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The Effect of Dobutamine Administration on Oxygen Saturation in Infant's Persistent Pulmonary Hypertension of The Newborn (PPHN)

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Abstract

Background: PPHN of infants are severe cases because the rate of disability and death in infants is relatively high, reaching around 10-20% of cases. Therefore, prompt, accurate, and rational management is needed to reduce cases number of records and deaths. The incidence of PPHN is 2-6 out of 1000 live births; in Surabaya, the incidence was 42 babies per 1000 live births from April to September 2017. Dobutamine is an effective therapy that can support good morbidity and mortality. Therefore, therapeutic options in infants with PPHN in the form of dobutamine are often used.

Objective: To determine the effect of dobutamine administration on oxygen saturation in infants with persistent pulmonary hypertension of the newborn (PPHN)

Method: A cross-sectional design with a consecutive sampling of 50 infants with PPHN who received dobutamine therapy at the Hospital of Siti Khodijah Muhammadiyah Sepanjang. Data collection using medical records.

Results: The average increase in oxygen saturation before and after being given dobutamine was 36.0%. No difference in the increase in oxygen saturation based on the duration of dobutamine administration. The dobutamine dose's effect on the oxygen saturation increase in infants with PPHN.

Conclusion: The results of this study indicate a significant effect of dobutamine administration on increasing oxygen saturation in PPHN infants.

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INTRODUCTION

Persistent Pulmonary Hypertension of the Newborn (PPHN) or also called Persistent fetal circulation. PPHN is a condition with pressure and pulmonary vascular resistance higher than systemic vascular pressure and resistance, resulting in right-to-left shunts (usually through the ductus arteriosus and/or foramen ovale), which is characterized by severe hypoxemia, acidosis that will exacerbate pulmonary arterial vasoconstriction[1,2].

The United States gave a report involving ten tertiary research centers stating that the incidence of PPHN was 1.9 per 1000 live births in neonates, while in the UK, it reached 0.43-5 per 1000 live births in neonates[3]. In PPHN, therapy has been given with various options to reduce morbidity and mortality rates in infants with PPHN[4,5], such as a study conducted in the United Kingdom using ECMO technology in a randomized trial. In Surabaya, the incidence of PPHN in infat is 42 per 1000 live births from April to September in 2017[6]. Although PPHN is always associated with birth in post-term babies, PPHN cases are often found in babies with pretem conditions[7].

There are many modalities to manage PPHN in infants, one of the therapies from the inotropic group that is often given to infants with PPHN is dobutamine. Dobutamine is the beta-agonist of choice for heart failure patients with systolic dysfunction[8]. Dobutamine has a more inotro-pic than a chronotropic effect on the heart through beta-1 adrenergic stimulation[1]. The choice of therapy in infants with PPHN is dobutamine and how much effect dobutamine has on the infant.

METHOD

This research is analytic, with the design used being cross-sectional, where this study is to determine the effect of dobutamine on oxygen saturation in infants with PPHN at Siti Khodijah Hospital Muhammadiyah Sepanjang.

This study began with collecting initial data in Siti Khodijah Muhammadiyah Hospital, Sepanjang NICU. The initial data then obtained secondary data from medical record data. Sampling used consecutive sampling on 50 infants with PPHN who received dobutamine therapy at Siti Khodijah Hospital Muhammadiyah Sepanjang.

Data collection in this study only used secondary data. Secondary data used medical records at Siti Khodijah Muhammadiyah Hospital, Sepanjang.

The data analysis used in this research is univariate and bivariate. Univariate analysis is a technique where data is analyzed on one variable independently without being associated with other variables. Bivariate analysis in this study can be called descriptive analysis, which will be carried out on the two variables studied, namely the independent variable (free) giving dobutamine with units of mcg/kg/minute which can affect the dependent variable (bound), namely oxygen saturation of infants with PPHN.

RESULT

This study aims to determine the effect of dobutamine on oxygen saturation in infants with PPHN. The characteristics of infants with PPHN can be seen from gender, weight, and grade of PPHN, then the effect on oxygen

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saturation by dobutamine in this study. The medical record data used in this study were 50 data on infants with PPHN. The data were analyzed by descriptive analysis to determine the number and percentage in each group. The relationship between variables was analyzed using bivariate analysis of non-parametric analysis test.

Characteristics of Infant with PPHN

Based on Table 1, of the 50 infants with PPHN in this study, 33 (66.0%) were male, while 17 other infants (34.0%) were female. This result indicates that male infants dominated the infants in this study. Infants in this study were eighteen with mild PPHN (36.0%), seven infants with moderate PPHN (14.0%), and 50 infants with severe PPHN (50.0%). Furthermore, the minimum weight of 50 infants with PPHN is 1.25 kg, and the maximum is 4.2 kg. The average weight of infants with PPHN at Siti Khodijah Muhammadiyah Hospital Sepanjang was 2.52 kg, with a standard deviation of 0.674 kg.

Infant Oxygen Saturation with PPHN

Table 2 shows that of the 50 infants with PPHN before being given dobutamine, the lowest oxygen saturation was 86.0%, and the highest was 99.0%. The mean value of oxygen saturation of the 50 infants was 93.5%, with a standard deviation of 3%.

For all infants with PPHN after being given dobutamine for several days, the lowest oxygen saturation was 94.0%, and the highest was 99.0%. The mean value of oxygen saturation of the 50 infants was 97.1%, with a standard deviation of 1.26%.

Table 1 Characteristics of Infants with PPHN

Variable		Sum	Percentage
Sex	Man	33	66,0%
	Women	17	34,0%
	Total	50	100,0%
Grade of PPHN	Mild	18	36,0%
	Moderate	7	14,0%
	Severe	25	50,0%
	Total	50	100,0%
Infant Weight (kg)	Minimum	1,25	
	Maximum	4,2	
	Means	2,52	
	Standard Deviation	0,674	

Table 2 Oxygen Saturation of Infants with PPHN

Dobutamine Administration	Oxygen Saturation				Z	p
	Minimum	Maximum	Means	SD		
Before	0,86	0,99	0,935	0,03	-5,750	0,000
After	0,94	0,99	0,971	0,126		

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Table 3 Effect of Duration Dobutamine Administration on Oxygen Saturation

Duration of Dobutamine	Oxygen Saturation Increase (Means)	Chi-Square	p
2 days	0,028	7,953	0,337
3 days	0,039		
4 days	0,042		
5 days	0,017		
6 days	0,050		
7 days	0,070		
8 days	0,035		
9 days	0,023		

Table 4 Effect of Dobutamine Dosage on Oxygen Saturation

Dosage (mcg)	Means±SD	Z	p
5	0,042 ±0,026	-2,134	0,033
5-3	0,024 ± 0,032		

The average increase in oxygen saturation before and after being given dobutamine was 36.0%. Wilcoxon test results also showed a significance value of 0.000 ($p < 0.05$). So, it can be concluded that dobutamine administration has a significant effect on the increase in oxygen saturation in PPHN infants.

Effect of Dobutamine Duration Administration on Increase in Oxygen Saturation

In Table 3, the Chi-Square test results also showed a significance value of 0.337 ($p > 0.05$). This result shows no difference in the increase in oxygen saturation in PPHN infants based on the duration of dobutamine administration.

Effect of Dobutamine Dosage on Increase in Oxygen Saturation

In Table 4, the average increase in oxygen saturation of infants with PPHN given dobutamine at a dose of 5 mcg is 4.2%, while the average increase in oxygen saturation of infants with PPHN given dobutamine at a dose of 5-3 mcg is 2,4%. This result shows that dobutamine at a dose of 5 mcg is more effective in increasing the oxygen saturation of infants with PPHN. Moreover, the Mann-Whitney test with a significance value of 0.033 ($p < 0.05$) indicates the dobutamine dose's effect on the oxygen saturation increase in infants with PPHN.

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DISCUSSION

Infant's Sex and Weight with PPHN

Based on previous research, the sex of the infant did not show any difference in infants with PPHN[9]. Although in this study, the male sex dominates the research data. In previous studies, babies with low birth weight have organs that are not yet fully mature, including the lungs[10]. However, in this study, the average weight of the babies obtained proved that the weight of infants with PPHN was still average.

Grades of PPHN Infant

Pulmonary Artery Systolic Pressure (PASP) in patients was divided into four categories, namely normal PASP 35 mmHg, mild (PASP 35-45 mmHg), moderate (PASP 45-60 mmHg). The PASP value was obtained from echocardiographic medical record data. Of the 50 infants with PPHN included in mild PPHN, as many as 18 patients, seven with moderate PPHN, and 25 with severe PPHN. Previous studies stated that PASP obtained from echocardiography is a much more general and applicable modality. Moreover, the grades showed more in the state of severe PPHN[11].

Effect of Dobutamine on Infants with PPHN

Dobutamine is a racemic mixture that stimulates beta-1 and beta-2 receptors. In addition, the enantiomer(-) is an alfa-agonist. Infusion rates produce a positive inotropic effect in humans. The beta-1 adrenergic effect on the myocardium is predominant and results in increased cardiac output with only a slight increase in heart rate. Dobutamine is the most widely used selective beta-1 agonist in patients with heart failure[12]. In blood vessels, the alfa-agonist (vasoconstrictive) effect of the enantiomer(-) is antagonized by the beta-2-agonist (vasodilation) effect. So, systemic resistance is usually slightly decreased. Dobutamine does not stimulate dopamine receptors. Dobutamine has a more inotropic than a chronotropic effect on the heart via beta-1 adrenergic stimulation[13].

Oxygen Saturation in Infants with PPHN

Right-to-left shunts may accompany right ventricular dysfunction in the atria due to decreased diastolic complaints and increased end-diastolic pressure. This diagnosis must be distinguished from PPHN caused by pulmonary vascular abnormalities. Signs more suggestive of primary heart disease than PPHN are as follows: cardiomegaly, weak pulse, differential pulse in the upper and lower extremities, pulmonary edema, grade 3+ heart murmur, persistent arterial O2 pressure (PaO2) <40 mmHg. Oxygen saturation is less than average, whereas the normal range is 95%-100%[14].

Effect of Type of Oxygen on Oxygen Saturation (SPO2) of Infants with PPHN

The oxygen given to each patient is different. Infants who were given Continuous Positive Airway Pressure (CPAP) oxygen were known to have an average increase in oxygen saturation of 3%. Meanwhile, infants who were given biphasic CPAP oxygen, Nasal O2, and CPAP AFF each experienced an increase of 2%. This condition indicates that infants with PPHN who were given CPAP oxygen had more oxygen saturation increases. Continuous Positive Airway Pressure (CPAP) is a device to maintain positive pressure in the neonate's airway during spontaneous breathing. CPAP is a simple and effective tool for managing

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respiratory distress in neonates. Correct use of CPAP has been shown to reduce difficulty in breathing, reduce dependence on oxygen, help repair and maintain residual lung capacity, prevent upper airway obstruction, prevent lung collapse, reduce apnea, bradycardia, and cyanotic episodes, and reduce the need for hospitalization. Intensive room. There are several criteria for the occurrence of respiratory distress in neonates which are indications for the use of CPAP, one of which is an infant with oxygen saturation <93% (preductal)[15].

Duration Dobutamine Administration and Dosage on Oxygen Saturation

The dose of dobutamine for infants in PPHN is the same as for dopamine. Low doses of 1-2 mcg/kg/min, and higher doses (>10 mcg/kg/min)[1]. Dobutamine is only given intravenously. Dobutamine in low doses: inotrope (beta-1 agonist) 2.5-5µg/kg/min, high doses cause afterload reduction (alfa-2 agonist) >10µg/kg/minute[16]. The main side effects are excessive tachycardia and arrhythmias in patients with significant coronary artery disease, which requires dose reduction. Tachyphylaxis accompanies each beta stimulant's use. Intermittent infusions of dobutamine may benefit some patients with chronic heart failure.

Effect of Dobutamine on Oxygen Saturation (SpO2) in Infants with PPHN

Dobutamine is a synthetic catecholamine modified from isoprenaline to reduce its chronotropic effect. Dobutamine has a half-life of about 2 minutes in children and adults, and beta acts on beta-1 and beta-2 receptors with little effect on alfa receptors, leading to an increase in myocardial contractility and heart rate and a slight decrease in peripheral vascular resistance. Perhaps this vasodilating effect has resulted in many studies suggesting that dobutamine is not as good as dopamine in improving blood pressure in hypotensive premature infants. However, in the few studies that have calculated this effect, dobutamine appears to be better than dopamine at improving blood pressure[13].

In Early Goal-Directed Therapy (EGDT), dobutamine is recommended if tissue hypoperfusion is found (SPO2 <70%), provided that CVP, hematocrit, and MAP have been corrected beforehand and reach normal values[17]. In some cases, it can be reduced by sepsis-induced cardiac dysfunction. In this case, dobutamine is administered (the dose can be increased to a maximum of 20 mcg/kg/min) to increase oxygen delivery to the periphery and prevent further organ dysfunction caused by hypoperfusion and ischemia. If dobutamine administration causes hypotension, norepinephrine is recommended to counteract the vasodilating effects of dobutamine[18,19].

CONCLUSION

Dobutamine influences increasing oxygen saturation in infants with PPHN. There was no difference in the increase in oxygen saturation in PPHN infants based on the duration of dobutamine administration. Dobutamine dose affects the increase in oxygen saturation in infants with PPHN. Dobutamine with a dose of 5 mcg is more effective than 5-3 mcg in increasing oxygen saturation in infants with PPHN.

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