

Factors associated with failure to wean children from mechanical ventilators

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Abstract

Background Patients with failure to wean from mechanical ventilators in 48 hours have increased risk of morbidity, however only a few protocols can be used for children.

Objective To assess possible factors associated with failure to wean from mechanical ventilators in the pediatric intensive care unit (PICU).

Methods This cross sectional study performed from June 2011 to June 2012 had 124 subjects with 79 patients who were successfully weaned and 45 patients who fail to be weaned from mechanical ventilators. Data was analyzed by 2x2 contingency tables. Results with P value <0.05 were further analysis by logistic regression multivariate analysis.

Results Factors associated with failure to wean from mechanical ventilators were abnormal electrolyte (P=0.001) and acid base status (P<0.001), lower ratio between tidal volume (TV)/inspiration time (IT) (P<0.001), lower mechanical load (P<0.001), and longer duration of mechanical ventilator use (P<0.001). Multivariate analyses revealed that the significant risk factors for failure to wean were TV/IT (OR 6.0; 95%CI 3.5 to 7.5; P=0.001), mechanical load (OR 11.5, 95%CI 10.3 to 15.5; P=0.002), and duration of mechanical ventilator use (OR 12.5; 95%CI 8.5 to 14.9; P=0.026).

Conclusions Lower ratio of TV/IT and mechanical load, as well as longer duration of ventilator use are factors associated with failure to wean from a mechanical ventilator. [Paediatr Indones. 2013;53:59-64.].

Keywords: weaning, mechanical ventilation, children, intensive care

Weaning from mechanical ventilation has been defined several different ways. One definition is a gradual reduction in ventilator support when patients are recovering from respiratory failure but are clearly not yet ready for spontaneous respiration.¹ For others, weaning is the act of disconnecting patients from the ventilator,² and for yet others, weaning constitutes both discontinuation from mechanical ventilation and extubation.³ Two deliberate steps are involved in weaning. First, patient readiness must be tested with physiological measurements, usually called weaning predictors.^{4,5} Second, the patient is evaluated while ventilator support is decreased, either gradually or abruptly.^{6,7} This two-step approach has been found to be more dependable than allowing physicians to wean in a desultory fashion.⁸ For this reason, we used

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weaning from mechanical ventilation definition as gradual reduction in ventilator support when patients are recovering from respiratory failure but are not yet ready for spontaneous respiration because weaning is a gradual process and not all of patient with successfully to wean also successfully extubated.

The first problem the clinician faces is the determination of patient readiness to resume independent ventilation.³ These determining predictors for weaning children from mechanical ventilation are important, not only to reduce the risk of re-intubation or to avoid delayed weaning resulting in longer pediatric intensive care unit (PICU) stays, but also to provide clearer weaning guidelines, especially for nursing staffs.^{9,10}

Despite the fact that failure to wean within 48 hours results in increased risk of morbidity and more frequent use of mechanical ventilation, methods for weaning children from respiratory support have never been rigorously studied.^{11,12} Therefore the objective of this study was to investigate possible factors associated with weaning failure in children on mechanical ventilator in PICU.

Methods

This cross sectional study was undertaken in the PICU at Cipto Mangunkusumo Hospital from June 2011 to June 2012. Subjects were pediatric PICU patients on mechanical ventilation during the study period. Logistic regression formula with $\alpha=0.05$ and 5% accuracy was used to calculate the required sample size, a minimum of 119 subjects.

We included patients aged 1 month – 18 year old, stable from respiratory failure (including stable from pathologic process of the lung such as infection, atelectasis, pneumothorax, pleural effusion, etc), and had stable hemodynamic. Patients with spontaneous extubation, history of prematurity, or reintubation caused by respiratory obstruction were excluded.

Data was analyzed by 2x2 contingency tables. Results with P value < 0.05 were further analyzed by logistic regression multivariate analysis. This study was approved by the Ethics Committee of University of Indonesia Medical School.

Results

During the study period there were 128 PICU patients using mechanical ventilation. Four patients were excluded because of spinal muscular atrophy diagnosis (1 subject) and respiratory tract obstruction during extubation (3 subjects). The basic characteristics of subjects are shown in **Table 1**. Seventy nine patients were successfully weaned, and the other 45 patients were failed.

Bivariate analysis revealed that abnormality of acid base status ($P < 0.001$) and electrolyte status ($P=0.001$), lower ratio of TV/IT ($P<0.001$), lower mechanical load ($P<0.001$), and longer duration of mechanical ventilator use ($P<0.001$) were associated with failure of weaning. Other variables, such as nutritional status ($P= 0.388$), use of premedication ($P= 0.737$), ratio of PaO₂/FiO₂ ($P= 0.997$), and ventilation pump function ($P=0.460$) did not have significant effects on failure to wean. Failure to wean from mechanical ventilation was significantly associated with dead in our subjects (**Table 2**).

Logistic regression analysis revealed that lower ratio of TV/IT, lower mechanical load, and longer duration of mechanical ventilator use were significant risk factors for failure to wean children from mechanical ventilators in the PICU, with odds ratio of 6 (95% CI 3.5 to 7.5), 11.5 (95% CI 10.3 to 15.5), and 12.5 (95% CI 8.5 to 14.9), respectively (**Table 3**).

Table 1. General characteristics of subjects

Characteristics	Total (n=124)
Age, n (%)	
≤2 years	69 (55.7)
>2 years	55 (44.3)
Gender, n (%)	
Male	61 (49.2)
Female	63 (50.8)
Nutritional status, n (%)	
Well-nourished	96 (77.4)
Malnourished	28 (22.6)
Reason for PICU admission, n (%)	
Oncology surgery	11 (8.9)
Neurosurgery	4 (3.2)
Digestive surgery	35 (28.2)
Non-surgical	74 (59.7)
Outcomes, n (%)	
Died	35 (28.2)
Survived	89 (71.8)

Table 2. Factors associated with failure to wean from mechanical ventilation

Variables	Weaning category		P value
	Successful	Failed	
Nutritional status, n (%)			
Well-nourished	66 (83.5)	30 (66.7)	0.388
Undernourished	13 (16.5)	15 (33.3)	
Acid-base status			
Normal	41 (51.9)	5 (11.1)	<0.001
Abnormal	38 (48.1)	40 (88.9)	
Electrolyte status			
Normal	75 (94.9)	34 (75.6)	0.001
Abnormal	4 (5.1)	11 (24.4)	
Premedication			
Used	63 (88.6)	37 (82.2)	0.737
Not used	16 (20.3)	8 (17.8)	
Gas exchange (PaO ₂ /FiO ₂)			
≤150	20 (25.3)	28 (58.3)	0.997
>150 – <200	8 (10.1)	(-)	
≥200	51 (64.5)	17 (31.7)	
TV*/IT** ratio			
≤8	16 (20.3)	39 (86.7)	<0.001
>8-14	63 (79.7)	6 (13.3)	
Mechanical load (P _{0.1} /TV/IT)			
≤0.25	65 (82.3)	13 (28.9)	<0.001
>0.25	14 (17.7)	32 (71.1)	
Ventilation pump function			
P _{0.1} ≤3.4	75 (94.9)	41 (91.1)	0.460
P _{0.1} >3.4	4 (5.1)	4 (8.9)	
Duration of mechanical ventilator use			
≤48 hours	32 (40.5)	1 (2.2)	<0.001
>48 hours	47 (59.5)	44 (97.8)	
Outcomes			
Survived	70 (88.6)	19 (42.2)	<0.001
Died	9 (11.4)	26 (57.8)	

*Tidal volume, **Inspiration time

Table 3. Multivariate analysis*

Variables	Weaning category		OR	P value	95%CI
	Successful	Failed			
TV/IT ratio					
≤8	16 (20.3)	39 (86.7)	6	0.001	3.5 to 7.5
>8-14	63 (79.7)	6 (13.3)			
Mechanical load (P _{0.1} /TV/IT)					
≤0.25	65 (82.3)	13 (28.9)	11.5	0.002	10.3 to 15.5
>0.25	14 (17.7)	32 (71.1)			
Duration of mechanical ventilator use					
≤48 hours	32 (40.5)	1(2.2)	12.5	0.026	8.5 to 14.9
>48 hours	47 (59.5)	44 (97.8)			

* Logistic regression

Discussion

Weaning methods used in adults on mechanical ventilators may not be appropriate for infants and children. This may be due to the unique aspects of the pulmonary physiology, respiratory mechanics and epidemiology of acute lung injury.¹³ Discontinuing mechanical ventilation as soon as it is no longer needed, is important for prevention of respiratory complications and physiological dependence on sedation and narcotics required to keep these pediatric patients comfortable and safe.^{14,15,16} Kurachek *et al* showed, that failed extubation was significantly associated with length of PICU stay (17 days versus 7 days in patients who were successfully extubated), and also reported that patients with failed extubation had significantly higher mortality (4% versus 0.8%).¹⁴ We found that 28% of patients with mechanical ventilation died during observation. Of these deaths, 57.8% ($P < 0.01$) were due to failed weaning from mechanical ventilation.

Our higher mortality rates may have been due to the non-surgical category of 59.7% of our PICU admissions. Almost all patients had been transferred to the PICU after an emergency ward stay of several days because of the limited number of PICU beds. Without close monitoring, such conditions may lead to increased risk of failure to wean. Based on these results, guidelines for weaning are needed for patients on mechanical ventilation in the PICU.

A preliminary study done in the same setting reveals 71.4% of subjects with severe malnourishment suffered failure to wean from mechanical ventilation.¹⁷ In contrast, in our study with more subjects (total subjects of $n = 124$ vs. $n = 84$) nutritional status was not significantly ($P = 0.388$) associated with failure to wean. As such, nutritional status should still be a consideration for weaning due to the inadequate performance of the respiratory muscles in malnourished subjects. Malnutrition decreases muscle mass and respiratory muscle strength both in humans and laboratory animals.¹

Randolph *et al* showed that duration of mechanical ventilator use in children was shorter than in adults (48 hours or less).¹³ However, 73% of our subjects had > 48 hours duration of mechanical ventilation use. Furthermore, 59.7% of our PICU patient admissions

were non-surgical rather than surgical, resulting in shorter lengths of stay. Therefore ventilator use for > 48 hours was significantly associated with failure to wean ($P = 0.026$). In addition multivariate analysis revealed that ventilator use for > 48 hours to be a risk factor for failure to wean (OR 12.5; 95%CI 8.5 to 14.9). Similarly, other studies¹⁸⁻²⁰ showed that > 48 hours on duration of ventilator use was an important variable associated with failure of extubation, even in large PICU population.

Acid-base disorders such as metabolic or respiratory alkalosis, do not affect skeletal muscle strength and may improve endurance. However the effect of metabolic or respiratory acidosis, on respiratory muscle function remains unclear. Respiratory muscle function may be impaired by decreased levels of phosphate, calcium, magnesium and potassium.¹ We found a significant association between abnormality of electrolyte as well as acid base status and failure to wean using bivariate analysis. However, multivariate analysis revealed no such associations.

Studies of pre-extubation steroid use in children as a means to reduce post-extubation stridor or re-intubations have revealed conflicting results. A recent study of the subject provides only a lukewarm endorsement of the practice.^{14,20-22} Kurachek *et al* showed that rescue interventions for post-extubation stridor (steroids, racemic epinephrine, and helium-oxygen gas) were significantly associated with extubation failure.¹⁴ Similarly, we found that the use of premedication (steroid, epinephrine) was not significantly associated with failure to wean from mechanical ventilation ($P = 0.737$).

In intensive care unit, adult patients with using rapid shallow breathing index (rapid spontaneous respiratory, low spontaneous tidal volume (TV) and rapid shallow breathing index (RSBI) occlusion pressure as have been used to predict weaning success.^{1,23} However, Leclerc *et al*²⁴ found that these criteria were poor predictors in children, because not all had showed tachypnea when failing to wean but a few showed bradypnea mainly due to over sedation and potentially decreasing respiratory drive.⁹ Therefore, this study used TV/IT ratio criteria and found a significant association between failure to wean (OR 6; 95%CI 3.5 to 7.5; $P = 0.001$) with value ≤ 8 .

Once a patient is able to sustain spontaneous breathing, a second judgment must be made,

preferably by a team approach and an organized problem-oriented plan to expedite successful discontinuation of mechanical ventilation.³ Weaning attempts that are unsuccessful indicate incomplete resolution of the illness that precipitate the need for mechanical ventilation, such as impaired gas exchange, poor neurological and muscular function and unstable cardiovascular function.^{1,2,3} Therefore, we evaluated parameters such as gas exchange, ventilator pump function and lung mechanical load as shown in **Table 2**. Gas exchange parameters ($\text{PaO}_2/\text{FiO}_2$) were not significantly associated with weaning failure ($P=0.997$).

Impaired ventilator pump may occur in conditions characterized by decreased respiratory drives (measure by airway occlusion pressure, $P_{0.1}$), abnormal respiratory mechanics (airway occlusion pressure divided with inspiratory impedance, $P_{0.1}/\text{TV}/\text{IT}$), diminished respiratory muscle performance and impaired cardiovascular performance.¹ We found that both TV/IT and mechanical load were significantly associated with weaning failure, (OR 6; 95%CI 3.5 to 7.5 $P=0.001$, OR 11.5; 95%CI 10.3 to 15.5; $P=0.002$, respectively).

A limitation of this study was its cross-sectional design. Therefore an association of cause and effect may be weak than that of a cohort study. A cross sectional was performed due to subject and medical record limitation. Another limitation was our not performing respiratory muscle function tests, since our institution did not have the facilities to do so.

In conclusion, abnormal acid-base and electrolyte status, lower TV/IT ratio, lower mechanical load, and longer duration of ventilator usage are significantly associated with failure to wean for mechanical ventilation. Multivariate analysis revealed that abnormal electrolyte and acid-base status, not significantly associated with failure to wean in our subjects.

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