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INTRODUCTION

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Abstract

13. In Vitro Antiplatelet Aggregation Activity of *Centella asiatica* (L.) Urban Ethanolic Extract

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Research Article

Comparison of Electrolyte Disturbance of Using Intravenous Aminophylline Versus Nebulization Salbutamol for Exacerbation Asthma in Surabaya, Indonesia

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ABSTRACT

Background: Uncontrolled asthma symptoms will exacerbate asthma. Aminofilin is now rarely used as asthma medication abroad because it shows major side effects, unlike in Indonesia, which is still widely used with relatively rare side effects events. Aminophylline have relatively more affordable price compared to salbutamol, the first-line option in the management of asthma exacerbations requirements. Both of these drugs have a risk of causing electrolyte disturbances, which could endanger the patients. Considering the individual drug side effects, so it important to study the safety of the medicine to ascertain whether there are differences in the incidence of electrolyte disturbances by both drugs.

Objective: The main objective of this study was to determine differences in the incidence of electrolyte disturbances in patients with asthma exacerbations prescribed with aminophylline and salbutamol at a hospital in Surabaya.

Method: This study design is a cross-sectional study of inpatient adult asthma exacerbations in emergency room (ER), using two groups, namely the group receiving intravenous aminophylline therapy (n = 22), and the group receiving nebulized salbutamol therapy (n = 21).

Result: There is no significant difference between in intravenous aminophylline anda nebulized salbutamol group. And there is no significant difference in sodium (p>0,866) and potassium (p>0,470) level in blood as a respon to the asthma exacerbations treatment by intravenous aminophylline compared to nebulized salbutamol.

Conclusion: Although there was no significant difference in the incidence of electrolyte disturbances in both drugs, but close monitoring is still needed to prevent any side effects incident.

Keywords: asthma exacerbations, electrolyte disturbance, aminofilin, salbutamol

INTRODUCTION

Asthma is a heterogeneous disease which can be caused by a variety of etiologies. These disease is one of the major health problems in the world[1]. Although new drugs and evidence-based guidelines have been developed in recent years however no major changes in the morbidity and mortality of asthma[2]. The incidence of worsening asthma symptoms can cause serious problems to the incidence of asthma exacerbations that can ended into death. Salbutamol is a bronchodilator which belonged to the short-acting beta-2 agonist (SABA), the first line option in the management of asthma exacerbations[1,3]. Contrast to methylxanthines (aminophylline and theophylline), salbutamol has higher efficiency than methylxanthines. Methylxanthine is used as an adjunctive therapy in the management of asthma if therapeutic effectiveness is not optimal, as well as its role in the management of asthma exacerbations is still controversial[1]. Theophylline belong to methylxanthines, but its use in asthma has been reduced due to the high frequency of side effects and relatively low effectiveness and slower[1,4]. Aminophylline is a derivative of theophylline with addition of ethylenediamine from a water soluble salt complex. Aslaksen e*t al.*(1981)[5] prove that aminophylline at a comparable concentration with intravenous and oral theophylline did not differ significantly in farmakokinetiknya or binding proteins in the blood, so it can be considered the same. Theophylline/ aminophylline has a narrow therapeutic range and narrow

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Table 1: Characteristics of Research Subjects in Related to Sex, Age, and Medical History

Characteristics	Details	intravenous aminophylline (n:22)	nebulized salbutamol (n:21)
Sex:	Male	5	10
	Female	11	11
Age (years):	17-25	3	5
	26-35	3	3
	36-45	4	3
	46-55	5	4
	56-65	1	5
	>65	0	1
	average:	39.25	42.38
Medical history:	asthma	15	18
	asthma + gastritis		1
	asthma + type 2 diabetes mellitus		1
	asthma + dyslipidemia	1	1

variations in hepatic metabolism and clearance so that might have risks of causing ADR (adverse drug reactions)[6]. Many evidences regarding the events of theophylline and aminophylline ADR have many uncovered yet[7-11]. so its use was abandoned in a foreign country, but in Indonesia, theophylline is still be used in the treatment of asthma exacerbations. In Indonesia, aminophylline/ theophylline is one of the asthma drug that is often used in the treatment of asthma exacerbations in the hospital. Aminophylline even is included in the list of DOEN (Daftar Obat Essensial Nasional) 2013. In East Java, aminophylline and theophylline in the treatment of acute asthma is still widely used in the treatment of asthma exacerbations main hospital[12-14]. The effect of a drug ADR can be individualized, including the effects of treatment with theophylline during treatment of asthma. Interindividual variability in the distribution and elimination kinetics of theophylline will result in differences in levels of theophylline in plasma, leading to clinical consequences which can not be predicted. The differences in therapeutic response in inidividual theophylline, can be either the dose or doses toxic subterapetik[15]. Genetic factors are among the factors that cause a different response to asthma therapy[16]. The use of beta-agonists and methylzanthine can increase the risk of an occurrence of hyponatremia hypokalemia. As has been observed by Mohammad et al. (2014)[17]. which examines electrolyte disturbance in chronic asthma (outpatient) and exacerbation of asthma. The results showed that incidence of hyponatremia is low (4%) in stable asthmatic patients dan no abnormalities were noted in serum sodium level the exacerbation of asthma. In contrast to the results in the levels of potassium, more patients with acute asthma exacerbation (54%) had hypokalemia and, there was a significant decrease in potassium level in these patients than those with stable bronchial asthma. Hypokalemia is a side effect that often occurs in both beta-2 agonist (salbutamol)[1] and methylxanthine (aminophylline). Information about the side effects from these drugs was limited and outdated as has been done by Whyte et al.(1988)[18] Hung et al., (1999)[19] Hung et al. (1999) suspected the existence of a mechanism similar to the effects of beta-2 agonist bronchodilation with the incidence of hypokalemia. It mentioned that salbutamol inhalation significantly improved asthmatic symptoms as demonstrated by increasing of expiratory flow and venous oxygen tension, and decreasing of respiratory rate, clinical scores, and venous PCO_2 tensions[19]. Although the incidence of hypokalemia tend to be more frequent, but they still need to be a concern in the treatment of asthma exacerbations. Therefore, it is necessary to study in this effect to patients Indonesia in order to determine differences in the incidence of electrolyte disturbances in patients with asthma exacerbations medicated with aminophylline and salbutamol at a hospital in Surabaya.

METHOD

This study design is cross-sectional study of inpatient in emergency room (ER). The variables of this study consisted of the independent variable, which were treatments exacerbations of asthma (aminophylline intravenous and nebulized salbutamol), and dependent variables which were sodium and potassium levels in the blood. Data were collected from January 2014 to June 2015 in some hospitals in Surabaya, Indonesia.

Population and Sample Research. The population were all patients with exacerbations of asthma in some ER in hospital in Surabaya. The study sample were all patients with exacerbation asthma in hospital in Surabaya who fulfill the inclusion and exclusion criteria of the study. Inclusion criteria for the study sample were: (1) aged adults (≥18 years)[20] ; and (2) willing to be the subject of research. Exclusion criteria for the study sample were: (1) Patient-lactating pregnant or taking oral contraceptives;[21] (2) Patients with impaired renal function or hepatic impairment; (3) The patient smoked or quit smoking <2 years, coffee consumption; (4) The patient had respiratory problems besides asthma that can affect clinical outcomes of the treatment.

Method Of Collecting Data. Ethics test has been carried out in each of several hospitals in Surabaya according to existing procedures. Then the data collection is done with stand-by in the ER. Currently no exacerbation of asthma patients who meet the criteria, then the patient was asked to fill his willingness and informed consent. The patient's body temperature measurements were taken immediately

Table 2: Frequency Distribution of Sodium Levels Before and After Administration of Exacerbation Treatment with Aminofilin Intravenous or Nebulized Salbutamol

Intervention Group	Intravenous Aminophylline (n:22)	Nebulized Salbutamol (n:21)	Total
Initial conditions before being given treatment (t_0)			
Hyponatremia (% of subjects)	0 (0.00%)	1 (2.32%)	1 (2.32%)
Normal (% of subjects)	22 (51.17%)	19 (44.19%)	41 (95.36%)
Hypernatremia (% of subjects)	0 (0.00%)	1 (2.32%)	1 (2.32%)
Total (% of sample)	22 (51.17%)	21 (48.83%)	43 (100%)
Conditions after being given treatment (t_1)			
Hypo-Natremia (% of subjects)	0 (0.00%)	1 (2.32%)	1(2.32%)
Normal (% of subjects)	22 (51.17%)	19 (44.19%)	41 (95.36%)
Hyper-Natremia (% of subjects)	0 (0,00%)	1 (2.32%)	1 (2.32%)
Total (% of sample)	22 (51.17%)	21 (48.83%)	43 (100%)

Table 3: Frequency Distribution of Changes in Sodium Levels After Administration of Exacerbation Treatment with Aminofilin Intravenous or Nebulized Salbutamol

Intervention Group	Intravenous Aminophylline (n:22)	Nebulized Salbutamol (n:21)	Total
Changes in the value t0 to t1 (ratio scale)			
Decreased (% of subjects)	8 (18.61%) Consist of: -1 = ∑ 3 -2 = ∑ 2 -3 = ∑ 3	6 (13,95%) Consist of: -1 = ∑ 2 -2 = ∑ 4	14 (32,56%)
Fixed (% of subjects)	6 (13.95%)	9 (20,93%)	15 (34,88%)
Increased (% of subjects)	8 (18.61%) Consist of: +1 = ∑ 6 +2 = ∑ 2	6 (13,95%) Consist of: +1 = ∑ 3 +3 = ∑ 1 +4 = ∑ 2	14 (32,56%)
Total (% of subjects)	22 (51.17%)	21 (48.83%)	43 (100%)
Changes in the value t0 to t1 (ratio scale)			
Worsen (% of subjects)	0 (0.00%)	0 (0,00%)	0 (0,00%)
Fixed (% of subjects)	22 (51.17%) Consist of: N-to-N= ∑ 22	21 (48,85%) Consist of: Ho-to-Ho= ∑ 1 N-to-N= ∑ 19 Hi-to-Hi= ∑ 1	43 (100%)
Recovered (% of subjects)	0 (0,00%)	0 (0,00%)	0 (0,00%)
Total (% of subjects)	22 (51.17%)	21 (48.83%)	43 (100%)

: hipo (under the normal level)
: normal
: hyper (above the normal level)

(to ensure the presence of infection), then performed blood sampling before getting treatment for an unknown levels of electrolyte (sodium and potassium). Samples were treated for 1 hour (aminophylline intravenous or nebulized salbutamol), then blood drawn back (t_1). Results of laboratory examination on t_0 and t_1 then compared to observe changes in the use of electrolyte nebulized salbutamol in patients with asthma exacerbations in Surabaya. The patient's body temperature measurements were taken immediately (to ensure the presence of infection), then performed blood sampling before getting treatment for an unknown levels of electrolyte (sodium and potassium). Samples were treated for 1 hour (aminophylline intravenous or nebulized salbutamol), then blood drawn back (t_1). Results of laboratory examination on t_0 and t_1 then compared to observe changes in the use of aminophylline intravenous electrolytes with nebulized salbutamol in patients with asthma exacerbations in Surabaya. The research sample was also interviewed about the clinical symptoms of hyponatremia and hypokalemia to determine differences in clinical symptoms. Conducted interviews to patients about medicines that are used before MRS (hospital admission) to determine whether the previous drug can affect the results or not. There are events

Table 4: Sodium Levels Test Changes Due to Aminofilin Intravenous Administration Compared to Nebulized Salbutamol Administration

Intervention Group		Test Differences between t0 and t1 in the same group** (Paired T-Test)	Test Differences between t_0 in groups** (Independent T-Test)	Test Differences between t_1 in groups** (Independent T-Test)
Intravenous Aminophylline (n:22)	Sodium level before the treatment (t_0)	0,004 (H_1 accepted)	0,736 (Not significant)	0,866 (Not significant)
	Sodium level after the treatment (t_0)			
Nebulized Salbutamol (n:21)	Sodium level before the treatment (t_0)	0,000 (H_1 accepted)		
	Sodium level after the treatment (t_0)			

* data is normal distribution if sig ≥ 0.05

**data is homogen (not significant) if sig >0,05, H_0 accepted and H_1 rejected

Table 5: Frequency Distribution of Potassium Levels Before and After Administration of Exacerbation Treatment with Aminofilin Intravenous or Nebulized Salbutamol

Intervention Group	Intravenous Aminophylline (n:22)	Nebulized Salbutamol (n:21)	Total
Initial conditions before being given treatment (t_0)			
Hypokalemia (% of subjects)	3 (6,98%)	3 (6,98%)	6 (13,95%)
Normal (% of subjects)	19 (44,19%)	18 (41,85%)	37 (86,05%)
Hyperkalemia (% of subjects)	0 (0.00%)	0 (0,00%)	0 (0,00%)
Total (% of sample)	22 (51.17%)	21 (48.83%)	43 (100%)
Conditions after being given treatment (t_1)			
Hypokalemia (% of subjects)	2 (4,65%)	5 (11,63%)	7 (16,28%)
Normal (% of subjects)	20 (46,51%)	16 (37,21%)	36 (83,72%)
Hyperkalemia (% of subjects)	0 (0,00%)	0 (0,00%)	0 (0,00%)
Total (% of subjects)	22 (51.17%)	21 (48.83%)	43 (100%)

in patients with hypokalemia before getting the test drug therapy salbutamol group, it is made possible patients already using asthma medication for type of reliever on the way to the hospital emergency room to help alleviate the symptoms. Analysis of the data in this study used t-test, to determine differences in the incidence of changes in the electrolyte. Levels of potassium and sodium in the blood is the data that is included in the scale ratio of the need to use Kolmogorov-Smirnov test to test for two independent samples, to determine the normality of the data distribution. If the value of P> 0.05 means that the differences are not significant so H_0 is accepted, while the value of P <0, 05 means that a significant difference so H_1 is received. Data interviews clinical conditions nominal data samples that can be analyzed descriptively.

RESULT AND DISCUSSION

Characteristics of the study subjects are shown in Table 1. In this study, the number of women were more than men, either in groups aminophylline intravenous or nebulized salbutamol. The age of the study subjects were in the productive age range, with average of 39.25 (intravenous aminophylline group) and 42.38 (nebulized salbutamol). A large part of their medical history was only had asthma without any other comorbidities **(**Table 1). At nebulized salbutamol's population group, there were 4 patients who should be excluded because blood tests must be done in a laboratory outside the hospital and possibly due to factors in the journey that causes lysis of blood be on t0 or t1, so it can not be known sodium/ potassium level. Measurement of sodium/ potassium levels in the blood of patients in different laboratories can affect the results, because every instrument has different precision and accuracy, so the range of normal values can be different for different laboratories. Exacerbation of asthma patients used in the study was the rate of mild-moderate asthma who do not require another asthma treatment such as corticosteroids. Because the systemic corticosteroids group for asthma medications, ADR form methylprednisolon can cause hypokalemia, its use may cause sodium retention and increased secretion of potassium which can cause hypertension and hypokalemia[22]. Diabetic patients will be at risk of electrolyte disturbances, especially if they use drugs

Table 6: Frequency Distribution of Changes in Potassium Levels After Administration of Exacerbation Treatment with Aminofilin Intravenous or Nebulized Salbutamol

Intervention Group	Intravenous Aminophylline (n:22)	Nebulized Salbutamol (n:21)	Total
Changes in the value t0 to t1 (ratio scale)			
Decreased (% of subjects)	8 (18.60%) Consist of: -0,2 = ∑ 5 -0,3 = ∑ 2 -0,4 = ∑ 1	13 (30.23%) Consist of: -0,1 = ∑ 2 -0,2 = ∑ 1 -0,3 = ∑ 2 -0,4 = ∑ 4 -0,5 = ∑ 1 -0,7 = ∑ 1 -0,8 = ∑ 1 -1,0 = ∑ 1	21 (48.83%)
Fixed (% of subjects)	9 (20.93%)	5 (11.63%)	14 (32.56%)
Increased (% of subjects)	5 (11.63%) Consist of: +0,1 = ∑ 3 +0,3 = ∑ 1 +0,4 = ∑ 1	3 (6.98%) Consist of: +0,1 = ∑ 1 +0,2 = ∑ 1 +0,8 = ∑ 1	8 (18.64%)
Total (% of subjects)	22 (51.17%)	21 (48.83%)	43 (100%)
Changes in the value t0 to t1 (ratio scale)			
Worsen (% of subjects)	0 (0.00%)	3 (6.98%) Consist of: N-to-Ho= ∑ 3	3 (6.98%)
Fixed (% of subjects)	21 (48.84%) Consist of: Ho-to-Ho= ∑ 1 N-to-N= ∑ 20	17 (39.53%) Consist of: Ho-to-Ho= ∑ 2 N-to-N= ∑ 15	38 (88.37%)
Recovered (% of subjects)	1 (2.33%) Consist of: Ho-to-N= ∑ 1	1 (2.33%) Consist of: Ho-to-Ho= ∑ 1	2 (4,65%)
Total (% of subjects)	22 (51.17%)	21 (48.83%)	43 (100%)

: hipo (under the normal level)
: normal
: hyper (above the normal level)

exacerbate asthma who are at risk of the disorder. And in this study sample there was one person who had a history of diabetes mellitus type 2 (Table 1), which at the time of the study also experienced hypokalemia. Although the provision of nebulized salbutamol therapy only decreases by 2 points hypokalemia condition (condition of asthma patients after therapy is hypokalemia), but this still needs to be a particular concern. According Liamis et al. (2014),[23] this electrolyte disturbances are particularly common in decompensated diabetics, especially in the context of diabetic ketoacidosis or nonketotic hyperglycemic hyperosmolar syndrome. These patients are markedly potassium-, magnesium- and phosphate-depleted[23]. Initial conditions in the intervention groups are relatively equal, that most have normal sodium level. Only in nebulized salbutamol group, there are 2 people who have levels outside the range, consist of 1 person experiencing hyponatremia (2.32%) and 1 person experiencing hypokalemia (2.32%). These conditions are also the same after intravenous administration of aminophylline therapy and intravenous salbutamol (Table 2). Changes in sodium levels before given treatment (t0) and after given therapy (t1) can be seen in Table 3. The results showed that the intravenous aminophylline group showed decreasing in sodium levels as much as the improvement after therapy, ie by 18.61%, despite of all the changes they are still in the normal range. In the group of nebulized salbutamol, more number of samples did not change levels of sodium (20.93%), although there are some that decreased (13.95%) and increase (13.95%) of the levels. Just like aminophylline intravenous group, the nebulized salbutamol group also showed normal range of sodium levels (Table 3). Sodium levels data of the group aminophylline intravenous and nebulized salbutamol shows in table 4, both before treatment (t0) and after treatment (t1) indicates that all data distributed normally ($p \geq 0.05$). Both groups equally showed a significant difference between the sodium level before and after treatment (p (0.004) <0,05 and p (0.000) <0.05), which means there is a significant change in sodium levels with administration of intravenous aminophylline and salbutamol therapy nebulized. This study used a quasi-experimental, and both groups interventional therapy derived from a different hospital (no random). To ascertain

Table 7: Potassium Levels Test Changes Due to Differences in Aminofilin Intravenous Administration Compared with Nebulized Salbutamol

		Test Differences between t0 and t1 in the same group** (Paired T-Test)	Test Differences between t_0 in groups** (Independent T-Test)	Test Differences between t_1 in groups** (Independent T-Test)
Intravenous Aminophylline (n:22)	Kalium level before the treatment (t_0) Kalium level after the treatment (t_0)	0.000 (H_1 accepted)	0.569 (Not significant)	0.470 (Not significant)
Nebulized Salbutamol (n:21)	Kalium level before the treatment (t_0) Kalium level after the treatment (t_0)	0.001 (H_1 accepted)		

* data is normal distribution if sig ≥ 0.05

**data is homogen (not significant) if sig >0.05, H_0 accepted and H_1 rejected

whether the two groups have the same sodium content databases then the data was analyzed using t-test between groups (t_0), and the result showed no significant difference in sodium content between the two groups in the time before t0 therapy (p>0.736), so that it can be ascertained that potassium levels in both groups was the same. In addition, the results of sodium levels after administration of the therapy also showed no significant difference between the two groups (p>0.866) (Table 4). Initial conditions of the intervention groups are relatively equal, that most have normal potassium levels. At nebulized aminophylline group, most of the samples have normal potassium levels (44.19%), although 6.96% of them had hypokalemia. Similarly with nebulized salbutamol group, most of the samples had normal potassium levels (41.85%), with 6.98% of them had hypokalemia. None of the subjectsshowed specific symptoms of hypokalemia although the potassium level is below the normal range. Similar conditions also occured during exacerbations of asthma after therapy in each group. In the group of intravenous aminophylline, the number of patients with normal potassium levels were increased to 46.51%. In the other side, the salbutamol group showed an increasing number of subjects that experienced hypokalemia to be 11.63% (Table 5). Changes in potassium levels before given treatment (t0) and after given therapy (t1) can be seen in Table 6. The results showed that most of the subject who received intravenous aminophylline therapy had higher levels of potassium which is fixed (20.93%). Based on the value of the normal range, all the samples in the group were in the normal range even there is one patient who experienced improvement from hypokalemia becomes normal. There is a theory that theophylline increases production of urine and enhances excretion of water and electrolytes[24]. The total number of patients with chronic asthma and low serum sodium levels was too small to draw a clear conclusion about its prevalence and clinical significance, further studies with a larger number of subjects are needed to evaluate the significance of this finding (Table 6). Contrast with nebulized salbutamol group, which is largely decreased the potassium levels as much as 30.23%, and only 11.63% were fixed. Based on the value of the normal range, this group also experienced improvements majority (39.53%), even one patient experienced improvement from hypokalemia becomes normal. However, the concern is that there are 3 subjects (6.98%) experienced worsening of normal potassium levels (t0) becomes hypokalemia (t1) even though they do not show specific symptoms of hypokalemia and not require treatment (Table 6). Asthma patients who used the drug may cause hypokalemia. In this case, β2 agonist that has been widely transparently reported salbutamol can lead to hypokalaemia. The β2 adrenergic receptor stimulation by sympathomimetic drugs such as bronchodilators can reduce levels of serum potassium. Therapeutic doses of nebulized salbutamol can lower potassium levels of 0,2 mmol/L to 0,4 mmol/L[25]. The incidence of hypokalemia in the aminophylline treatment group was less than salbutamol. Hypokalemia can occur due to the transfer of potassium from the intravascular to normal intraseluler. Distribution of potassium between cells and the extracellular fluid is maintained by Na-K-ATPase pumping reside in cell membranes. In certain circumstances may an increasing in the rate of potassium into the cell transients. Hypokalemia is usually associated with increasing morbidity and mortality, in particular because of arrhythmia or sudden cardiac death. Hypokalemia is a result of the overall deficit or shift potassium serum potassium into the intracellular compartments in the body[26]. Besides, there is also a theory that hypokalemia may occur due to active inhibition of potassium secretion in the cortical collecting tubule, possibly the caused by the stimulation of membrane-dependent sodium potassium adenosine triphosphatase that results in hyper polarization of the cellular membrane potential[27]. In this study clinical interview conducted directly to the subject of research and also assisted by his family. Hypokalemia clinical symptoms such as

arrhythmias, can not be known because it requires an electrocardiogram (ECG) to determine the cardiac patient records. The ECG examination was not done because the patient objected to undress like commonly done for heart disease patients. Hypokalemia contribute to an increased risk of arrhythmia, it occurs most frequently in acute myocardial infarction (MI) at pulse rate greater than 100x/min. Hypokalemia can cause patients to experience muscle fatigue or cramps and serious cardiac aritmia and sudden death. Treatment of hypokalemia, In general, each 1mmol/L potassium fall below 3.5 mmol/L in accordance with the total body deficit of 100-400 mEq. When possible, potassium supplements should be given orally. Of salt available, potassium chloride is most commonly used as the most effective for the common cause of potassium depletion. The use of IV should be restricted to patients who have severe hypokalemia, signs and symptoms of hypokalemia, or inability to tolerate oral therapy. Potassium must be administered in salt, because dextrose so as to stimulate the secretion of insulin and worsen intracellular potassium shifts. Generally, 10 to 20 mEq of potassium diluted in 100 mL of 0,9% saline and administered through a peripheral vein over 1 hour. If the infusion rate exceeds 10 mEq/hr, ECG should be monitored[26]. Data potassium levels of the group aminophylline intravenous and nebulized salbutamol shows in table 7, both before treatment (t0) and after treatment (t1) indicates that all data normal distribution ($p \geq 0.05$). Both groups equally showed a significant difference between the potassium levels before and after treatment ($p(0.000)<0.05$ and $p(0.001)<0.05$), which means that there is a significant change in potassium levels with administration of intravenous aminophylline and salbutamol therapy nebulized. The two groups have the same potassium levels databases then analized with t-test between groups (t_0), and the result showed no significant difference in potassium levels between the two groups before t0 therapy ($p>0.569$), so that it can be ascertained condition potassium levels in both groups was the same. The results of potassium levels after administration of the therapy also showed no significant difference between the two groups ($p> 0.470$) (Table 7). Both β2-agonist and aminophylline group was known can cause hypokalemia as adverse drug reaction event[28,29]. Nebulized salbutamol administration for the emergency treatment of acute exacerbations of asthma associated with a statistically significant decrease in serum potassium levels decreased significantly[29]. Salbutamol cause hypokalemia which correlates with a decrease in respiratory rate (RR), and an increase in venous oxygen tension (pO_2) and peak expiratory flow (PEF). These findings suggest that the same mechanism is involved in eliciting hypokalemia and bronchodilation[19]. Hypokalemia in patients with asthma can be life-threatening plasma potassium concentration of 1.7 mEq/L and can be exacerbated by a combination treatment with other drugs such as diuretics, corticosteroids and theophylline which resulted in loss of potassium[28]. Paralysis can suddenly occur in both lower limbs due to improper treatment. Administration of inhaled β2-agonist continuously can cause paralysis due to hypokalaemic though is the drug of choice to overcome asthma exacerbations[30].

CONCLUSION

There is no significant difference in levels of sodium and potassium in the treatment of asthma exacerbations by intravenous aminophylline compared with nebulized salbutamol. And the majority of subjects showed normal values in its levels of potassium and sodium, both of intravenous aminophylline or nebulized salbutamol.

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