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ORIGINAL ARTICLE

Intratracheal Administration of Budesonide with Surfactant in Very Low Birth Weight Infants to Prevent Bronchopulmonary Dysplasia

Mohammed Mahmoud Shehab[1], Elshymaa Safwat Elhassanein Elkhawaga[2*], Lotfy Mohamed Elsayed[1], Mohammed Ali Abdo [1], Mohamed Ahmed Ibrahim[2],

[1] Pediatric Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[2] Pediatric Department, NICU,Alahrar Teaching Hospital.Egypt

***Corresponding author:**
Elshymaa Safwat Elhassanein Elkhawaga

Email:
elkhawagashymaa289@gmail.com

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ABSTRACT

Background: Respiratory distress syndrome (RDS) is a leading cause of premature infant death. One of the most successful therapies for Bronchopulmonary dysplasia (BPD) is anti-inflammatory medication using corticosteroids. However, systemic corticosteroid administration is not suggested due to long-term side effects. We aim to study the effect of early intratracheal instillation of surfactant/budesonide with surfactant in preterm infants with severe Respiratory distress syndrome (RDS). **Methods:** This cross sectional study was carried out in the Pediatric Department, on 60 preterm infants weighing less than 1,500g who were admitted to the neonatal intensive care unit (NICU) of Zagazig University Hospital, during the period from November 2021 to November 2022. The treatment group (surfactant and budesonide) was given a mixture of 0.25 mg/kg (1 mL/kg) of budesonide and 100 mg/kg (4 mL/kg) of surfactant, and the control group (surfactant only) was given 100 mg/kg (4 mL/kg) of surfactant only. **Results:** There was no statistical significant difference between studied groups as regard Surfactant redoes, BPD, BPD moderate to severe, duration of non-invasive ventilation, duration of invasive ventilation, death, intraventricular hemorrhage (IVH), ROP and NEC. Among Surfactant- budesonide group; 16.7% Surfactant redoes, 26.7% BPD, 16.7% death, 6.7% IVH, 16.7% ROP, 0 % NEC and median duration of non-invasive ventilation is 3 days for surfactant- budesonide and control groups. **Conclusions:** Early intratracheal administration of budesonide and surfactant in preterm infants with sever RDS might decrease BPD and mortality without disturbing surfactant function.
Keywords: RDS; bronchopulmonary dysplasia; budesonide;preterm infant; pulmonar

INTRODUCTION

Respiratory distress syndrome (RDS) is one of the leading causes of preterm newborn death. Bronchopulmonary dysplasia (BPD) is one of the most deadly persistent respiratory disorders in preterm neonates after RDS therapy. Despite advances in RDS newborn care in the post-surfactant period, the incidence of BPD has not decreased [1]. It is considered that host immunological responses and pulmonary inflammation play important roles in the pathophysiology of BPD.The survival of smaller preterm newborns has increased thanks to Neonatal care has made technological and conceptual advances, such as the common use of prenatal corticosteroids and gentle ventilatory procedures in the post-surfactant era; yet, the incidence of bronchopulmonary dysplasia (BPD) has not decreased [2,3].

One of the best ways to avoid BPD is anti-inflammatory medication with corticosteroids [4]. Systemic corticosteroids, however, can have long-term negative effects, including poor physical development, small head size, and neurodevelopmental problems such neuromotor and cognitive abnormalities[5]. Direct application of corticosteroids to the lungs can reduce systemic side effects while increasing local anti-

inflammatory effects. Even when corticosteroids are inhaled as aerosol particles, there are restrictions on how much corticosteroid can reach newborn babies' distal lungs. A glucocorticoid with potent local anti-inflammatory properties is budesonide. Budesonide intratracheal instillation employing surfactant as a carrier dramatically improved pulmonary status, according to a pilot research [6]. Inhaled budesonide may be superior to systemic steroids for the treatment of BPD in preterm neonates. Because of its powerful topical effects, early administration of inhaled budesonide has been found to lower the incidence of BPD among premature neonates Bassler et al[7]. However, it can be difficult to provide inhaled glucocorticoids to premature newborns. It was demonstrated that budesonide alone administered straight into the trachea proved ineffective [8]. It is technically difficult and has limited benefits to provide inhaled glucocorticoids to premature newborns [9,10].This study aimed to determine whether early intratracheal budesonide instillation with surfactant in infants with severe Respiratory distress syndrome (RDS) might reduce bronchopulmonary dysplasia (BPD).

METHODS

This cross sectional study was carried out in pediatric department, Zagazig University, Hospital during the period from November 2021 to November 2022. Who necessitate surfactant therapy is thought to have an increased chance of getting BPD. The included 60 infants were divided into two groups written informed consent was obtained from all participants parents based on the medication given: **Group (I)** Control group, surfactant only; and **Group (II)** Treatment group, surfactant and budesonide. The inclusion criteria were determined within 4 hours after birth and included any preterm less than 1.500 g, These infants were deemed to be at a high risk of developing bronchopulmonary dysplasia (BPD) based on radiographic evidence of severe respiratory distress syndrome (RDS) (grades III–IV), mechanical ventilation, fraction of inspired oxygen (FIO2) at least 0.5, absence of severe congenital anomalies, or lethal cardiopulmonary disorder. Very low birth weight infants (VLBWIs) children with moribund conditions at birth, chromosomal abnormalities, congenital cardiac anomalies, and congenital pulmonary anomalies were excluded because these conditions could be confounding factors by affecting pulmonary function and survival, making them unsuitable for evaluating the effectiveness or safety of budesonide with surfactant. Chest radiography and assisted breathing results were used to make the diagnosis of Respiratory Distress Syndrome (RDS), and the attending physician made the choice to undergo surfactant replacement**[11].** All cases in the study were subjected to the following/all newborn critical care unit admissions' medical records:

Infant demographic factors included; Birth weight, gender, Apgar score, gestational age, and small for gestational age (SGA). Maternal demographic factors included; Treatment with antenatal corticosteroids (ANC), gestational diabetes in mothers (GDM), pregnancy-induced hypertension in mothers (PIH), and chorioamnionitis.

Surfactants were infused into the trachea via an orogastric tube and an endotracheal tube. The treatment group received a budesonide/survanta mixture of 0.25 mg/kg (1 mL/kg) (Pulmicort nebulizing suspension, Astra Zeneca, Lund, Sweden) and 100 mg/kg (4 mL/kg) (Infasurf®, ONY, Inc., Amherst, NY, USA). Survanta 100 mg/kg (4 mL/kg) was given to the control group exclusively. Survanta had a concentration ratio of 100 mg: 0.25 mg, or 4: 1 ml. Budesonide dosage was determined based on previous research [6, 12].

Ethics Considerations:

The institutional review board (IRB#6954-23-5-2021), Faculty of Medicine, Zagazig University approved the entire study plan. Written informed consent was obtained from all participants' parents. At all study levels, confidentiality and personal privacy were respected. This study was carried out in accordance with the Declaration of Helsinki, which is the International Medical Association's code of ethics for human subject research.

Statistical analysis:

The data was analyzed using SPSS software, version 18 (SPSS Inc., PASW statistics for Windows version 18). The median (minimum and maximum values) was used to characterize non-normally distributed data, whereas the mean was used to characterize regularly distributed data as established by the Kolmogrov-Smirnov test. The findings were found to be significant at the (0.05) level.

RESULTS

Table (1) illustrates non statistically significant difference between studied groups as regard gestational age, birth weight, sex, SGA, APGAR at 1 and 5 minutes. Mean gestational age is 30.3 weeks versus 29.73, mean birth weight is 1078.33 versus 1081.67, median APGAR score at 1 min is 5 versus 3, and APGAR score at 5 min is 7 versus 6 for Surfactant- budesonide group & control groups, respectively. Sex distribution among

studied groups is 17/13, 15/15 male / female ratio for Surfactant- budesonide group & control groups, respectively. Small for gestational age represents 26.7% and 23.3% for Surfactant - budesonide group & control groups respectively.

Table (2) demonstrate non statistically significant difference between studied groups as regard Surfactant redoes, BPD, BPD moderate to severe, duration of non invasive ventilation, Duration of invasive ventilation, Death, IVH, ROP and NEC. Among Surfactant- budesonide group ; 16.7% Surfactant redoes, 26.7% BPD, 16.7% death , 6.7% IVH , 16.7% ROP, 0 % NEC and median duration of non invasive ventilation is 3 days for Surfactant- budesonide and control groups. Among control group; 26.7% Surfactant redoes, 36.7% BPD, 26.7% death, 6.7% IVH , 23.3% ROP, 0 % NEC and median duration of BPD is 3 days for Surfactant- budesonide and control groups . Median duration of invasive ventilation is 20 versus 23 days for Surfactant- budesonide and control groups.

Table (3) demonstrates non statistically significant difference between studied groups as regard IVH, ROP and NEC. Among Surfactant-budesonide group; 6.7% IVH, 16.7 % ROP and 0 % NEC. Among control group; 6.7% IVH, 23.3% ROP and 0 % NEC respectively.

Table (4) illustrates statistically significant lower mean gestational age among cases with positive BPD than negative BPD cases (28.74±1.59 versus 30.61±1.96, respectively). Median birth weight of the studied neonates is lower among cases with positive BPD than negative cases (800 versus 1200) with statistically significant difference between them. APGAR score was lower among cases with positive BPD than cases with negative BPD at 1 &5 minutes (5 versus 3) and (7 versus 4), respectively. Maternal PIH is significantly higher among cases without BPD than cases with BPD.

Table (5) demonstrates that univariate analysis for predictors of bronchopulmonary dysplasia among studied cases are; Gestational age, Birth weight, APGAR AT 1 M and APGAR AT 5 M. Multivariate analysis of the significant factors illustrates that APGAR score at 5 minute is the only statistically significant predictor of BPD with every increase one point in the score decreases risk of BPD by 0.227 (odds ratio :0.227; 95% CI :0.056 -0.929).

Table (6) illustrates that univariate analysis for predictors of moderate to severe bronchopulmonary dysplasia among studied cases are; APGAR AT 1 M and APGAR AT 5 M with every increase one point in APGAR score at 1 minute decrease risk by 0.622 and in APGAR 5 minutes decreases risk by 0.571. Multivariate analysis of the significant factors illustrates that none of them was statistically significant predictor.

Table (7) demonstrates that univariate analysis for predictors of death among studied cases are; gestational age, birth weight, sex, APGAR SCORE at 1 and 5 minutes, maternal DM, chorioamnionitis. Multivariate analysis of the significant factors illustrates that presence of chorioamnionitis is statistically significant predictor of death, presence of chorioamnionitis increase risk of death by 6.83 more times.

Table (1): Comparison of gestational age , birth weight and sex between studied groups.

Baby	Surfactant- budesonide group (n=30)	Control group (n=30)	test of significance
Gestational age/weeks	30.30±2.09	29.73±1.98	t=1.08 p=0.285
Birth weight/gm	1078.33±287.58	1081.67±236.53	t=0.049 p=0.961
Sex **Male** **Female**	 17(56.7) 13(43.3)	 15(50) 15(50)	X^2=0.268 p=0.605
SGA **-VE** **+VE**	 22(73.3) 8(26.7)	 23(76.7) 7(23.3)	X^2=0.089 p=0.766
APGAR AT 1 M	5(0-7)	3(0-6)	Z=0.723 P=0.470
APGAR AT 5 M	7(3-8)	6(3-7)	Z=1.42 P=0.155

Parameters described as mean ± SD , median (min-max) and number (%), Z:Mann Whitney U test X2=Chi-Square test , t :Student t test

Table (2): Comparison of BPD & mortality between studied groups

BPD & mortality	Surfactant- budesonide group (n=30)	Control group (n=30)	test of significance
Surfactant redose	5(16.7)	8(26.7)	X^2=0.884 p=0.532
BPD	8(26.7)	11(36.7)	X^2=0.693 p=0.405
BPD moderate to severe	5(16.7)	7(23.3)	X^2=0.417 p=0.519
Duration of non invasive ventilation	3(1-7)	3(1-7)	z=0.754 p=0.451
Duration of invasive ventilation	20(3-29)	23(2-29)	z=0.176 p=0.860
Death	5(16.7)	8(26.7)	X^2=0.884 p=0.347
IVH	2(6.7)	2(6.7)	P=1.0
ROP	5(16.7)	7(23.3)	X^2=0.417 p=0.519
NEC	0	0	P=1.0

Parameters described as median (min-max) and number (%), Z:Mann Whitney U test X2=Chi-Square test , FET :Fischer exact test.

Table (3): Comparison of Outcome between studied groups

Outcome associated with Prematurity	Surfactant- budesonide group (n=30)	Control group (n=30)	test of significance
IVH	2(6.7)	2(6.7)	P=1.0
ROP	5(16.7)	7(23.3)	X^2=0.417 p=0.519
NEC	0	0	P=1.0

Parameters described as number (%) , X2=Chi-Square test , FET :Fischer exact test

Table (4): Relation between baby, mother characters and incidence of BPD among studied cases.

	total number	BPD		test of significance
		-ve	+ve	
Gestational age / weeks	60	30.61±1.96	28.74±1.59	t=3.64 p=0.001*
Birth weight/ gm	60	1200(750-1500)	800(700-1450)	z=2.47 p=0.014*
Sex Male Female	32 28	19(59.4) 22(78.6)	13(40.6) 6(21.4)	X^2=2.54 p=0.111
SGA -VE +VE	45 15	33(73.3) 8(53.3)	12(26.7) 7(46.7)	X^2=2.08 p=0.149
APGAR AT 1 M	60	5(0-7)	3(0-5)	z=3.92 p<0.001*

APGAR AT 5 M	60	7(3-8)	4(3-7)	z=4.39 p<0.001*
ANC	60	41(68.3)	19(31.7)	….
Maternal GDM	6	5(83.3)	1(16.7)	X^2=0.693 p=0.405
Maternal PIH	9	9(100)	0	X^2=4.91 p=0.027*
Chorioamnionitis	18	10(55.6)	8(44.4)	X^2=1.94 p=0.227
Drug treatment **Surf- budesonide group** **Control group (surfactant group)**	30 30	22(73.3) 19(63.3)	8(26.7) 11(36.7)	X^2=0.693 p=0.405

Parameters described as mean ± SD, median (min-max) and number (%), Z:Mann Whitney U test X2=Chi-Square test , t :Student t test , *statistically significant

Table (5): Predictors of bronchopulmonary dysplasia among studied cases.

Predictors of BPD	**Univariate analysis**		**Multivariate analysis**		
	p value	**COR (95%CI)**	**B**	**p value**	**AOR (95%CI)**
Gestational age / weeks	0.002*	0.578(0.407-0.819)	-0.593	0.198	0.553(0.224-1.36)
Birth weight/ gm	0.016*	0.997(0.995-0.999)	0.004	0.167	1.00(0.998-1.01)
Sex **Male (R)** **Female**	0.116	0.399 (0.127-1.25)			
SGA **-VE (R)** **+VE**	0.155	2.41(0.717-8.02)			
APGAR AT 1 M	0.001*	0.564(0.400-0.796)	0.791	0.178	2.21(0.698-6.97)
APGAR AT 5 M	<0.001*	0.422(0.269-0.661)	-1.48	0.039*	0.227(0.056-0.929)
Maternal GDM	0.419	0.400(0.043-3.68)			
Maternal PIH	0.999	Undefined			
Chorioamnionitis	0.168	2.26(0.709-7.17)			
Drug treatment **Surf- budesonide group(r)** **Control group**	0.407	1.59(0.531-4.78)			
Overall % predicted =76.7%					

AOR: Adjusted odds ratio, COR: Crude odds ratio, R: reference group β: regression coefficient

Table (6): Predictors of moderate to severe bronchopulmonary dysplasia among studied cases.

Predictors	**Univariate analysis**		**Multivariate analysis**		
	p value	**COR (95%CI)**	**β**	**p value**	**AOR (95%CI)**
Gestational age/weeks	0.06	0.712(0.500-1.01)			
Birth weight/gm	0.214	0.998(0.996-1.0)			
Sex **Male (R)** **Female**	0.306	0.500(0.133-1.88)			
SGA **-VE (R)**	0.145	2.71(0.709-10.39)			

+VE					
APGAR AT 1 M	0.007*	0.622(0.441-0.878)	-0.375	0.426	0.688(0.274-1.73)
APGAR AT 5 M	0.01*	0.571(0.373-0.875)	-0.039	0.944	0.962(0.324-2.86)
Maternal GDM	0.830	0.782(0.083-7.39)			
Maternal PIH	0.999	Undefined			
Chorioamnionitis	0.09	3.0(0.812-11.08)			
Drug treatment Surf- budesonide group(r) Control group	0.520	1.52(0.423-5.47)			
Overall % predicted =78.3%					

AOR: Adjusted odds ratio, COR: Crude odds ratio, R: reference group , β: regression coefficient

Table (7): Predictors of death among studied cases.

Predictors of death	**Univariate analysis**		**Multivariate analysis**		
	p value	**COR (95%CI)**	**B**	**p value**	**AOR (95%CI)**
Gestational age / weeks	0.009*	0.594(0.402-0.877)	0.037	0.954	1.04(0.289-3.73)
Birth weight/ gm	0.019*	0.997(0.994-0.999)	0.001	0.864	0.999(0.992-1.010
Sex Male Female(R)	0.02*	6.81(1.36-34.16) 1	2.15	0.06	1.12(0.012-1.29)
SGA -VE (R) +VE	0.054	1 3.62(0.976-13.42)			
APGAR AT 1 M	0.006*	0.625(0.446-0.876)	-0.593	0.348	0.553(0.160-1.91)
APGAR AT 5 M	0.034*	0.650(0.437-0.967)	0.852	0.259	2.35(0.534-10.29)
Maternal GDM	0.004*	28.75(2.96-279.54)	2.61	0.07	13.56(0.742-240.1)
Maternal PIH	0.999	undefined			
Chorioamnionitis	<0.001*	16.25(3.63-72.66)	1.922	0.029*	6.83(1.22-38.32)
Drug treatment Surfactant - budesonide group (r) Control group	0.351	1.82(0.518-6.38)			
overall % predicted =88.3%					

AOR: Adjusted odds ratio, COR: Crude odds ratio, R: reference group β: regression coefficient

DISCUSSION

In terms of gestational age, birth weight, sex, SGA, and APGAR at 1 and 5 minutes, the current study found no statistically significant differences between the analyzed groups. Pregnancy age on average (30.3 weeks versus 29.73), mean birth weight (1078.33 versus 29.73), median APGAR score at 1 min (5 versus 3) and APGAR score at 5 min (7 versus 6) for Surfactant- budesonide group & control groups, respectively. Sex distribution among studied groups is 17/13, 15/15 male / female ratio for Surfactant- budesonide group & control groups, respectively. Small for gestational age represents 26.7% and 23.3% for Surfactant budesonide group & control groups respectively. which is consistent with the research of **Gharehbaghi et al** [13] who reported that there was no statistical significant difference between intervention group (budesonide + surfactant) and control group (surfactant) as regard gestational age (28.2±1.7 versus 28.4±1.5, P = 0.38), birth weight (1055±192versus 1089±168, P = 0.27),sex [male 38 (59.3%), versus 40 (62.5%), p= 0.445], APGAR at 1 minute [5.9±1.7 versus 6.1±1.7] and 5 minutes (7.6±1.9 versus 7.8±1.4). The groups under study shared similar initial features.

Also, **Vemireddy et al**[14] reported that the study comprised and randomly assigned 109 neonates:

in the intervention group, 54 (budesonide + surfactant), there was no statistically significant difference between the studied groups with relation to gestational age, with 55 in the control group (surfactant) (26.3 ± 0.4 versus 25.9 ± 0.4, P = 0.245) , birth weight (778.1 ± 46.7 versus 763.2 ± 43.5, P = 0.644) , sex [male 29/54 (53.7%), versus 25/55 (45.4%), p= 0.445], SGA [5/54 (9.2%) versus 4/55 (7.2%), p= 0.741] APGAR at 1 minute [(5 (1-8) versus 5 (1-9)] and 5 minutes [7 (3-9) versus 7 (2-9)].

The results of the current investigation revealed no statistically significant differences between the study groups in terms of surfactant redoes, BPD, BPD mild to severe, length of non-invasive ventilation, or duration of invasive ventilation, Death , IVH, ROP and NEC. Among Surfactant-budesonide group ; 16.7% Surfactant redoes, 26.7% BPD, 16.7% death, 6.7% IVH, 16.7% ROP, 0 % NEC and median duration of non invasive ventilation is 3 days for Surfactant-budesonide and control groups. Among control group ; 26.7% Surfactant redoes, 36.7% BPD, 26.7% death, 6.7% IVH, 23.3% ROP and 0 % NEC. Median duration of invasive ventilation is 20 versus 23 days for Surfactant- budesonide and control groups. Similar to our results. Which coincide with the study of **Vemireddy et al** [14] who reported that primary outcomes examined in his study were incidence of death, BPD, and combined BPD or death. **Yeh et al**[6] showed that budesonide with in comparison to surfactant only therapy, surfactant could reduce the prevalence of BPD, mortality, and survival without BPD without noticeably raising side effects.

According to the results of the current investigation, there were no statistically significant differences between the analyzed groups in terms of IVH, ROP, and NEC. group of surfactants-budesonide; 6.7%IVH, 16.7 % ROP and 0% NEC. Among control group; 6.7% IVH, 23.3% ROP and 0% NEC respectively. Which in agreement with the study of Vemireddy et al[14] who stated that there was no statistically significant difference between the control group and the intervention group (budesonide + surfactant) (surfactant) as regard the incidence of IVH [5/54 (9.2%) versus 14/55 (25.4%), P = 0.041] , NEC [4/54 (7.4%) versus 5/55 (9%). P= 1.000] and ROP [6/54 (11.1%) versus 5/55 (9%), P = 0.761]. Also, similar to the current studies of **Gharehbaghi et al**[13] and **Yeh et al**., [15], they reported that there was no statistically significant difference in the incidence of IVH, NEC, and ROP in the two examined groups between the intervention group (budesonide + surfactant) and the control group (surfactant).

The current investigation revealed that cases with positive BPD had statistically significantly lower mean gestational ages than instances with negative BPD (28.74±1.59 versus 30.61±1.96, respectively). Median birth weight of the studied neonates is lower among cases with positive BPD than negative cases (800 versus 1200) with statistically significant difference between them. APGAR score was lower among cases with positive BPD than cases with negative BPD at 1 &5 minutes (5 versus 3) and (7 versus 4), respectively. Maternal PIH is significantly higher among cases without BPD than cases with BPD. Which in agreement with the study of **Jassem-Bobowicz et al**[16] who reported that the Apgar score in the patients who developed BPD was lower at 1 min and 5 min (1 minute 5.1 vs. 6.8, p p < 0.001; 5 minute 6.9 vs. 7.8, p p < 0.001), statistically significant lower birth weight (1002gm versus 1394gm, p= <0.001) and significant lower Gestational age (27.5 versus 30.3, p= <0.001) in patients with BPD than in patients without BPD. But in contrast to our results Maternal PIH is significantly higher among cases without BPD than cases with BPD. Also, **Landry & Menzies** [17] demonstrated that patients with BPD had considerably lower birth weights than patients without BPD. The Apgar rating at 1 min and 5 min were lower significantly among cases with positive BPD than cases with negative BPD.

The current study showed that univariate analysis for predictors of bronchopulmonary dysplasia among studied cases are ; Gestational age, Birth weight, APGAR AT 1 M and APGAR AT 5 M. Multivariate analysis of the significant factors illustrates that APGAR score at 5 minute is the only statistically significant predictor of BPD with every increase one point in the score decreases risk of BPD by 0.227 (odds ratio: 0.227; 95% CI: 0.056 -0.929). Which is consistent with the research of **Alshehri et al**[18] who concluded revealed Gestational Age, Birth Weight, Sex, small for Gestational Age, and 5 Minute Apgar Score were the most important prediction factors of BPD. Also, **Ramos-Navarro et al [**19] reported that the predictive factors for BPD in neonatal birth weight, gestational age, and postpartum resuscitation. Male gender, intrauterine growth restriction, and oligohydramniosis could be separate prenatal risk factors. If the risk of developing BPD can be early identified and assessed, it is crucial to avoid and manage its occurrence[20].

In the present study, predictors of moderate to severe bronchopulmonary dysplasia were identified using univariate analysis among studied

cases are; APGAR AT 1 M and APGAR AT 5 M with every increase one point in APGAR score at 1 minute decrease risk by 0.622 and in APGAR 5 minutes decreases risk by 0.571. Multivariate analysis of the significant factors illustrates that none of them was statistically significant predictor which in agreement with the study of **Trembath & Laughon**[21] who found that lower 1 and 5-minute Apgar Scores, male sex, lower birth weight, and gestational age were risk factors for newborns developing BPD. Sharma et al[22] who came to the conclusion that BPD There is a substantial association between severity and apgar scores at 1 and 5 minutes Landry & Menzies[17] demonstrated that the risk of developing BPD rose by 16% with each point reduction from the 1 min Apgar score related to the severity of BPD (OR 1.16 [95% CI 1.1 to 1.3]), and **Roberts et al** [23].It was discovered that premature infants with BPD had lower 5 minute Apgar scores than non-BPD neonates. BPD development was connected to postnatal asphyxia.

The current study showed that univariate analysis for predictors of death among studied cases are ; age at conception, birth weight, sex, and Maternal diabetes, chorioamnionitis, and APGAR SCORE at 1 and 5 minutes. The results of the multivariate analysis of the important factors show that chorioamnionitis is a statistically significant predictor of death, increasing the probability of death by 6.83 times.

The main risk factors for BPD include prematurity and low birth weight[24]. Only 20% of babies born at 28 weeks are diagnosed with BPD, compared to more than 80% of babies born between 22 and 24 weeks, 95% of BPD babies are VLBW [25]. Other prenatal risk factors include chorioamnionitis, male sex, intrauterine growth restriction (IUGR), and race or ethnicity and smoking [26]. Twin studies suggest that Genetic risk factors may have a role in the development of BPD, and the hunt for genetic markers for BPD is still continuing [27].

CONCLUSIONS

In preterm infants with severe RDS, early intratracheal injection of budesonide and surfactant may reduce BPD and mortality without impairing surfactant function.

To support our findings, additional prospective randomized controlled multicentric trials using various surfactant formulations, many preterm infants, and extended follow-up are needed.

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