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Original Article

Factors associated with oxygenation improvement in children with ARDS

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Abstract

Background In pediatric patients, acute respiratory distress syndrome (ARDS) has a high mortality rate of approximately 25%. In surviving children, ARDS may result in sequelae, such as restrictive or obstructive lung dysfunction, muscle weakness and hypotrophy, as well as psychiatric, intelligence, and memory problems.

Objective To identify prognostic factors related to oxygenation improvement in children with ARDS.

Methods We conducted a prospective cohort study in the pediatric intensive care unit (PICU) of Sardjito Hospital, Yogyakarta. We included 20 children aged 29 days to 18 years who fulfilled the ARDS criteria. They underwent lung recruitment maneuver for 1 hour. Logistic regression analysis was used to assess for possible associations between potential prognostic factors and oxygenation improvement.

Results None of the subjects had significant hemodynamic changes or hypercapnea during lung recruitment. Two prognostic factors from our univariate analysis, namely type of ARDS (RR 0.17; 95% CI 0.023 to 1.23; P= 0.079) and severity of ARDS (RR 0.74; 95% CI 0.007 to 0.84), were analyzed by multivariate logression test. However, the results were not statistically significant for type of ARDS (RR 0.33; 95% CI 0.009 to 1.41) or severity of ARDS (RR 0.11; 95%CI 0.009-3.25).

Conclusion We do not identify any prognostic factors, including type and severity of ARDS, associated with oxygenation improvement in children with ARDS. **[Paediatr Indones. 2014;54:42-5.]**

Keywords *: ARDS, oxygenation improvement*

Acute respiratory distress syndrome (ARDS) is an acute dysfunction of the lung characterized by sudden onset of tachypnea and oxygen-refractory hypoxemia, the presence of diffuse patchy infiltrates on chest x-ray, PaO_2/FiO_2 ratio <200, and decreased lung compliance, but not associated with cardiogenic pulmonary edema or chronic disease.[1] ARDS has a high mortality rate of approximately 25%. It also results in sequelae in surviving children such as restrictive and obstructive lung dysfunction, muscle weakness and hypotrophy, as well as psychiatric, intelligence, and memory problems.[2,3,4]

The lung recruitment maneuver is an effective way to reverse the collapse of alveoli, the best technique being a lung-protective strategy using low-tidal volume ventilation.[5,6] As the mortality rate has decreased in the last decade from 35% to 21%, there may be other factors related to oxygenation improvement in ARDS.[7]

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Methods

We conducted a cohort study in the PICU at Sardjito Hospital, Yogyakarta from July to November 2012, involving children aged 29 days to 18 years who fulfilled the ARDS criteria (acute decrement of PaO_2/FiO_2 ratio <200, within 36 hours onset, and no cardiac abnormality). Subjects' parents consented to their participation in this study. Patients presenting with neuromuscular diseases, chronic lung diseases, bulla or bleb, pneumothorax, fluid and inotropic refractory shock, were excluded. This study was approved by the Medical and Health Research Ethics Committee, Universitas Gadjah Mada Medical School.

We evaluated several prognostic factors that may influence the improvement of PaO_2 in children with ARDS, namely severity and type of ARDS, corticosteroid use, pediatric risk of mortality (PRISM) III scores, and type of lung recruitment maneuver. ARDS severity was classified AS non-severe (PaO_2/FiO_2 ratio >100) or severe (PaO_2/FiO_2 ratio <100), whereas ARDS type was classified as pulmonary or extrapulmonary ARDS. The PRISM III scores were grouped as <8 or >8. The lung recruitment maneuver was grouped into positive end-expiratory pressure (PEEP) 9 cm H_2O and < 9 cm H_2O. The primary outcome was oxygenation improvement defined as maximum PaO_2 increment, which we classified into two quantiles, adequate, or inadequate.

All subjects were medicated by midazolam infusion in a supine position. The PRISM III scores were assessed within the first 24 hours of PICU admission. Subjects were ventilated using cuffed, standard-size endotracheal tubes. The lung recruitment maneuver was performed based on the PICU standard procedure, consisting of pressure controlled mandatory ventilation (P-CMV) mode, 100% oxygen concentration, inspiratory: expiratory ratio 1:1-1.5, tidal volume 5-7 mL/kg with maximum peak inspiratory pressure (PIP) 30-35 cmH_2O, as well as PEEP started at 5 cm H_2O and increased 1 cm H_2O every 15 minutes until the maximum PaO_2 was achieved. We measured PaO_2 at 0, 30, and 60 minutes using an immediate response mobile analysis system (*IRMA®*) device and blood gas analysis (BGA) cartridge (*Diametrics Inc.®* , St. Paul, Minnesota, USA). Accuracy of this device had been tested against benchmarked laboratory testing.[8] In addition to PaO_2, we also closely observed heart rate, capillary refill time, oxygen saturation, non-invasive blood pressure and mean arterial pressure. Lung recruitment maneuver was discontinued in subjects with bradycardia, hypotension, mean arterial pressure (MAP) decreased >20 mm Hg, and/or hypercapnea > 55 mm Hg.

We analyzed the influence of prognostic factors on PaO_2 improvement using univariate logistic regression. Prognostic factors with $P < 0.25$ were included in a multivariate analysis. Statistical significance was defined using RR and 95% confidence interval (CI). All statistical analyses in this study were performed using *IBM® SPSS® version 20 software for Mac*.

Results

We included 20 children with ARDS who completed the study enrollment. **Table 1** shows the basic characteristics of study subjects.

No significant hemodynamic changes, such as hypotension, decreased mean arterial peressure (MAP), increased heart rate and prolongation of capillary refill time (CRT), were seen in our subjects (**Figure 1**). Hypercapnea was also not observed in any subjects. Subjects' mean $PaCO_2$ was 35.2 ± 8.2 cm H_2O.

The PaO_2 improvement were classified into two categories, based on two quantiles with a cut-off point increase of 22 cm H_2O. The primary outcome, i.e., oxygenation improvement, was analyzed using univariate logistic regression test. This analysis revealed two factors with $P < 0.25$: type of ARDS (RR 0.17; 95% CI 0.023 to 1.23; P= 0.079) and severity of ARDS (RR 0.17; 95% CI 0.007 to 0.84; P = 0.035) (**Table 2**).

Table 1. Baseline characteristics of subjects

Characteristics	
Mean age (SD), months	23.3 (42.5)
Gender, n	
Boys	13
Girls	7
Diagnosis, n	
Pneumonia	8
Sepsis	5
Post-laparotomy	2
Meningoencephalitis	3
Others	2

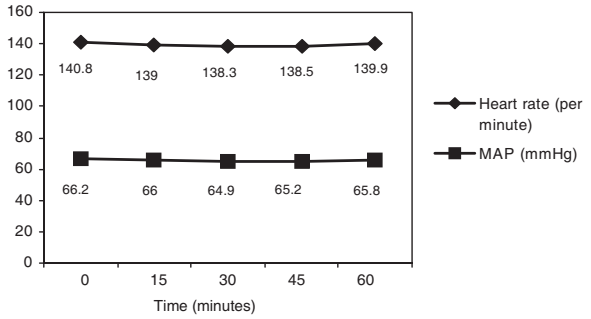

Figure 1. Hemodynamic observation during enrollment

Discussion

This study results which indicated that the type of ARDS in children did not influence PaO_2 were contradictory with other previous study in adult ARDS patients which concluded lung stiffness and alveoli collapse was more severe in pulmonary ARDS.[9] Another study showed PaO_2 increment to be higher in extrapulmonary ARDS.[10] However, those studies did not analyze potential covariates which could affect oxygenation improvement.[9] On the other hand, one study found no significant mortality difference between pulmonary and extrapulmonary ARDS, and that low-tidal volume ventilation (6 mL/kg) resulted in lower mortality compared to conventional tidal volume (12mL/kg) (30% vs. 40%).[11] A possible explanation of these differing results is that the previous studies did not include potential covariates, such as intra-abdominal problems that might be accompanied by aspiration pneumonia or sepsis complicated by ventilator-associated pneumonia.[11,12]

The PaO_2/FiO_2 ratio >100 was found to not be a prognostic factor for adequate oxygenation improvement, inconsistent with the results from ARDS Definition Task Force study that concluded PaO_2/FiO_2 ratio to be a prognostic factor for mortality and length of hospitalization. In the Task Force study, the mortality rates of PaO_2/FiO_2 200-300, PaO_2/FiO_2

Table 2. Univariate logistic regression of factors affecting oxygenation in children with ARDS

Outcomes	Oxygenation improvement		RR	95% CI	P value
	Inadequate n	Adequate n			
ARDS					
Extrapulmonary	4	8	0.17	0.023-1.23	0.079
Pulmonary	6	2			
Severity of ARDS					
Non-severe	4	6	0.74	0.007-0.84	0.035
Severe	9	1			
Steroid use					
Yes	2	3	0.58	0.075-4.56	0.61
No	8	7			
PEEP					
9 cm H_2O	3	3			
<9 cm H_2O	7	7	1.0	0.15-6.78	1.00
PRISM III					
<8	6 (30)	5 (25)	1.5	0.26-8.82	0.65
>8	4 (20)	5 (25)			

Multivariate logistic regression analysis revealed that neither severity of ARDS nor type of ARDS were significant independent factors for adequate oxygenation improvement (**Table 3**).

Table 3. Multivariate logistic regression analysis of factors affecting oxygenation in children with ARDS

Outcomes	RR	95% CI	P value
ARDS			
Extrapulmonary	0.33	0.009 – 1.41	0.35
Pulmonary			
Severity of ARDS			
Non-severe	0.11	0.009 – 3.25	0.09
Severe			

100-200, and PaO_2/FiO_2 <100, were 27% (95% CI 24-30%), 32% (95% CI 29-34%), and 45% (95%CI 42-48%) (P<0.001), respectively.[13]

A limitation of this study was that PaO_2 measurements were performed only three times. Performing PaO_2 measurements more than three times with higher PEEP might increase oxygen improvement. It appears that higher PEEP (until 18 cmH_2O) in children is safe for lung and hemodynamics.[14] A study with a larger sample size is recommended to increase statistical power.

Corticosteroid administration was not proven to be effective for ARDS, consistent with another randomized, controlled trial that showed no difference in 60 day mortality in patients receiving methylprednisolone (29.2% vs. 29.6%, P = 1.0).[15]

In summary, the severity and type of ARDS are not the prognostic factors for oxygenation improvement in children presenting with ARDS.

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