

Relationship between Oxygenation Index and Extubation Outcome in Neonates using Mechanical Ventilator

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Abstract:-

Background: Mechanical ventilation is a life-saving intervention for neonates with respiratory failures. Through intubation, mechanical ventilators help patients achieving normal oxygen and carbon dioxide levels in the artery and minimizing heavy breaths. However, the use of mechanical ventilation, especially on prolonged case, in neonates can cause complications. The process of weaning off mechanical ventilation, therefore, needs to be carefully carried out to minimize re-intubation. One of the clinical parameters measured prior to extubation is oxygenation index (OI), which is the measurement of oxygen exchange in the lungs representing lung dysfunction. **Objective :** to analisis the relationship between oxygenation index and extubation outcome in neonatus using mechanical ventilation. **Material and Methods:** This research was an observational cross-sectional research to assess the relationship between the success of extubation and OI in neonates using mechanical ventilation in Haji Adam Malik hospital, Medan, Indonesia between February and May 2022. **Results:** OI <4.5% was categorized as low and OI >4.5% was categorized as high. There were 50 neonates involved in this research, where 5 (10%) neonates were below 28 weeks' gestational age and 7/50 (14%) neonates had extubation failure. The mean OI was 1.62%, where 47 (94%) neonates had low OI and 3 (6%) neonates had high OI. The relationship OI and the success of extubation on neonates was analyzed using Fischer's exact test. All three neonates with high index had extubation failure. On the other hand, only 4 (8.5%) out of 47 neonates with low OI had extubation failure. The analysis by Fischer's exact test showed a significant relationship between OI and the success of extubation in neonates using mechanical ventilation ($p=0.002$). **Conclusion:** Low oxygenation index can be used as succesfull of extubation in neonatus.

Keywords:- Oxygenation index, mechanical ventilator, neonates.

I. INTRODUCTION

Mechanical ventilation is a life-saving intervention in children and neonates with respiratory failure through intubation procedure.^{1,2} Mechanical ventilation helps to reach normal oxygen and carbon dioxide levels in the artery, minimizes heavy breathing, and comforts the patients. Gas exchange on mechanical ventilation is maintained by minimizing lung damage (alveolar damage, oedema, inflammation, and lung fibrosis), hemodynamic disorders, and other side effects such as nerve damage. Ventilator induces lung damage through barotrauma (high pressure), volutrauma (high volume), atelectrauma, and biotrauma (increased in inflammation).^{3,4}

The indication of mechanical ventilation (MV) depends on the gestational age and clinical condition of the neonates – in addition to blood gas analysis. In newborn baby, MV indication could be: i) severe apnea (bagging required) with more than one period of apnea within an hour, ii) increase in partial pressure of CO₂ (PaCO₂) to more than 60 mmHg and pH below 7.25, also poor clinical condition, iii) fraction of inspired oxygen (FiO₂) to less than 40% and poor clinical condition, iv) neonates with gestational age of less than 25 weeks.^{3,5-9} The use of mechanical ventilation, especially on prolonged case, in neonates can cause complications, such as ventilator-related pneumonia, airway trauma, and bronchopulmonary dysplasia (BPD).¹⁰

One way to reduce the risk of damage due to mechanical ventilation is to reduce the duration of use.¹¹ Weaning from mechanical ventilation is the process to lower the ventilator support so that neonates can slowly detach the use of ventilator.² The process was done through extubation. The extubation process in the patients should be well observed to minimize re-intubation.¹²

Rapid extubation on premature babies could cause extubation failure and lead to re-intubation. The most reported reasons for extubation failure in the neonatal intensive care unit (NICU) were apnea (68.1%), hemodynamic disorder due to infection (54.2%), and neurological disorder (34.7%). The time frame after extubation to determine the extubation failure varies from 24, 48, or 72 hours, to 7 to 10 days.¹¹ Thus, in addition to subjective assessment, objective assessment, such as hemodynamic stability and the adequacy of oxygen and airways, is required.^{13,14}

There has not been any standardized criteria for successful extubation in neonates to date. The criteria are often associated with other tests, such as cuff-leak test in endotracheal tube (ETT) and spontaneous breathing trial (SBT), with or without continuous positive airway pressure (CPAP).^{1,15,16,17} One of the clinical parameters measured prior to extubation is oxygenation index, a parameter used to assess the severity of respiratory failure due to hypoxia in neonates.¹¹ It is an efficient measurement of oxygen exchange in the lungs, which is a good representative to lung dysfunction, measured based on.^{18,19}

$$\text{Oxygenation Index} = \frac{[\text{FiO}_2 \times \text{MAP (mean airway pressure} \times 100)]}{\text{PaO}_2}$$

Where:

$$\text{MAP} = \frac{[\text{PEEP} + (\text{PIP} - \text{PEEP})]}{3}$$

The study by Barros et al Rocha et al had shown a positive correlation between oxygenation index and the duration of mechanical ventilation use. Thus, could help in the early prognosis of the disease requiring the use of ventilator.^{18,19} This study was done to assess the relationship between the success of extubation and oxygenation index in neonates using mechanical ventilation.

II. MATERIAL AND METHODS

This was an observational cross-sectional research to assess the relationship between oxygenation index and the success of extubation in neonates using mechanical ventilation. This research was conducted at the NICU of Haji Adam Malik Hospital, Medan, Indonesia from February to May 2022. Research samples were neonates aged 0 to 28 days old using mechanical ventilation. Research samples were calculated using the unpaired test formula (Sostroasmori and Ismail, 2014) with a minimum of 40 subjects. The data was obtained from the medical records. Information on ventilator settings and oxygenation index from the beginning to weaning from ventilator in neonates was taken from the medical records.

Oxygenation index measured the fraction of inspired oxygen based on the following formula^{18,19}, where oxygenation index <4.5% was categorized as low and >4.5% was categorized as high.

$$\text{Oxygenation index} = \frac{[\text{FiO}_2 \times \text{MAP (mean airway pressure} \times 100)]}{\text{PaO}_2}$$

In this study, extubation on neonates using mechanical ventilation was assessed by clinical parameters AGDA and SpO₂. Extubation failure was determined based on the need for reintubation within 72 hours.

A. Research ethics

The parents or guardians of the research subjects were given explanations about the research and were asked for consent to be involved in the research. This research was approved by the Health Research Ethical Committee, Faculty of Medicine of Universitas Sumatera Utara and Haji Adam Malik hospital, Medan, Indonesia.

B. Data Analysis

Data collected was processed and analyzed with SPSS v20.0. Univariate analysis was done to describe the characteristics of research subjects. Categorical data was presented in frequency and percentage, while numerical data was shown as mean±standard deviation for normal distribution data, else median if the data was not normally distributed. The relationship between oxygenation index and the success of extubation was analyzed using chi-square test. Fischer's exact test was used if chi-square test did not fulfill the parametric criteria (expected count >25%). Significance was at p<0.05.

III. RESULTS

A. Research subject data characteristic

There were 50 neonates using mechanical ventilators treated at the the NICU of Haji Adam Malik hospital, Medan, Indonesia. The complete characteristic data is presented on Table 1. In this study, the population of male neonates were higher than females, with a mean age of 9.85 days. There were 5 (10%) neonates below the 28 weeks' gestational age and only 7(14%) neonates had extubation failure.

Subject characteristics	n = 50
Gender, n (%)	
Male	30 (60)
Female	20 (40)
Gestational age, n (%)	
< 28 weeks	5 (10)
28 – 32 weeks	10 (20)
32 – 36 weeks	8 (16)
> 36 weeks	27 (54)
Age, days	
Mean (SD)	9.85 (12.09)
Body weight, gram	
Mean (SD)	2342 (950.05)
Body height, cm	
Mean (SD)	47.1 (1.77)
Extubation success, n (%)	
Success	43 (86)
Fail	7 (14)

Table 1: Research subject characteristic data

B. Blood test result

Blood test showed that the following parameters, FiO₂, MAP, PIP, pH, dan SaO₂, were significant between neonates of successful and failed extubation with p<0.05. The comprehensive blood test results and the relationship based on the success of extubation success can be seen on table 2.

Blood analysis	Extubation success		p
	Fail	Success	
FiO ₂ , %			
Median (Min – Max)	55 (25 – 100)	30.5 (21 – 45)	0.008 ^a
SpO ₂			
≤ 90%	3 (37.5)	5 (62.5)	0.113 ^b
90 – 95 %	3 (8.8)	31 (91.2)	
95 – 100%	1 (12.5)	7 (87.5)	
MAP, mmHg			
Mean (SD)	7.22 (1.31)	5.52 (1.29)	0.011 ^c
PIP			
Mean (SD)	21.67 (3.93)	14.62 (3.85)	0.011 ^c
PEEP			
Median (Min – Max)	5 (5 – 6.5)	5 (4 – 6)	0.192 ^a
pH			
Median (Min – Max)	7.23 (7.11-7.37)	7.36 (7.22-7.52)	0.021 ^a
pCO ₂			
Mean (SD)	34.83 (8.52)	38.95 (8.97)	0.586 ^c
PaO ₂			
Median (Min – Max)	150.5 (91-170)	169 (107-203)	0.153 ^a
HCO ₃			
Mean (SD)	18.95 (4)	20.76 (5.83)	0.323 ^c
TCO ₂			
Median (Min – Max)	16.95 (12.9-19.5)	17.4 (3.8-146)	0.605 ^a
BE			
Mean (SD)	-9.37 (3.41)	-9.17 (6.66)	0.399 ^c
SaO ₂ , %			
Median (Min – Max)	98.5 (95-99)	99 (97-100)	0.004 ^a
Hb, gr/dL			
Median (Min – Max)	11.55 (9.5-17.8)	13.35 (9.2-28)	0.476 ^a
Leukocytes, thousand/μL			
Median (Min – Max)	14.9 (4.79-22.39)	13.63 (1.92-80.95)	0.476 ^a
Thrombocytes, thousand/μL			
Median (Min – Max)	180.5 (5-246)	193 (2-746)	0.150 ^a
Neutrophiles			
Mean (SD)	72.27 (10.38)	63.36 (15.63)	0.090 ^c
Lymphocytes			
Mean (SD)	17.02 (7.22)	19.48 (10.26)	0.436 ^c
CRP			
Median (Min – Max)	0.7 (0.7-1.4)	0.7 (0.7-6.22)	0.090 ^a
Procalcitonin			
Median (Min – Max)	5.75 (0.08-100)	1.35 (0.05-40.37)	0.108 ^a

Table 2: Blood test result and extubation outcome

^aMann Whitney, ^bKruskal Wallis, ^cT Independent

C. Oxygenation index analysis

Table 3 shows the results of the oxygenation index on neonates using mechanical ventilation at the NICU of Haji Adam Malik hospital, Medan, Indonesia. The mean oxygenation index was 1.62%, where 47 (94%) neonates had low oxygenation index and 3 (6%) neonates had high oxygenation index.

Variable	n = 50
Oxygenation index (%)	
Mean (SD)	1.62 (1.41)
Low	47 (94)
High	3 (6)

Table 3: Oxygenation index analysis

The relationship between oxygenation index and the success of extubation on neonates was analyzed using Fischer’s exact test. All three neonates with high index had extubation failure. On the other hand, only 4 (8.5%) out of 47 neonates with high oxygenation index had extubation failure. The analysis by Fischer’s exact test showed a significant relationship between oxygenation index and the success of extubation in neonates using mechanical ventilation (p=0.002).

Variables	Extubation Success		p	PR (CI 95%)
	Fail	Succeed		
Oxygenation Index				
High	3 (100)	0	0.002 ^a	11.75
Low	4 (8.5)	43 (91.5)		(4.062-30.00)

Table 4: Relationship between oxygenation index and extubation success on neonates using mechanical ventilation

^aFischer's Exact

IV. DISCUSSION

Subjective and objective assessment is required to determine the readiness for extubation.^{13,14} One of the clinical parameters to assess extubation readiness on patients with mechanical ventilation is oxygenation index (OI). It is used to assess the severity of respiratory failure due to hypoxia on neonates¹¹ and is an efficiency measurement of oxygen exchange in the lungs that can better represent lungs dysfunction. Normal OI value has not been disclosed, as OI was only calculated on patients with severe condition or when intubated.^{19,20}

There were 43 (86%) patients with successful extubation. Gestational age was considered as one of the success factors for extubation process. Low birth weight was also a contributing factor for successful or failed extubation.²¹ There were only 5 (10%) neonates with gestational age <28 weeks in this study. A prospective study on prediction of extubation readiness with randomized control trial method mentioned that extubation success was 71% in full term babies, 60 – 73% in very premature babies, and 80 – 86% in premature babies.^{18,19} This data explained the rate of extubation success with the gestational age of neonates involved in this study.

In a study by Deguines et al in France, premature babies below 32 weeks were evaluated for the extubation outcome against parameters, such as pH, PaCO₂, PIP, and PEEP. However, no statistical significance was observed between mechanical ventilation parameters and gasometric parameters.²² The result of the study was conflicting the study done by Jurkevicz et al, which showed that the pre-extubation pH of the successful and failed extubation groups were 7.36 ± 0.07 and 7.40 ± 0.07 , respectively, indicating no significant difference between the two. However, based on the average MAP (7.72 ± 0.77) and FiO₂ (0.25 ± 0.05) against the success of extubation resulted with a p value of 0.03 (Jurkevicz et al., 2021). This study showed the FiO₂, MAP, PIP, pH and SpO₂ parameters were significant between neonates with successful and failed extubation outcome ($p < 0.05$). This result might be due to the standard weaning protocols used on invasive mechanical ventilation. Some literatures showed that data, such as pH, PaCO₂, and HCO₃ could be used as parameters to assess the extubation success on neonates' population.^{23,24}

The studies on the correlation between oxygenation index and the use of mechanical ventilation in neonates are still limited. Many studies, however, have been carried out to

children subjects, but with various results on the risk of failed extubation and death. A 20-month long study by Peters et al. on 118 children with mechanical ventilation showed high extubation failure with 22% mortality rate.²⁵ This study, however, did not assess the outcome of neonates with mechanical ventilation.

Muniraman et al in 2019 found that oxygenation index had a high sensitivity and specificity to predict the extubation success outcome on neonates.²⁶ Some studies showed a correlation between oxygenation index and extubation outcome, as well as mortality. A study in 2009 by Kao et al found that increased oxygenation index from day 1 – 3 of ventilator use was a predictor of extubation failure and high mortality.²⁷ Ghuman et al found a significant relationship in the oxygenation index between died and survived patients in 95 paediatric subjects with mechanical ventilation.²⁸ Trachel et al stated that higher oxygenation index during the ventilator use had a risk of extubation failure and lead to higher risk of mortality, although the cut-off points for oxygenation index to predict mortality had not been established.²⁹

A study done by Khan, Brown, and Venkataraman showed that oxygenation index >4.5 had a high risk of reintubation and found that 24.1% of their subjects had prolonged use of mechanical ventilation.³⁰ Rocha et al. found a relationship between higher oxygenation index (average OI >7) measured between day 2 and 6 of prolonged ventilator use and increased risk of extubation failure ($p < 0.05$).¹⁹ A further study by Barros et al on oxygenation index and extubation failure showed a significant positive correlation on oxygenation index measured on day 3 ($r = 0.52$) and day 5 ($r = 0.65$).¹⁸ This study showed a significant relationship between oxygenation index and the success of extubation in neonates using mechanical ventilation with $p = 0.002$ and PR 11.75.

The results of this study could help researchers and doctors to assess the readiness for extubation on neonates based on the oxygenation index. It could give a description on the predictor for extubation failure to prevent reintubation in neonates. This was the first study done in Sumatera Utara to assess the relationship between oxygenation index on extubation success in neonates using mechanical ventilation. However, blood tests on research subjects were not done prior to extubation, thus, there were no comparison on the blood analysis pre- and post-extubation.

V. CONCLUSION

There was a relationship between oxygenation index and extubation outcomes in neonates with mechanical ventilation with $p = 0.002$ and PR 11.75.

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