Original Article

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Association between initial use of bubble CPAP and mortality in the neonatal ICU: A retrospective cohort study

Associação entre o uso inicial de bubble CPAP e mortalidade em UTI neonatal: um estudo de coorte retrospectivo

Asociación entre el uso inicial de CPAP de burbuja y la mortalidad en la UCI neonatal: un estudio de cohorte retrospectivo

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ABSTRACT

Introduction: Neonatal respiratory distress is a relevant cause of morbidity and mortality. Bubble Continuous Positive Airway Pressure (BCPAP) is a noninvasive ventilatory modality used in the management of these patients. **Objectives:** To evaluate the association between initial BCPAP use and mortality in newborns with respiratory distress, as well as related clinical outcomes. **Methods:** A retrospective cohort study conducted in the neonatal intensive care unit of a tertiary hospital between September 2021 and August 2023. Newborns diagnosed with respiratory distress were included, while those with immediate intubation, extensive resuscitation, Apgar score ≤1 at 1 minute or ≤3 at 5 minutes, or transferred patients were excluded. Clinical variables and outcomes were analyzed, and logistic regression was performed with mortality as the outcome. **Results:** A total of 218 newborns were included and classified according to initial ventilatory support: noninvasive ventilation (NIV, n=94), BCPAP (n=60), and orotracheal intubation (OTI, n=64). Mortality was lower in the BCPAP group (3.3%) compared with the OTI group (28.1%). The OTI group had a higher proportion of extreme prematurity and lower birth weight. In logistic regression, the initial ventilatory modality was associated with mortality (OR: 14.2; p<0.001). Length of hospital stay was shorter in the BCPAP group compared with the OTI group (p<0.001). **Conclusion:** BCPAP use was associated with lower mortality and shorter hospital stay compared with OTI. Baseline differences between groups limit causal inferences and suggest confounding by disease severity.

Keywords: Respiratory Distress Syndrome; Newborn; Continuous Positive Airway Pressure; Intensive Care Units; Neonatal; Cohort Studies; Retrospective Studies.

RESUMO

Introdução: O desconforto respiratório neonatal é causa relevante de morbimortalidade. O *Bubble Continuous Positive Airway Pressure* (BCPAP) é uma modalidade ventilatória não invasiva utilizada no manejo desses pacientes. **Objetivos:** Avaliar a associação entre o uso inicial do BCPAP e a mortalidade em recém-nascidos com desconforto respiratório, bem como desfechos clínicos associados. **Métodos:** Coorte retrospectiva realizada em unidade de terapia intensiva neonatal de hospital terciário entre setembro de 2021 e agosto de 2023. Incluíram-se recém-nascidos com diagnóstico de desconforto respiratório; excluíram-se aqueles com intubação imediata, ressuscitação extensiva, escore de Apgar ≤1 no primeiro minuto ou ≤3 no quinto minuto, ou transferidos. Analisaram-se variáveis clínicas e desfechos, com regressão logística, tendo o óbito como desfecho. **Resultados:** Foram incluídos 218 recém-nascidos, distribuídos conforme o suporte ventilatório inicial: ventilação não invasiva (VNI, n=94), BCPAP (n=60) e intubação orotraqueal (IOT, n=64). A mortalidade foi menor no grupo BCPAP (3,3%) em comparação ao grupo IOT (28,1%). O grupo IOT concentrou maior prematuridade extrema e menor peso ao nascer. Na regressão logística, a modalidade ventilatória inicial associou-se à mortalidade (OR: 14,2; p<0,001). O tempo de internação foi reduzido no grupo BCPAP em comparação ao grupo IOT (p<0,001). **Conclusão:** O uso de BCPAP associou-se a menor mortalidade e menor tempo de internação em comparação à IOT. Diferenças basais entre grupos limitam inferências causais e sugerem confusão por gravidade.

Palavras-Chave: Síndrome do Desconforto Respiratório do Recém-Nascido; Pressão Positiva Contínua nas Vias Aéreas; Unidades de Terapia Intensiva Neonatal; Estudos de Coorte; Estudos Retrospectivos.

RESUMEN

Introducción: La dificultad respiratoria neonatal es una causa importante de morbilidad y mortalidad. La presión positiva continua de burbuja en la vía aérea (BCPAP) es una modalidad de ventilación no invasiva utilizada en el manejo de estos pacientes. **Objetivos**: Evaluar la asociación entre el uso inicial de BCPAP y la mortalidad en recién nacidos con dificultad respiratoria, así como los resultados clínicos asociados. **Métodos**: Estudio de cohorte retrospectivo realizado en una unidad de cuidados intensivos neonatales de un hospital terciario entre septiembre de 2021 y agosto de 2023. Se incluyeron recién nacidos con diagnóstico de dificultad respiratoria; se excluyeron aquellos con intubación inmediata, reanimación extensa, puntaje de Apgar ≤1 al minuto o ≤3 a los cinco minutos, o aquellos transferidos. Las variables clínicas y los resultados se analizaron mediante regresión logística, con la muerte como resultado. **Resultados**: Se incluyeron 218 recién nacidos, distribuidos según el soporte ventilatorio inicial: ventilación no invasiva (VNI, n = 94), BCPAP (n = 60) e intubación orotraqueal (ITO, n = 64). La mortalidad fue menor en el grupo BCPAP (3,3%) en comparación con el grupo OTI (28,1%). El grupo OTI presentó mayores tasas de prematuridad extrema y menor peso al nacer. En la regresión logística, el modo ventilatorio inicial se asoció con la mortalidad (OR: 14,2; p < 0,001). La duración de la hospitalización se redujo en el grupo BCPAP en comparación con el grupo OTI (p < 0,001). **Conclusión**: El uso de BCPAP se asoció con menor mortalidad y menor duración de la hospitalización en comparación con OTI. Las diferencias basales entre los grupos limitan las inferencias causales y sugieren factores de confusión debido a la gravedad.

Palabras Clave: Síndrome de Dificultad Respiratoria Neonatal; Presión Positiva Continua en la Vía Aérea; Unidades de Cuidados Intensivos Neonatales; Estudios de Cohorte; Estudios Retrospectivos.

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INTRODUCTION

Neonatal respiratory distress (RD) is characterized by the newborn's (NB) difficulty in establishing adequate breathing after birth.[1] It is one of the main causes of morbidity and mortality in preterm newborns (PTNB).[1,2] Between 2018 and 2023, mortality from neonatal RD in Brazil corresponded to approximately 2,000 deaths annually.[3]

Respiratory distress syndrome (RDS) is the most common cause of RD in PTNB, due to alveolar surfactant deficiency.[2] Other etiologies of RD include transient tachypnea of the newborn (TTN), meconium aspiration syndrome (MAS), pulmonary infections, and heart disease.[4] The main risk factors for the development of RD include premature birth, perinatal asphyxia, cesarean delivery without labor, gestational diabetes mellitus (GDM), and pregnancy-induced hypertension (PIH).[5-7]

Historically, treatment for neonatal RD involves invasive procedures, such as mechanical ventilation (MV).[1,8] Although essential in certain cases, MV is associated with serious complications, such as barotrauma, infections, bronchopulmonary dysplasia (BPD), and increased mortality.[9] Randomized clinical trials have demonstrated that less invasive ventilatory support, such as Continuous Positive Airway Pressure (CPAP), when applied to selected patients, was associated with a lower occurrence of MV-related complications.[9,10]

CPAP consists of applying positive pressure to the airways of spontaneously breathing newborns.[10] This pressure contributes to maintaining functional residual capacity (FRC), facilitating gas exchange, promoting the production of endogenous surfactant, and reducing the respiratory effort of babies.[11]

Among the nasal CPAP modalities, Bubble CPAP (BCPAP) is widely used due to its operational simplicity and low cost.[12] This system uses bubbles to generate pressure oscillations that keep the alveoli open, promoting adequate ventilation to meet the needs of the newborn. and reducing respiratory effort.[10,12] This study aims to analyze the association between the use of BCPAP and clinical outcomes, compared with other ventilatory modalities in newborns with respiratory distress syndrome.

METHODS

Study design

This is a longitudinal observational study of the retrospective cohort type, conducted in accordance with the STROBE Statement standards.

Context

The study was based on newborns diagnosed with respiratory distress syndrome (ICD-10: P22 - Respiratory distress of the newborn) admitted to the Neonatal Intensive Care Unit (NICU) of the Alto Vale Regional Hospital (HRAV), between September 2021 and August 2023. All data were collected from electronic medical records. The study was approved by the Research Ethics Committee of UNIDAVI (opinion no. 6.902.331).

Participants

The inclusion criteria were all newborns admitted to the NICU of HRAV, from September 2021 to August 2023, with a diagnosis of respiratory distress syndrome (RD), identified by the International Classification of Diseases (ICD-10) codes related to respiratory conditions of the perinatal period (P22, P220-P229, P240, P28, P285-P289).

Newborns who required extensive resuscitation at birth, those with an Apgar score ≤1 at one minute and ≤3 at five minutes, and newborns transferred to other institutions were excluded. Transfers occurred mainly due to the need for care support not available in the originating unit, including specialized surgical procedures or management of more complex clinical conditions.

Variables

The variables analyzed included neonatal characteristics (gestational age, birth weight, sex, and Apgar score), maternal and gestational data (maternal age, number of prenatal visits, comorbidities, gestational complications, medication use, mode of delivery, and interventions performed), RD etiology, neonatal

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therapeutic support (use of antibiotics, vasoactive drugs, surfactant, umbilical catheter, nitric oxide, and adrenaline), and types of ventilatory support, classified as non-invasive ventilation (NIV), Bubble CPAP (BCPAP), and endotracheal intubation (ETI). The NIV group included oxygen therapy modalities without continuous positive airway pressure application, such as nasal cannula, hood, and halo, used in newborns with mild RD, and were analyzed in a grouped manner, considering their use as initial respiratory support of lower clinical complexity. Information related to ventilatory support (start site, duration, need for changes in modality, and associated complications) and clinical outcomes (length of hospital stay and condition at the end of hospitalization) were evaluated. For multivariate analysis, complications were grouped as a dichotomous variable (presence vs. absence).

Newborns were classified according to initial ventilatory support, reflecting the therapeutic strategy adopted in early stabilization and reducing time bias (immortal time bias). It is recognized, however, that BCPAP failure requiring escalation to intubation can introduce classification bias. In cases of BCPAP failure requiring advanced neonatal resuscitation, management followed the protocols of the Neonatal Resuscitation Program. Thus, the occurrence of adrenaline use in newborns classified in the BCPAP group refers to events after the failure of the initial modality, and do not represent the concomitant use of BCPAP and adrenaline.

Data sources and study size

We analyzed 231 electronic medical records, of which 218 met the eligibility criteria. The study included all eligible cases registered during the study period, characterizing a census-based convenience sample, without prior calculation of the sample size.

Quantitative variables

Quantitative variables included maternal age (years), number of prenatal visits, gestational age at birth (weeks), birth weight (grams), Apgar score at 1 and 5 minutes, duration of ventilatory support (days), and length of hospital stay (days).

Statistical analysis

Statistical analyses were performed using IBM® SPSS Statistics, version 26.0.0, and graphs were created using GraphPad® Prism, version 8.2.1. The presence of outliers and the normality of the data were assessed. Continuous variables were expressed as median and interquartile range (IQR), and categorical variables as frequency (n) and percentage (%). Comparisons between ventilatory support groups were performed using the Kruskal-Wallis and Pearson's chi-square or Fisher's exact tests, as appropriate. For mortality outcome analysis, the Mann-Whitney, chi-square, or Fisher's exact tests were used. Adjusted residuals (AR) were used to identify specific associations. Variables with significant associations were included in a logistic regression model, considering mortality as the dependent variable. A statistical significance level of $p \leq 0.05$ was adopted. Given the limited number of events, the model results were interpreted with caution, considering possible collinearity between variables indicative of clinical severity. No adjustment for multiple comparisons was performed, and the secondary analyses were considered exploratory.

RESULTS

General characterization of the sample according to ventilatory support

The sample included 218 newborns diagnosed with RD, distributed according to initial ventilatory support: NIV (n=94), BCPAP (n=60), and IOT (n=64).

The IOT group had a higher frequency of newborns with gestational age <28 weeks (23.0%; AR=3.4; p<0.001) and birth weight <1,000g (23.0%; AR=5.3; p<0.001). In the NIV group, term newborns predominated (76.3%; AR=5.0), while the BCPAP group had a higher proportion of neonates between 28-32 weeks (27.6%; AR=3.3). The distribution of birth weight varied significantly between the groups (p < 0.001). Newborns weighing between 2,500-4,000 g were more frequent in the NIV group (78.6%; AR=4.4), while newborns weighing

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<1,000 g were more frequent in the IOT group (23.0%; AR=5.3). The BCPAP group had a higher proportion of newborns weighing between 1,500-2,499 g (31.7%; AR=1.7). Adjusted residuals indicate significant associations between higher birth weight and the use of NIV, and between extremely low birth weight and the need for IOT (Table 1).

RD etiologies differed significantly between the groups (p<0.001). Early unspecified RD was the most frequent cause in the sample (54.6%), predominating in the NIV group (72.3%; AR=4.6). Neonatal pneumonia occurred in 16.5% of cases, with a higher prevalence in the BCPAP group (21.7%). DR syndrome occurred in 10.1% of the sample and was more frequent in the BCPAP (16.7%; AR=2.0) and IOT (15.6%; AR=1.7) groups (Table 1). There was a predominance of males in the sample (54.1%), with significant difference between the groups (p=0.023), with a higher proportion of females in the NIV group (56.4%) and higher frequency of males in the BCPAP (60.0%) and IOT (64.1%) groups (Table 1). Information regarding the Apgar score, mode of delivery, and maternal variables is presented in Supplementary Table 1.

Among the therapeutic interventions, the use of antibiotic therapy was more frequent in the IOT group (95.3%; AR=5.8; p<0.001). Vasoactive drug administration was more frequent in the IOT group (54.0%; AR=7.2), while the BCPAP group had a lower rate (23.3%; AR=3.0) (p<0.001). Surfactant use was higher in the IOT group (54.7%; AR=7.0), followed by the BCPAP group (25.0%; AR=0.3) (p<0.001). Umbilical catheter insertion showed significant differences between the groups, being observed in 87.5% of patients in the IOT group (AR=8.6) and in 60.0% of the BCPAP group (AR=3.1), while it was not observed in the NIV group (0.0%; AR=10.8) (p<0.001). The use of nitric oxide and adrenaline was more frequent in the BCPAP and IOT groups (Table 1).

The initiation of ventilatory support was more frequent in the delivery room in the IOT group, while the BCPAP and NIV groups showed a higher initiation in the NICU (p<0.001). The need to change ventilatory support occurred mainly in the BCPAP and NIV groups (p<0.001). The total time of ventilatory support was significantly longer in the IOT group, intermediate in the BCPAP group, and shorter in the NIV group (p<0.001). Detailed data are shown in Table 1.

Regarding complications associated with ventilatory support, pneumothorax was the most prevalent, present in 4.1% of newborns, more frequent in the IOT group (9.4%; AR=5.5), followed by the BCPAP group (5.0%) (*p=0.015*). BPD was identified in 3.7% of the sample, with a higher prevalence in the IOT group (12.5%; AR=1.3), followed by the BCPAP group (6.7%; AR=1.5). Pulmonary hemorrhage was observed in 2.3% of newborns and occurred exclusively in the BCPAP (3.3%) and IOT (4.7%) groups. Pleural effusion was the least frequent complication, identified only in the IOT group (1.6%). (Table 1).

The length of hospital stay also differed between the groups (*p<0.001*), being longer in the IOT group, with a median of 17.0 days (IQR: 8.0-35.75), followed by the BCPAP group, with 11.0 days (IQR: 8.0-17.0). The NIV group had the shortest length of stay, with a median of 4.0 days (IQR: 2.0-7.25) (Figure 1a).

In the total sample, the mortality rate was 9.2% and the median length of stay was 8.0 days (IQR: 4.0-15.25). Mortality varied significantly between groups (*p<0.001*), being highest in the IOT group (28.1%; AR=6.2), followed by the BCPAP group (3.3%; AR=1.8), with no deaths recorded in the NIV group (0%; AR=4.1) (Figure 1b).

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Figure 1. Length of hospital stay and mortality rate according to the type of ventilatory support. **Figure a.** Length of hospital stay (in days) according to the type of ventilatory support used. * : statistically significant difference between the groups. **Figure b.** Mortality rate according to the type of ventilatory support. * : statistically significant difference between the groups.

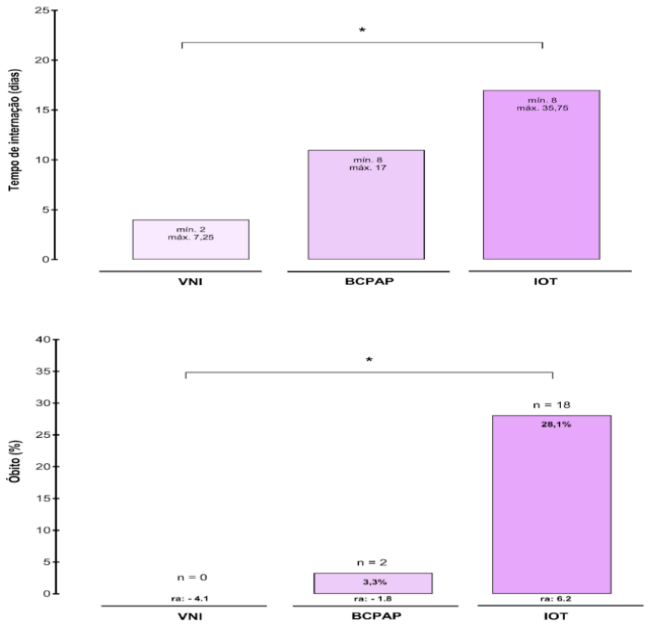

Table 1. Clinical characteristics, therapeutic interventions, and complications of the overall sample according to the type of ventilatory support

Variables	Total N = 218 n (%)	VNI N = 94 n (%)[ar=number]	BCPAP N = 60 n (%)[ar=number]	IOT N = 64 n (%)[ar=number]	*p-value*
Newborn's data					
Gestational age					
< 28	14 (6.6)	0 (0.0)$^{-3.4}$	0 (0.0)$^{-2.4}$	14 (23.0)$^{6.1}$	**<0.001**
28 - 32	31 (14.6)	0 (0.0)$^{-5.3}$	16 (27.6)$^{3.3}$	15 (24.6)$^{2.6}$	
33 - 36	46 (21.7)	22 (23.7)$^{0.6}$	19 (32.8)$^{2.4}$	5 (8.2)$^{-3.0}$	
37 - 41	121 (57.1)	71 (76.3)$^{5.0}$	23 (39.7)$^{-3.1}$	27 (44.3)$^{-2.4}$	
Birth weight (g)					
<1000	16 (7.8)	0 (0.0)$^{-3.5}$	2 (3.3)$^{-1.5}$	14 (23.0)$^{5.3}$	**<0.001**

<1500	17 (8.3)	0 (0.0)$^{-3.6}$	6 (10.0)$^{0.6}$	11 (18,0)$^{3.3}$	
<2500	38 (18.5)	11 (13.1)$^{-1.7}$	19 (31.7)$^{3.1}$	8 (13.1)$^{-1.3}$	
2500 - 4000	124 (60.5)	66 (78.6)$^{4.4}$	31 (51.7)$^{-1.7}$	27 (44.3)$^{-3.1}$	
>4001	10 (4.9)	7 (8.3)$^{1.9}$	2 (3.3)$^{-0.7}$	1 (1.6)$^{-1.4}$	
RD Etiologies					
ERD not specified	119 (54.6)	68 (72.3)$^{4.6}$	24 (40.0)$^{-2.7}$	27 (42.2)$^{-2.4}$	**<0.001**
Neonatal pneumonia	36 (16.5)	12 (12.8)$^{-1.3}$	13 (21.7)$^{1.3}$	11 (17.2)$^{0.2}$	
RDS	22 (10.1)	2 (2.1)$^{-3.4}$	10 (16.7)$^{2.0}$	10 (15.6)$^{1.7}$	
SAM	13 (6.0)	4 (4.3)$^{-0.9}$	5 (8.3)$^{0.9}$	4 (6.3)$^{0.1}$	
TTRN	11 (5.0)	7 (7.4)$^{1.4}$	4 (6.7)$^{0.7}$	0 (0.0)$^{-2.2}$	
Cardiopathies	7 (3.2)	1 (1.1)$^{-1.6}$	2 (3.3)$^{0.1}$	4 (6.3)$^{1.6}$	
Malformations and others	6 (2.8)	0 (0.0)$^{-2.2}$	1 (1.7)$^{-0.6}$	5 (7.8)$^{2.9}$	
Perinatal anoxia	3 (1.4)	0 (0.0)$^{-1.4}$	0 (0.0)$^{-1.1}$	3 (4.7)$^{2.7}$	
Apnea of prematurity	1 (0.5)	0 (0.0)$^{-0.9}$	1 (1.7)$^{1.6}$	0 (0.0)$^{-0.6}$	
Neonatal interventions and therapeutic support					
Antibiotic therapy	144 (66.7)	33 (35.9)$^{-8.3}$	50 (83.3)$^{3.2}$	61 (95.3)$^{5.8}$	**<0.001**
Vasoavtive drugs	48 (22.3)	0 (0.0)$^{-6.8}$	14 (23.3)$^{0.2}$	34 (54.0)$^{7.2}$	**<0.001**
Surfactant	50 (23.5)	0 (0.0)$^{-6.8}$	15 (25.0)$^{0.3}$	35 (54.7)$^{7.0}$	**<0.001**
Umbilical catheter	92 (43.0)	0 (0.0)$^{-10.8}$	36 (60.0)$^{3.1}$	56 (87.5)$^{8.6}$	**<0.001**
Nitric oxide	7 (3.3)	0 (0.0)$^{-2.3}$	1 (1.7)$^{-0.8}$	6 (9.5)$^{3.3}$	**0.003**
Adrenaline	35 (16.1)	1 (1.1)$^{-5.2}$	10 (16.7)$^{0.1}$	24 (37.5)$^{5.5}$	**<0.001**
Complications arising from the use of ventilatory support					
Pneumothorax	9 (4.1)	0 (0.0)$^{-2.7}$	3 (5.0)$^{0.4}$	6 (9.4)$^{2.5}$	**0.015**
Pleural effusion	1 (0.5)	0 (0.0)$^{-0.9}$	0 (0.0)$^{-0.6}$	1 (1.6)$^{1.6}$	
Pulmonary hemorrhage	5 (2.3)	0 (0.0)$^{-2.0}$	2 (3.3)$^{0.6}$	3 (4.7)$^{1.5}$	
Broncodysplasia	8 (3.7)	0 (0.0)$^{-2.5}$	4 (6.7)$^{1.5}$	4 (12.5)$^{1.3}$	**0.043**

UTI: urinary tract infection, PIH: pregnancy-induced hypertension, GDM: gestational diabetes mellitus, MgSO4: magnesium sulfate, ERD: early respiratory distress, MAS: meconium aspiration syndrome, TTN: transient tachypnea of the newborn, RDS: respiratory distress syndrome.
Source: The authors.

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Logistic regression analysis for mortality prediction

In logistic regression analysis, prematurity was associated with a higher chance of death (OR: 5.7; 95% CI: 1.863-17.916; p=0.002). The location of initial care showed a significant association with mortality (OR: 0.5; 95% CI: 0.012-0.236; p<0.001). Variables related to greater clinical severity, such as the use of an umbilical catheter (OR: 14.5; 95% CI: 3.291-64.713; p<0.001), antibiotic therapy (OR: 5.0; 95% CI: 1.127-22.181; p=0.034), vasoactive drugs (OR: 29.9; 95% CI: 8.285-108.471; p<0.001), adrenaline (OR: 19.5; 95% CI: 6.789-56.332; p<0.001) and nitric oxide (OR: 16.0; 95% CI: 3.291-77.791; p=0.001) were factors independently associated with mortality. The use of surfactant showed a statistically significant association with a lower chance of death (OR: 0.07; 95% CI: 0.025-0.217; p<0.001). The presence of complications was associated with a higher risk of mortality (OR: 2.3; 95% CI: 1.334-4.214; p=0.003). The type of initial ventilatory support was associated with mortality (OR: 14.2; 95% CI: 3.631-55.565; p<0.001), an interpretation that should be cautious as it mainly reflects differences in baseline severity between the groups and possible collinearity with therapeutic interventions (Table 2).

Table 2. Logistic regression of clinical variables associated with mortality in newborns with respiratory distress syndrome

Variables	Death		
	OR	**95% CI**	***p-value***
Preterm	5.7	(1.863-17.916)	**0.002**
Gestational age	1.0	(0.706-1.509)	0.871
Birth weight (g)	0.9	(0.632-1.309)	0.609
Starting point	0.5	(0.012-0.236)	**<0.001**
Etiologies	1.1	(0.978-1.145)	0.082
Umbilical catheter	14.5	(3.291-64.713)	**<0.001**
Antibiotic therapy	5.0	(1.127-22.181)	**0.034**
Vasoactive drugs	29.9	(8.285-108.471)	**<0.001**
Adrenaline	19.5	(6.789-56.332)	**<0.001**
Surfactant	0.07	(0.025-0.217)	**<0.001**
Nitric oxide	16.0	(3.291-77.791)	**<0.001**
Complications	2.3	(1.334-4.214)	**0.003**
Type of ventilatory support	14.2	(3.631-55.565)	**<0.001**

OR: odds ratio, CI: Confidence interval. Type of ventilatory support: NIV, BCPAP or IOT.
Source: The authors

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DISCUSSION

The findings of this study are consistent with the literature in showing that the use of BCPAP is associated with more favorable clinical outcomes when compared to IOT, especially in newborns with less clinical severity.[13] In the present study, newborns initially managed with BCPAP had a lower frequency of complications related to ventilatory support, shorter hospital stay, and lower mortality compared to the IOT group. The type of initial ventilatory support showed significant association with mortality (OR: 14.2), a finding that should be interpreted considering that MV tends to be used in newborns with more complex clinical conditions, and not as evidence of a direct causal effect of the technique.[8]

A greater need for IOT was observed among extremely premature newborns (<28 weeks) and those with low birth weight, especially <1,500g. On the other hand, newborns with gestational age between 28-32 weeks and those with weight >1,500g had a higher frequency of initial use of BCPAP. These findings are consistent with the literature, which associates lower gestational age and low birth weight with greater pulmonary immaturity and the need for more invasive ventilatory support.[14,15]

In the adjusted model, variables such as etiology of RD, birth weight, and gestational age were not associated with mortality. Evidence describes BCPAP as a frequently used strategy as initial support because it allows for ventilatory stabilization without immediate intubation, and its indication should consider the clinical context.[9,16] Thus, initial ventilatory support should also be understood as a marker of clinical severity, and not just as an intervention.[8,13]

The literature indicates that BCPAP failure rates vary between 20% and 30%, especially in cases of greater clinical severity, making escalation to intubation necessary.[17,18] In this study, a failure rate of 33.4% was observed in the BCPAP group, which is consistent with the literature. Despite this, 19 newborns remained on BCPAP without needing initial intubation, suggesting that this strategy may, in selected cases, postpone or avoid exposure to complications associated with MV.

The use of vasoactive drugs was lower in the BCPAP group in this study, compared with the intubation group, possibly reflecting a profile of greater hemodynamic stability, although subject to confounding due to severity. These findings are consistent with previous evidence suggesting that MV may be associated with greater cardiovascular instability due to adverse effects such as increased intrathoracic pressure, reduced venous return, and impact on cardiac function.[15,17] Similarly, the higher frequency of adrenaline use observed in the IOT group should be interpreted as a marker of greater clinical severity and need for advanced neonatal resuscitation, in accordance with the Neonatal Resuscitation Program protocols, and should not be directly attributed to the initial ventilatory mode.[20,21]

Previous studies describe that the initial use of BCPAP may be associated with a lower need for intubation and more favorable clinical outcomes, although it is not effective in all cases.[9] Our study demonstrates that the initial respiratory support mode was associated with neonatal mortality, with a higher proportion of deaths in the IOT group (28.1%) compared to the BCPAP group (3.3%) (*p<0.001*). Similar results have been described in the literature, which associates less invasive strategies with a lower occurrence of MV-related complications, such as infections and lung injuries, which may contribute to more favorable outcomes.[22,23]

A study published in 2024, involving 440 newborns with gestational age <32 weeks, showed an association between the use of BCPAP as primary support and lower mortality rates.[23] In addition, less invasive ventilatory strategies, such as BCPAP, are associated with shorter MV time and reduced length of hospital stays, fundamental aspects in neonatal recovery.[24]

In this study, the BCPAP group had a shorter hospital stay compared to the IOT group (*p<0.001*), possibly reflecting baseline differences between the groups.

This study showed a lower prevalence of pulmonary complications in the BCPAP group compared to the IOT group. The higher frequency of pneumothorax, BPD, and

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pulmonary hemorrhage in the IOT group is consistent with previous studies describing an association between mechanical ventilation and a higher occurrence of adverse pulmonary events.[9,25] These results reinforce the role of BCPAP as an initial alternative, when clinically indicated, with the potential to reduce complications.

Our findings attest a lower need for invasive interventions in the BCPAP group, including less surfactant use and less frequent antibiotic therapy, compared to the IOT group. These results are aligned with the literature, which associates the use of BCPAP with less exposure to invasive interventions.[23,26] The high frequency of antibiotic therapy among intubated newborns reflects the relationship between IOT and greater vulnerability to infections.[27] Such associations may reflect confounding by indication and collinearity with severity markers, and should be interpreted with caution.

This study has limitations inherent to the retrospective cohort design, including the possibility of selection bias and classification bias. Stratification by gestational age or birth weight was not performed due to the limited number of events and the risk of loss of statistical power. Initial ventilatory support may reflect the baseline severity of newborns, acting as a severity marker. Multiple secondary comparisons were performed without adjusting for multiplicity, increasing the risk of type I error. Finally, the logistic regression model included several covariates given a small number of outcomes, which can lead to overfitting and unstable estimates

CONCLUSION

This study showed an association between the use of BCPAP and lower mortality and length of hospital stay in newborns with respiratory distress syndrome (RDS), when compared to intubation. Differences in the clinical profile between the groups limit causal inferences. The findings reinforce the role of BCPAP as an initial respiratory support strategy in selected newborns, highlighting the importance of appropriate clinical indication and rigorous monitoring for therapeutic escalation when necessary

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Supplementary Table 1. Apgar score, mode of delivery, and maternal variables

Variables	Total N = 218 n (%) / Med (IIQ)	NIV N = 94 n (%)[ar=number] / Med (IIQ)	BCPAP N = 60 n (%)[ar=number] / Med (IIQ)	IOT N = 64 n (%) [ar=number] / Med (IIQ)	*p-value*
Newborn's data[2]					
Sex[2]					
Female	100 (45.9)	53 (56.4)$^{2.7}$	24 (40.0)$^{-1.1}$	23 (35.9)$^{-1.9}$	**0.023**
Male	118 (54.1)	41 (43.6)$^{-2.7}$	36 (60.0)$^{1.1}$	41 (64.1)$^{1.9}$	**<0.001**
Apgar [1]					
1st minute	7.0 (5.0-8.0)	7.0 (6.0-8.0)	8.0 (6.0-8.0)	6.0 (4.0-7.75)	**0.005**
5th minute	8.0 (7.75-9.0)	8.0 (8.0-9.0)	9.0 (8.0-9.0)	8.0 (7.0-9.0)	**0.008**
Maternal and gestational data[1]					
Age	27.0 (22.5-32.0)	27.0 (24.0-32.0)	27.0 (22.0-33.5)	28.0 (23.0-32.0)	0.973
Prenatal	8.0 (6.0-11.0)	9.0 (7.0-12.0)	8.0 (5.5-11.0)	7.0 (5.0-10.0)	**0.002**
Comorbidities[2]					
Hypothyroidism	31 (18.7)	17 (22.4)$^{1.1}$	9 (18.8)$^{0.0}$	5 (11.9)$^{-1.3}$	0.377
Arterial hypertension	19 (11.4)	10 (13.2)$^{0.6}$	5 (10.4)$^{-0.3}$	4 (9.5)$^{-0.5}$	0.809
Depression / anxiety	12 (7,2)	6 (7,9)$^{0.3}$	3 (6,3)$^{-0.3}$	3 (7,1)$^{0.0}$	0,942
Others	17 (10,2)	10 (13,2)$^{1.1}$	4 (8,3)$^{-0.5}$	3 (7,1)$^{-0.8}$	0,514
Pregnancy complications [2]					

UTI	47 (25.8)	22 (29.7)$^{1.0}$	12 (22.6)$^{-0.6}$	13 (23.6)$^{-0.4}$	0.604
PIH	36 (19.8)	12 (16.2)$^{-1.0}$	16 (30.2)$^{2.3}$	8 (14.5)$^{-1.2}$	0.076
GDM	40 (22.0)	23 (31.1)$^{2.5}$	10 (18.9)$^{-0.6}$	7 (12.7)$^{-2.0}$	**0.037**
Others	38 (20.9)	10 (13.5)$^{-2.0}$	8 (15.1)$^{-1.2}$	20 (36.4)$^{3.4}$	**0.003**
Medications in use[2]					
Levothyroxine	31 (15.1)	15 (16.1)$^{0.4}$	10 (19.2)$^{1.0}$	6 (10.0)$^{-1.3}$	0.371
Methyldopa	34 (16.7)	17 (18.7)$^{0.7}$	10 (19.2)$^{0.6}$	7 (11.7)$^{-1.3}$	0.453
Metformin	17 (8.4)	8 (8.8)$^{0.2}$	7 (13.5)$^{1.5}$	2 (3.3)$^{-1.7}$	0.152
Antidepressants	11 (5.4)	7 (7.7)$^{1.3}$	2 (3.8)$^{-0.6}$	2 (3.4)$^{-0.8}$	0.434
Others	32 (15.7)	15 (16.5)$^{0.3}$	12 (22.6)$^{1.6}$	5 (8.3)$^{-1.9}$	0.109
Mode of delivery[2]					
Vaginal	67 (31.2)	29 (31.5)$^{0.1}$	12 (20.0)$^{-2.2}$	26 (41.3)$^{2.1}$	**0.039**
Cesarean	148 (68.8)	63 (68.5)$^{-0.1}$	48 (80.0)$^{2.2}$	37 (58.7)$^{-2.1}$	
Interventions and gestational conditions[2]					
$MgSO_4$	20 (20.4)	1 (4.3)$^{-2.2}$	5 (14.3)$^{-1.1}$	14 (35.0)$^{3.0}$	**0.008**
Antenatal corticosteroid	41 (32.8)	2 (4.8)$^{-4.7}$	16 (38.1)$^{0.9}$	23 (56.1)$^{3.9}$	**<0.001**
Antibiotic therapy	81 (54.4)	32 (53.3)$^{-0.2}$	21 (46.7)$^{-1.2}$	28 (63.6)$^{1.5}$	0.269
Ruptured bag	67 (37.6)	23 (32.9)$^{-1.1}$	14 (25.9)$^{-2.1}$	30 (55.6)$^{3.3}$	**0.004**
Positive Streptococcus B	16 (16.8)	10 (20.0)$^{0.9}$	0 (0.0)$^{-2.0}$	6 (21.4)$^{0.8}$	0.121
Ventilatory support[2]					
Starting in the delivery room[2]	82 (37.6)	13 (13.8)$^{-6.3}$	24 (40.0)$^{0.4}$	45 (70.3)$^{6.4}$	**<0.001**
Starting in the NICO[2]	136 (62.4)	81 (86.2)$^{6.3}$	36 (60.0)$^{-0.4}$	19 (29.7)$^{-6.4}$	
Need for change[2]	43 (20.2)	24 (25.6)	19 (33.4)	0 (0.0)	**<0.001**
Time (days)[1]	4.0 (2.0-10.0)	2.0 (1.0-2.0)	6.0 (3.0-9.0)	14.0 (5.0-26.5)	**<0.001**

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