Neonatal Ed. pii: fetalneonatal-2017-314172.
2. Ferreira CH, Carmona F, Martinez FE. Prevalence, risk factors and outcomes associated with pulmonary hemorrhage in newborns. J Pediatr (Rio J). 2014;90:316-22.
3. Bozdağ Ş, Dilli D, Gökmen T,et al. Comparison of two natural surfactants for pulmonary hemorrhage in very low-birth-weight infants: a randomized controlled trial. Am J Perinatol. 2015;32:211-8.