Journal of Tropical Pharmacy and Chemistry

Journal homepage: https://jtpc.farmasi.unmul.ac.id

Cost-Effectiveness of Length of Stay of Intravenous Aminophylline and Nebulized Salbutamol in Asthma Exacerbations

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Abstract

Asthma is a heterogeneous disease which is also one of the major health problems in the world. Uncontrolled asthma symptoms will exacerbate asthma, which is the biggest cause of the patient into the ER. Salbutamol is a bronchodilator that belonged to the short-acting beta-2 agonist (SABA), which is an obligatory choice in the management of asthma exacerbations. Unlike the aminophylline group in Indonesia which is still often used widely and rarely appear in the side effects of its use. The main objective of this study was to evaluate the cost-effectiveness of nebulized salbutamol versus intravenous aminophylline for reduction in asthma symptoms, improvement in lung function, and a long hospital stay. The study involved 57 adults asthma exacerbation patients without complication who received treatment in the ER, were studied by using quasi-experimental methods in this study cost-effectiveness analysis to compare intravenous aminophylline (n:27) versus nebulized salbutamol (n:30) therapy to determine the most cost-effective. Intravenous aminophylline therapy was more cost-effective than nebulized salbutamol in reducing the symptoms of asthma and PEF value improvement. Clinical outcome of the length of hospital stay outcome both had the same effective, and cost analysis results showed intravenous aminophylline (US$5.38) cheaper than nebulized salbutamol (US$5.71). intravenous aminophylline was more effective in reducing asthma symptoms than nebulized salbutamol (Pvalue=0.001). Meanwhile, the average decrease in lung function intravenous aminophylline than nebulized salbutamol, although not significantly different (Pvalue=0.507). Aminophylline therapy was more cost-effective in reducing asthma symptoms and improvement in lung function compared nebulized salbutamol in exacerbations asthma patients. But cost-effectiveness researchers need to measure substance abuse outcomes in terms of Quality-Adjusted Life Years (QALY), as this will make their findings more relevant to the development of treatment policy.

Keywords: asthma, salbutamol, aminophylline, outcome, cost

Received: 19 May 2022 **Accepted**: 02 May 2024

DOI: https://doi.org/10.25026/jtpc.v8i1.435

How to Cite:

Lorensia, A., Ikawati, Z., Andayani, T. M., Maranatha, D., 2024. Cost-Effectiveness of Length of Stay of Intravenous Aminophylline and Nebulized Salbutamol in Asthma Exacerbations. *J. Trop. Pharm. Chem.* **8**(1). 35-47. **DOI**: https://doi.org/10.25026/jtpc.v8i1.435

1 Introduction

Asthma is a heterogeneous disease that can attack from all ages and economic factors, is one of the major health problems in the world [1], Asthma is a chronic inflammatory disorder of the airways, with many cells and cellular elements play a role [1,2]. Worsening asthma symptoms exacerbate asthma acute or sub-acute symptoms and lung function of asthmatic patient status conditions are usually [1]. Salbutamol and aminophylline (theophylline) are used for the treatment of exacerbations asthma [1], including in Indonesia [3,4]. Although salbutamol is the first line of exacerbations asthma [1], previous studies have concluded there is no difference in effectiveness between both of them. A study of randomized controlled trials (RCTs) was identified by Travers et al. [5], not found evidence consistent benefit on intravenous beta-2 agonist or intravenous aminophylline for asthma exacerbations (asthma attacks) [1]. While research by Roberts et al. said there was no difference in the effectiveness of salbutamol and aminophylline the first 2 hours, but aminophylline significantly reduces the length of hospital stay [6]. Small doses of theophylline are known not only can relax airway smooth muscle but also to have anti-inflammatory and immunomodulatory effects, which is the basic theory for the treatment of asthma [7,8]. In Indonesia, the use of aminophylline is still frequently used in the primary therapy of asthma exacerbations in the hospital because it is effective and rarely cause ADR events even when taken in conjunction with other asthma treatment [9,10,11,12]. Even when safety aminophylline compared with salbutamol showed no significant difference between the incidence of hypokalemia and hyponatremia [13]. Although the overseas use of theophylline/aminophylline has been abandoned because it is a drug with a narrow therapeutic range so that a risk of causing ADR [14]. Evidence regarding ADR events of theophylline and aminophylline had a lot of revealed [8,13,15,16,17], so its use abroad has been abandoned.

Differences in effects of aminophylline and salbutamol can be due to different individual characteristics, genetic factors are the main factors that cause a different response to asthma therapy [18,19,20], and drug response can be determined by the relationship between genotype [21,22,23,24]. Indonesian people, especially the Javanese most have gene polymorphism CYP1A2*1F [25]. A genotype at CYP1A2*1F allele are a fast metabolizer, compared with genotype C which is a slower metabolism. Therefore, CYP1A2*1F gene polymorphism (A/A) has a metabolism faster than C/C or C/A, thus causing more lower drug levels [26].

Exacerbations of asthma should receive attention is important because the high risk of causing suffering to patients and their families

as well as increased spending on the health system substantially [27]. The social and economic problems of asthma exacerbations are associated with direct costs (direct costs) of health care use and indirect costs (indirect costs) related to lost productivity [27,28]. Therefore, studies of cost-effectiveness analysis (CEA) to assess the direct costs (direct cost) required (input) and the resulting clinical outcome (output), by comparing the difference in cost (incremental costs) and the different effects (incremental effects) [29,30,31]. In 2003, a study of 401 adult asthma patients showed an annual total cost of illness per person (total per-person annual disease costs) by an average of $4,912. The direct costs by 65% and indirect costs (indirect costs) of approximately 35% of the total costs used in the treatment [32]. In Indonesia, the research conducted by Lorensia et al. [33], Involved patients in this study were 54 Patients, with the total number of problems were 259 cases. The cost of drug-related problems was US$1,983.29. This study demonstrates that effective and rational treatment can influence treatment costs. Therefore, research is needed to consider the selection of drugs in terms of the cost needed in terms of treatment and effectiveness of the drug as a therapeutic outcome.

2 Methods

2.1 Research Design.

The research design was quasi-experimental, so it does not randomize. Each hospital just to get treatment for asthma exacerbations same in all subjects, namely asthma therapy with nebulized salbutamol therapy or intravenous aminophylline.

2.2 Population and Sample.

The population was all patients with exacerbations of asthma in a hospital in Surabaya. Samples research (research subjects) are all patients with asthma exacerbations in all hospitals in Surabaya who meet the inclusion and exclusion criteria of the study. The inclusion criteria are research subjects: (i) Patients aged adults (≥18 years); (ii) Patients are willing to become a subject of research; (iii) The level of mild-moderate asthma exacerbations, because at that level should not be added corticosteroid or other asthma therapies, and patients with severe exacerbations of asthma at a rate of up to life-threatening need additional therapy such as anticholinergics and corticosteroids [1], that could affect the study results. Exclusion criteria research subjects are: (i) Patients who use contraception; (ii) The pregnant patient-lactating; (iii) Patients with chronic renal function impairment; (iv) Patients with chronic liver disease; (v) Patient smoked or quit smoking <2 years; (vi) coffee consumption; and (vii) Patients admitted to getting asthma exacerbation therapy before coming to the emergency room because another therapy/other asthma therapies can affect the outcome of the research is a clinical outcome and ADRs.

Sampling on the subject of the research is consecutive sampling because it is not obtained to frame the subject, so do capture subjects that meet the inclusion and exclusion criteria, who came to the hospital during a certain period. In this study, the great unknown population because the population is experiencing an exacerbation of asthma in a hospital in Surabaya, so it is assumed the general population is not known, based on the formula of Medical Statistics calculating a subject with proportions a subject with [34], then most minimal research subjects each group in this study was 26 people.

2.3 Therapeutic intervention.

Subjects were divided into two groups: the test group (intravenous aminophylline group) and the control group (nebulized salbutamol group). In the intravenous aminophylline group, patients received intravenous aminophylline therapy, slowly with a slow bolus of 6 mg/kg for 20 minutes, followed by infusion (0.9% NaCl) at 5 mcg/kg/hr. Theophylline 1 mg is equivalent to 1:25 mg aminophylline [34,35,36], and the nebulized salbutamol group, patients received nebulized salbutamol therapy 2×5 mg or 2 mL of 0.5% (+2 mL saline) [37,38].

2.4 Outcome.

The outcome used in this study was a reduction in symptoms, lung function improvement (with measurement PEF), and length of hospital stay.

2.5 Cost.

The costs taken into account in the study came from the perspective of the hospital, which was composed of direct costs, such as the cost of medicine, medical measures, the services of medical personnel, and equipment costs related to asthma therapy. Indirect costs and the intangible cost was not counted in this study because it uses a research perspective hospital to be observed during the treatment of asthma patients to get treatment at the hospital.

2.6 Data analysis.

The method of the CEA (Cost-Effectiveness Analysis) will be calculated:

2.6.1 Cost analysis.

Determine the ratio between the cost of the treatment given to the subject of research. Costs were observed originating from the hospital perspective, namely direct costs include nurse service costs, the cost of physician services, the cost of medical equipment, as well as the cost of drugs.

2.6.2 ACER (Average Cost-Effectiveness Ratio).

ACER is the ratio of the cost-effectiveness/benefit (effectiveness) of the treatment given to the subject of research.

The data on the characteristics of the two groups will be tested for homogeneity with chi-square test and if the P value> 0.05 means that the data was no difference between the two groups. Outcomes in the form of number of asthma symptoms (breathness, wheezing, chest tightness, and cough) and improvement in lung function based on peak expiratory flow value (L/Second), were tested on data collection before and after the intervention. Both groups were tested differently by chi-square test and if H0 was rejected when $p<0.05$ and if there wasn't a difference between the two groups.

3 Results and Discussion

3.1 Characteristics of Research Subjects.

The study involved 27 subjects of research on intravenous aminophylline groups and 30 in the nebulized salbutamol group, with a more descriptive can be seen in **Table 1**. Comorbidities/co-morbidities (comorbidities) was a disease that accompanies asthma (exacerbations of asthma), such as hypertension, type 2 diabetes mellitus, etc. Morbidities associated with worsening health, clinical management more complex, and increased health care costs [39,40,41]. Comorbidities experienced by research subjects in the nebulized salbutamol group as gastritis can affect the ADR parameter that causes nausea, vomiting, but in this study, the patients do not experience nausea and vomiting (**Table 1**).

Table 1. Frequency Distribution Baseline Subject Research Aminophylline Intravenous and Nebulized Salbutamol Group

Characters Baseline		Intravenous Aminophylline Group (n=27)		Nebulized Salbutamol Group (n=30)		Homogeneity
Gender	Female	14	(50.85%)	19	(63.33%)	0.176
	Male	13	(48.15%)	11	(36.67%)	
Age (years)	Late adolescence (17-25)	5	(18.52%)	7	(23.33%)	0.075
	Early adult (26-35)	5	(18.52%)	5	(16.67%)	
	Late adult (36-45)	7	(25.93%)	5	(16.67%)	
	Ederly early (46-55)	8	(29.63%)	6	(20.00%)	
	Ederly late (56-65)	2	(7.41%)	6	(20.00%)	
	>65	0	(0.00%)	1	(3.33%)	
	Average	40.11		40.83		
Accompanying diseases	dyslipidemia, type 2 diabetes mellitus	0	(0.00%)	1	(3.33%)	0.000
	dyslipidemia, hyperuricemia	0	(0.00%)	1	(3.33%)	
	type 2 diabetes mellitus, gastritis	0	(0.00%)	1	(3.33%)	
	gastritis	0	(0.00%)	1	(3.33%)	
	none	27	(100.00%)	26	(86.67%)	
Employment	household assistant	10	(37.04%)	10	(33.33%)	0.854
	entrepreneur	9	(33.33%)	10	(33.33%)	
	employee	4	(14.81%)	5	(16.67%)	
	student	4	(14.81%)	4	(13.33%)	
	does not work	0	(0.00%)	1	(3.33%)	

If the P value> 0.05 means that data is no difference between the two groups

3.2 Outcome: Decrease in asthma symptoms.

In Table 2, each of the symptoms experienced by each subject of study was accumulated and assessed a reduced number of symptoms. Then test with Kolmogorov-Smirnov normality, and continued test of independent sample t-test (ratio scale) when the parametric data. No differences in the initial conditions before the patient gets treatment between the two groups, but the groups of intravenous aminophylline were more effective in reducing asthma symptoms experienced by patients (most patients decreased 4 symptoms (55.56%) compared to the nebulized salbutamol group. Symptoms normally generated during exacerbation shortness of breath, the sound when breathing (wheezing), a sense of pressure in the chest. These symptoms occur reversibly and recurrent episodic [1]. Symptoms of shortness of symptom of asthma were the most common. At symptoms of shortness, the initial conditions showed no difference between the two groups and after the therapy showed improvement of symptoms significantly and there is a significant difference after therapy which shows that the group of aminophylline intravenously produces an improvement of symptoms greater than with nebulized salbutamol group. All patients who complained of shortness and tightness disappear before therapy by administration of the intervention in both groups **(Table 2)**.

Table 2. Number of Asthma Symptoms (Breathness, Wheezing, Chest Tightness, and Cough)

Time data collection	Total Symptom	Intravenous Aminophylline Group (n=27)		Nebulized Salbutamol Group (n=30)		Total	P value*
0	1	3	(11.11%)	2	(0.00%)	5	0.570
	2	4	(14.81%)	6	(20.00%)	10	
	3	5	(18.52%)	11	(36.67%)	16	
	4	15	(55.56%)	11	(36.67%)	26	
Average		3.18		3.03		3.10	
1	0	27	(100.00%)	16	(53.33%)	43	0.002
	1	0	(0.00%)	6	(20.00%)	6	
	2	0	(0.00%)	3	(10.00%)	3	
	3	0	(0.00%)	3	(10.00%)	3	
	4	0	(0.00%)	2	(6.67%)	2	
Average		0.00		0.97		0.51	
1-0	+1	0	(0.00%)	1	(3.33%)	1	0.001
	0	0	(0.00%)	2	(6.67%)	2	
	-1	3	(11.11%)	6	(20.00%)	9	
	-2	4	(14.81%)	10	(33.33%)	14	
	-3	5	(18.52%)	7	(23.33%)	12	
	-4	15	(55.56%)	4	(13.33%)	19	
Average $_{1-0}$		-3.19		-2.07		-2.60	
Changes in the value 0 to 1		There is a difference between 0 and 1		There is a difference between 0 and 1			

Total symptom= breathness+wheezing+chet thightness+cough (each symptom rated: 1)
0 = time before the beginning of therapy of asthma exacerbations
1 = time after the initial therapy of asthma exacerbations
1-0 = change / difference after prior therapy with an asthma exacerbation. The "+" means an increase in symptoms of 0 to 1; the sign "-" means to decrease the symptoms of 0 to 1
* if H0 is rejected when p <0.05. Meaning: There isn't a difference between the two groups

In **Table 2**, there was a difference between the initial conditions of the two groups before therapy in wheezing symptoms, but no difference in complaints of wheezing after receiving treatment between the two groups and wheezing conditions largely reduced in the two groups. At symptom distress in the chest and coughing, no differences in initial conditions before the patient gets treatment between the two groups, but the groups of intravenous aminophylline more effectively relieve pressure in the chest and coughing compared nebulized salbutamol group [42]. Symptoms of spontaneous cough were a reflex of the body for their foreign objects to clog or irritate the respiratory tract. Coughing is also

one of the symptoms that appear in asthma exacerbations [43,44], due to bronchoconstriction and inflammation causes blockage of the airways.

Intravenous aminophylline more effective than nebulized salbutamol in addressing the symptoms of shortness, a sense of pressure in the chest, and coughing in the first hour (**Table 2**). Another study by Travers et al. [5], a randomized controlled trial (RCT) using the Cochrane Airways Group Register, comparing intravenous aminophylline and beta-2 agonist administered intravenously in asthma exacerbations was hospitalized. In the RCT, is not found evidence consistent benefit both intravenous beta-2 agonist or aminophylline intravenously to patients with acute asthma. It supports research by Munro dan Jacobs [45], of 71 multiple small research trials that compared the effectiveness of intravenous aminophylline and intravenous salbutamol, found that intravenous salbutamol no better than aminophylline in reducing air obstruction in patients with asthma.

3.3 Outcome: Improvement in lung function.

Comparison of the repair value of PEF between the two groups using the test independent sample t-test (ratio scale), which had previously been tested for normality with the Kolmogorov-Smirnov with a p-value of 0.001 (intravenous aminophylline) and 0.001 (nebulized salbutamol), which means continued with test non-parametric. And after administration of asthma therapy, there was no difference in improvement PEF values between the two group therapy **(Table 3)**.

Table 3. Lung Function Improvements Based on Peak Expiratory Flow Value (L/Second)

Time data collection		Intravenous Aminophylline Group (n=27)	Nebulized Salbutamol Group (n=30)	P value*
0	Average	49.07	24.33	0.233
	SD	82	73	
1	Average	76.48	34.17	0.190
	SD	125	112	
1-0	Average	1.44	1.23	0.507
	SD	50	62	
Changes in the value 0 to 1		0,3463 There is a difference between 0 to 1	0.6873 There is a difference between 0 to 1	

PEF = Peak Ezpiratory Flow
0 = time before the beginning of therapy of asthma exacerbations
1 = time after the initial therapy of asthma exacerbations
1-0 = change/ difference after prior therapy with an asthma exacerbation. The "+" means an increase in symptoms of 0 to 1; the sign "-" means to decrease the symptoms of 0 to 1
* if H0 is rejected when p <0.05. Meaning: There isn't a difference between the two groups

Peak Expiratory Flow (PEF) values predicted peak expiratory rate, a measure of air velocity that can be exhaled lung fastest, after taking a deep breath is expressed in liters per second (L/s). Peak flow meter use rate the PEF. Peak current flow in a patient may indicate changes before a patient experienced an exacerbation [46,47]. Previous studies using PEF value as an asthma therapy clinical outcome had been done by Tattersfield et al. [48], Burkhart et al. [49], dan Turner et al. [50].

In **Table 3**, there was no difference in improvement PEF values between the two group therapy. Other studies that have been done by Littenberg [51], that comparisons between aminophylline therapy with other therapies such as salbutamol, epinephrine, or any other bronchodilators, it was found that there was no difference between aminophylline with the control group. Sensitivity analysis of suspect aminophylline therapy is not effective on its own and more effective when combined with beta-2 agonists. Although studies have been conducted widely, the available research does not provide sufficient evidence to support or reject the use of aminophylline in the treatment of acute severe asthma. Other previous research comparing the two drugs in the treatment of exacerbations of asthma are not yet available, and the reference supporters some studies compared the two drugs in the class or similar, on the condition of chronic

asthma (asthma is stable). As was done by Hartnett dan Marlin [52], comparing theophylline tablets with salbutamol MDI in patients with chronic asthma, salbutamol therapy concluded that further enhance the value of FEV1 after 180 minutes compared to theophylline. However, theophylline showed a longer duration of action and resulted in an increase in FEV1 significantly after 360 minutes, and concluded there was no significant difference to the total effect of the two drugs after 360 minutes. Another study in the form of s conducted by Davies et al. [53], in adult patients with chronic asthma, showed that during the two weeks of treatment, patients receiving salmeterol improve morning PEF value higher than theophylline. The previous study that looked at a combination of both compared to single therapy has also been performed by Dawson dan Fergusson [54], in asthma patients aged children, concluded that the combination therapy salbutamol and theophylline better in enhancing the value of PEF compared single theophylline. In contrast to the results of Nakano et al. [55], which compared aminophylline and nebulized salbutamol, it is known that treatment with aminophylline had the same benefits as nebulized salbutamol therapy in the recovery of lung function.

Measurement of lung function in this study assesses PEF (peak expiratory flow) with a peak flow meter with the same type and brand. The condition of patients who are experiencing an asthma exacerbation also affect the ability of the subject of current research to blow a peak flow meter for such a device would be affected the amount of air inhaled (inspired) and the amount of exhaled air (expiration), while at patients with exacerbations of asthma patients with impaired limitations in expiratory[1]. In addition, other factors that may affect PEF measurements, such as body weight and socioeconomic status [56,57].

Measurement of the best value the patient is not the parameter best value assessment of pulmonary function, because the best value patient should be derived from the value at the time the patient is not experiencing exacerbations of asthma, and the value is used as a benchmark to determine the variability of asthma control the patient with a reference when the value of PEF less than 80% of the value best patient then the patient is at risk for exacerbations of asthma or exacerbations [1]. The PEF value in the study came from the highest value of the peak flow meter blown subject of study which is the best value of the three measurements in the time before getting treatment and the best value of 3 times the measurement at the time after therapy. Then assessing the effectiveness of therapies derived from the improvement, the further the difference then showed a better improvement. One of the parameters of asthma exacerbations effectiveness of therapy is long hospitalization, assuming a more optimal therapy will require further treatment and requires a longer treatment. All the study subjects treated for one day and nothing requiring further treatment or even hospitalization.

A similar study was not found, but one previous study in asthma patients aged children by Roberts et al. [6], comparing intravenous aminophylline with intravenous salbutamol with the method of the randomized double-blind study, in 40 patients with children who have severe asthma exacerbations. This study suggests that the child severe asthma, there was no significant difference in the effectiveness of salbutamol with an IV bolus of aminophylline in the treatment of the first 2 hours, even on the whole, the infusion of aminophylline is superior because it reduces the length of stay in hospital significantly.

Some patients received adjunctive therapy in the form of oxygen, the unit amount of oxygen administered in the hospital is unknown and the cost of providing oxygen in the ER of US$ 1.39 based policies in the hospital where the study, in which oxygen therapy is given to patients with asthma exacerbations if saturation oxygen patients between 90-95% [1].

3.4 Costing.

Data in this study takes into account the cost of direct medical costs than patients without seeing non-medical costs, as it uses the perspective of the hospital. All three hospitals had great pricing standards that vary, therefore, be a limitation of the study that should determine the standard costs used for three different hospitals are. Selection of standard charge was not based on Standard Data research costs are not using System Indonesian

Case Base Groups (INA-CABGs) when appropriate PERMENKES or regulation of health minister No. 27 (2014) in the implementation of Health Insurance in the Social Security System in the Social Security Agency) 2014 according to the letter of the Director of Health Services BPJS No. 3889/III.2/0514 and Circular Letter No. Menkes KF/Menkes/167/III/2014 [58], because at the INA-CBGs use package systems based illnesses suffered by patients fare better medical services and non-medical data so that the costing based on the handling of the diagnosis, which resulted in all therapies have similar costs **(Table 4)**.

In **Table 4**, e-catalog data only includes infusion rates of 500 ml 0.9% NaCl, while used in the study was 0.9% Infusion of NaCl 25 ml and 100 ml are not listed in e-catalogs are reviewed in January 2015 and is not listed also in DPHO-XXXII edition of 2013. the infusion of NaCl was used in the study is the product of PT.Otsuka Indonesia, was based on a hospital policy research site and e-catalogs that use the same PT. Otsuka Indonesia as a provider of goods.

Table 4. Determination of the Costs that are used in Research Per Patient

Groups	Direct Cost		Reference
Intravenous Aminophylline Group	Drugs	Aminophylline injection of 24 mg / ml 10 ml	e-catalog 2014
		Infusion of NaCl 100 ml (Otsu-NS)	Not based on the e-catalog of 2014 because it is not listed in the e-catalog dosage form 100 ml
	Services of medical personnel	Physician services	PERMENKES RI NO 59 (2014) [59]
		Nurses Services *	
		Pharmaceutical care*	
		Medical treatment*	*)
	medical devices	10 mL syringe injection	e-catalog 2014
		adult Infuset	e-catalog 2014
		Alcohol swab (before the injection is done as an antiseptic)	*)
Nebulized Salbutamol Group	Drugs	Ventolin (Salbutamol fluid 0.1%) Packaging: Dus, 4x5 Plastic Bottle @ 2.5 ml	e-catalog 2014
		0.9% saline solution for nebules @ 25 ml (Otsu-NS)	Not based on the e-catalog of 2014 because it is not listed in the e-catalog dosage form 100 ml
		Oxigen	*)
	Services of medical personnel	Physician services	PERMENKES RI NO 59 (2014) [59]
		Services nurses	
		Pharmaceutical care	
	medical devices	Micromise nebulizer	*)
		Alcohol swab	*)

* No details of the volume per patient / per use. Data based on the price at hospital

Table 5. Cost Analysis of Intravenous Aminophylline and Nebulized Salbutamol

Cost (US$)	Intravenous Aminophylline Group (n=27)	Nebulized Salbutamol Group (n=30)
Drugs	2.45	0.97
Medical treatment	0.50	2.32
Physician & nurse services	2.42	2.42
Hospitalization costs	0.00	0.00
TOTAL	5.38	5.71
Independent t-test	P = 0.001 H0 as p <0.05. Meaning: the cost components, no significant differences between nebulized salbutamol group and intravenous aminophylline group Conclusion: Costs that were used in intravenous aminophylline group was significantly greater than in nebulized salbutamol group	

Average cost was used in the intravenous aminophylline group and nebulized salbutamol group in **Table 5**, showed that there are significant differences between the two groups, where the group of nebulized salbutamol greater costs compared with intravenous aminophylline (**Table 5**).

3.5 Cost-Effectiveness Analysis.

Selection of outcome in asthma exacerbations based on parameters improvement of Global Initiative for Asthma [1], and similar previous research in the form of pharmacoeconomics research to treat exacerbations of asthma that has been done by Vezina et al. [60], Lorensia and Bahari [61], Domínguez-Ortega et al. [62], and Andrew et al. [63].

Table 6. Cost-Effectivenes Analysis of Intravenous Aminophylline and Nebulized Salbutamol

Description Calculation CEA		Intravenous Aminophylline Group (n=27)	Nebulized Salbutamol Group (n=30)
Cost (US$)		5.38	5.71
Clinical Outcome:	Average$_{1-0}$	3.19	2.07
Decrease in asthma symptoms	ACER	24,352.66	39,827.05
Clinical Outcome:	Peak Expiratory Flow (L/second) $_{1-0}$	1.44	1.23
Improvement in lung function	ACER	53,947.92	67,026.02

1-0 = change/difference after prior therapy with an asthma exacerbation. The "+" means an increase in symptoms of 1-0; the sign "-" means to decrease the symptoms of 1-0

Table 6, showed that testosterone treatment exacerbations of asthma with intravenous aminophylline more cost-effective in reducing the symptoms of asthma compared to nebulized salbutamol and in the improvement of the value of peak expiratory flow compared to nebulized salbutamol. Long hospitalization was not observed for all study subjects hospitalized for 1 hour and no one gets an extension duration of therapy.

Based on tests of homogeneity of the characteristics of the study subjects was known that the characteristic morbidities have significant differences. **Table 1** showed the gender distribution between the two different groups. At the age of children, the prevalence of asthma in boys and girls. Whereas in adulthood, the prevalence of women was more likely to suffer from severe asthma and the onset of asthma is lower than that of men. This was due to an increase in ovarian hormones and testosterone which decrease the airway in asthma. Changes in asthma symptoms during the life phase of an adult woman, including pregnancy and menopause, during sex. hormones change dramatically [1,64].

3.6 Research limitations

3.6.1 Research design.

The research design used in this study was quasi-experimental, where the selection of subjects intervention group was not randomized (random), in contrast to the experimental true.

3.6.2 Hospitals.

Hospital type different affects the severity of the patients who come for treatment. Due to a tiered system of treatment, the hospital is at the top level (tertiary care facilities) have patients who are relatively more complications and more severe illness severity compared to lower health facilities.

3.6.3 Different routes of drug administration.

On the implementation of interventions for intravenous aminophylline, some of the study subjects had difficulty mounting the infusion. This is likely due to an asthma attack increased inflammatory mediators, one of the most influential is the increase in adrenalin and histamine that cause vasoconstriction in the pulmonary circulation and vasoconstriction of the systemic blood vessels [65,66]. Vasoconstriction of the blood vessels and the anxiety level of patients likely to cause difficulties in intravenous injection, whereas patients require immediate attention so that there is some potential research subjects who participated in the study were canceled due to difficulties in the initial injection. The time needed to find a vein in performing the injection also affects the length of the subject of research at the hospital.

While in the treatment of exacerbations of asthma with nebulized salbutamol, treatment preparation easier because the use of nebulized without invasive action. Beta-2 agonist (salbutamol) relaxes smooth muscle of the

airways and inhibits microvascular leakage and improves mucociliary transport by cilia activity or influencing the composition of mucus secretion. Agonists stimulate adenylate cyclase and increase the formation of cAMP in airway tissues. Bronchodilation caused by cAMP. The level of intracellular cAMP can be enhanced with adrenoceptor agonist, which increases the rate of synthesis by adenylate cyclase (AC); or by phosphodiesterase (PDE) inhibitor such as theophylline, which slows the rate of degradation. Bronchoconstriction can be inhibited by a muscarinic antagonist and possibly by an adenosine antagonist [67].

3.6.4 Sampling methods.

This study using consecutive sampling, because not found a subject framework, where previously unknown patients with asthma exacerbations so that researchers should be on stand-by waiting in each hospital. The weakness of this method is that there are several potential research subjects who missed the subject of research, which may be because sometimes researchers can not/ do not immediately come to a place of research, so that prospective research subjects can not be involved in research.

3.6.5 PEF measurement.

The research subjects never see and use a peak flow meter, and no demonstration of recurring due to the condition of patients who require immediate treatment (before therapy), whereas at the time of measurement before getting therapy is the first measurement time for all of the study subjects. Also other factors that could affect the measurement of PEF include gender, height and weight, and socioeconomic status [56,57].

4 Conclusions

Intravenous aminophylline therapy was more cost-effective than nebulized salbutamol in reducing the symptoms of asthma and PEF value improvement. In this study, the characteristics of the respondents in the form of gender (p=0.176), age (p=0.075), and employment (p=0.854) showed no difference between the two groups. Meanwhile, comorbidities (P=0.000) indicated that there were differences between the two groups and could affect the results of the study. Clinical outcome of the length of hospital stay outcome both had the same effective, and cost analysis results showed intravenous aminophylline (US$ 5.38) cheaper than nebulized salbutamol (US$ 5.71). intravenous aminophylline was more effective in reducing asthma symptoms than nebulized salbutamol (Pvalue=0.001). Meanwhile, the average decrease in lung function intravenous aminophylline (1.44) than nebulized salbutamol (1.23), although not significantly different (Pvalue=0.507).

5 Declarations

5.1 Acknowledgments

Funding sources: this research was funded by the Institute of Research and Community Service of the Universitas Surabaya.

5.2 Author Contributions

The names of the authors listed in this journal contributed to this research.

5.3 Funding Statement

This research was not supported by any funding sources.

5.4 Conflicts of Interest

The authors declare no conflict of interest.

5.5 Ethic

Ethical has been approved by the Commission on Health Research Ethics dr. Ramelan Hospital, Surabaya No. 01/EC/KERS/2014.

6 References

[1] Global Initiative for Asthma (GINA). Global Strategy for Asthma Management & Prevention (Update), USA. 2019.
[2] Bush, A. (2019). Pathophysiological Mechanisms of Asthma. Front Pediatr, 7(68):1–17.
[3] Kementerian Kesehatan. Keputusan Menteri Kesehatan Republik Indonesia, Nomor 312/MENKES/SK/IX/2015, tentang Daftar Obat Essensial 2015, Jakarta, Kementerian Kesehatan Republik Indonesia.
[4] Kementerian Kesehatan. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.02.02/MENKES/523/2015, tentang

Formularium Nasional, Jakarta, Kementerian Kesehatan Republik Indonesia.
[5] Travers, A.H., Jones, A.P., Camargo, C.A., Milan, S.J., and Rowe, B.H. (2012). Intravenous beta(2)-agonists versus intravenous aminophylline for acute asthma. Cochrane Database Syst Rev, 12:CD010256.
[6] Roberts, G., Newsom, D., Gomez, K., Raffles, A., Saglani, S., and Begent, J. (2003). Intravenous salbutamol bolus compared with an aminophylline infusion in children with severe asthma: a randomised controlled trial. Thorax, 58:306–10.
[7] Tilley, S.L. (2011). Methylxanthines in asthma. Handb Exp Pharmacol, 200:439–56.
[8] Barnes, P.J. (2010). Theophylline. Pharmaceuticals (Basel), 3(3):725–47.
[9] Lorensia, A., Wahjuningsih, E., Canggih, B., and Lisiska, N. (2011). Pharmacist's Strategies in Treating Asthma Bronchiale Outpatient. Jurnal of Tropical Pharmacy and Chemistry, 1(3):177–91.
[10] Lorensia, A., Wahjuningsih, E., and Supriadi. (2012). Safety of Aminophylline for Asthma Therapy in Delta Surya Hospital at Sidoarjo. Indonesia journal of Clinical Pharmacy, 1(4):154–61.
[11] Lorensia, A., Canggih, B., and Wijaya, R.I. (2013). Analysis of Adverse Drug Reactions in Asthma Patients in a Hospital, Surabaya. Jurnal Farmasi Indonesia, 6(3):142–50.
[12] Lorensia, A., Wahyudi, M., Yudiarso, A., and Kurnia, S.E.D. (2020). Effect of illness perception on improving asthma symptoms with omega-3 fish oil therapy: Pre-post design. Journal of Applied Pharmaceutical Science, 10(6):62–71.
[13] Lorensia, A., Ikawati, Z., Andayani, T.M., Maranatha, D., and Wahjudi, M. (2016). Comparison of Electrolyte Disturbance of Using Intravenous Aminophylline Versus Nebulization Salbutamol for Exacerbation Asthma in Surabaya, Indonesia. International Journal of Pharmaceutical and Clinical Research, 8(4):221–8.
[14] Dalabih, A., Harris, Z.L., Bondi, S.A., and Arnold, D.H. (2012). Contemporary aminophylline use for status asthmaticus in pediatric ICUs. Chest, 141(4):1122–3.
[15] Mahemuti, G., Zhang, H., Li, J., Tieliwaerdi, N., and Ren, L. (2018). Efficacy and side effects of intravenous theophylline in acute asthma: a systematic review and meta-analysis. Drug Des Devel Ther, 12:99–120.
[16] Saint, G.L., Semple, M.G., Sinha, I., and Hawcutt, D.B. (2018). Optimizing the Dosing of Intravenous Theophylline in Acute Severe Asthma in Children. Paediatr Drugs, 20(3):209–14.
[17] Cooney, L., Sinha, I., and Hawcutt, D. (2016). Aminophylline Dosage In Asthma Exacerbations in Children: A Systematic Review. PLoS One, 11(8):e0159965.
[18] Lorensia, A., Ikawati, Z., Andayani, T.M., Maranatha, D., and Wahyudi, M. (2019). CYP1A2 Gene Polymorphism and Theophylline Level in Asthma. The Indonesian Biomedical Journal, 11(1):63–9.
[19] Fenech, A.G., Grech, G. (2011). Pharmacogenetics: Where do we stand?. Journal of the Malta College of Pharmacy Practice, 11:25–33.
[20] Tse, S.M., Tantisira, K., and Weiss, S.T. (2011). The Pharmacogenetics and Pharmacogenomics of Asthma Therapy. Pharmacogenomics Journal, 11(6):383–92.
[21] Uslu, A., Ogus, C., Ozdemir, T., Bilgen, T., Tosun, O., and Keser, I. (2010). The effect of CYP1A2 gene polymorphisms on Theophylline metabolism and chronic obstructive pulmonary disease in Turkish patients. Biochemistry and Molecular Biology reports, 43(8):530–4.
[22] Obase, Y., Shimoda, T., Kawano, T., Saeki, S., Tomari, S.Y., Mitsuta-Izaki, K., Matsuse, H., Kinoshita, M., and Kohno, S. (2003). Polymorphisms in the CYP1A2 gene and theophylline metabolism in patients with asthma. Clinical Pharmacology and Therapeutics, 73(5):468–74.
[23] Roden, D.M., Wilke, R.A., Kroemer, H.K., and Stein, C.M. (2011). Pharmacogenomics: the genetics of variable drug responses. Circulation, 123(15):1661–70.
[24] Sanchez-Ibarra, H.E., Reyes-Cortes, L.M., Jiang, X.L., Luna-Aguirre, C.M., Aguirre-Trevino, D., Morales-Alvarado, I.A.M., Leon-Cachon, R.B., Lavalle-Gonzalez, F., Morcos, F., and Barrera-Saldana, H.A. (2018). Genotypic and Phenotypic Factors Influencing Drug Response in Mexican Patients With Type 2 Diabetes Mellitus. Front Pharmacol, 9(320):1–11.
[25] Queljoe, D.D., Wahjudi, M., Erdiansyah, M., Suryadinata, R.V., and Lorensia, A. (2014). Pilot Study on Genetic Polymorphisms CYP1A2*1F on Asthma Patients and Nonasthma in Indonesia. Indonesia journal of Clinical Pharmacy, 4(1):8–16.
[26] SNPedia. 2016, rs762551. [ONLINE] Available at: https://www.snpedia.com/index.php/Rs762551 [Accessed 12 Desember 2020].
[27] Nunes, C., Pereira, A.M., and Morais-Almeida, M. (2017). Asthma costs and social impact. Asthma Res Pract, 3(1):1–11.

[28] Souiotis, K., Kousoulakou, H., Hillas, G., Bakakos, P., Toumbis, M., Loukides, S., and Vassilakopoulos, T. (2017). Direct and Indirect Costs of Asthma Management in Greece: An Expert Panel Approach. Front. Public Health, 5(67):1–6.

[29] Cookson, R., Mirelman, A.J., Griffin, S., Asaria, M., Dawkins, B., Norheim, O.F., Verguet, S., and Culyer, A. (2017). Using Cost-Effectiveness Analysis to Address Health Equity Concerns. Value Health, 20(2):206–12.

[30] Thomas, R., Chalkidou, K. Cost–effectiveness analysis. 2016. In: Cylus J, Papanicolas I, Smith PC, editors. Health system efficiency: How to make measurement matter for policy and management. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2016. (Health Policy Series, No. 46.) 6. [ONLINE] Available at: https://www.ncbi.nlm.nih.gov/books/NBK436886/. [Accessed 12 Desember 2020].

[31] Savitz, L.A., Savitz, S.T. (2016). Can delivery systems use cost-effectiveness analysis to reduce healthcare costs and improve value?. F1000Res, 5(F1000):1–6.

[32] Chipps, B.E., Foggs, M.B. (2015). Asthma Management and the Allergist: Better Outcomes at Lower Cost. American College of Allergy. [ONLINE] Available at: https://college.acaai.org/sites/default/files/Asthma%20management.pdf. [Accessed 12 Desember 2020].

[33] Lorensia, A., Wijaya, R.I., and Canggih, B. (2013). Cost-Effectiveness Study related to Inpatient Selection of Bronchial Asthma Medication at a Private Hospital in Surabaya. Jurnal Ilmiah Sains & Teknologi, 7(1):56–63.

[34] Singh, A.S., Masuku, M.B. (2014). Sampling Techniques & Determination of Sample Size in Applied Statistics Research: An Overview. International Journal of Economics, Commerce and Management, 2(11):1–22.

[35] National Asthma Council Australia. 2006. Asthma Handbook: Version 2.0 Management Adults. [ONLINE] Available at: https://www.asthmahandbook.org.au/static/files/Australian-Asthma-Handbook-v2.0-Management-%E2%80%93-Adults.pdf. [Accessed 1 Maret 2021].

[36] Fong, N. (2011). Aminophylline/Theophylline: Loading and maintenance dose, NHS Trust: East Lancashire Hospitals. 2011

[37] Barnard, A. (2005). Management of an Acute Asthma Attack, Australian Family Physician, 34(7):531–4.

[38] Luo, Z., Liu, E., Luo, J., Li, S., Zeng, F., Yang, X., and Fu, Z. (2010). Nebulized hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis. Pediatr Int, 52(2):199–202.

[39] Kankaanranta, H., Kauppi, P., Tuomisto, L.E., and Ilmarinen, P. (2016). Emerging Comorbidities in Adult Asthma: Risks, Clinical Associations, and Mechanisms. Mediators of Inflammation, 3690628:1–23.

[40] Veenendaal, M., Westerik, J.A.M., Bemt, L.V.D., Kocks, J.W.H., Bischoff, E.W., and Schermer, T.R. (2019). Age- and sex-specific prevalence of chronic comorbidity in adult patients with asthma: A real-life study. NPJ Prim Care Respir Med, 29(14):1–7.

[41] Mahdavian, M., Power, B.H., Asghari, S., Pike, J.C. (2018). Effects of Comorbidities on Asthma Hospitalization and Mortality Rates: A Systematic Review. Can Respir J, 6460379:1–7.

[42] Lorensia, A., Wahyudi, M., Yudiarso, A., Kurnia, S.E.D. (2020). Effect of illness perception on improving asthma symptoms with omega-3 fish oil therapy: Pre-post design. Journal of Applied Pharmaceutical Science, 10(6):62–71.

[43] Niimi, A. (2011). Cough and Asthma. Curr Respir Med Rev, 7(1):47–54.

[44] Morjaria, J.B., Rigby, A.S., Morice, A.L. (2017). Asthma phenotypes: do cough and wheeze predict exacerbations in persistent asthma?. European Respiratory Journal, 50(1701366):1–9.

[45] Munro, A., Jacobs, M. (2004). Is intravenous aminophylline better than intravenous salbutamol in the treatment of moderate to severe asthma?. Emerg Med J, 21:78–80.

[46] Lorensia, A., Wahjudi, M., Yudiarso, A., Suryadinata, R.V., and Ratnasari, R. (2020). Pilot Study of Lung Function Improvement in Peak Expiratory Flow (PEF) Value Using Fish Oil Containing Omega-3 Therapy in Asthma. Global Medical & Health Communication, 8(3):211–8.

[47] Hua, J., Zhang, W., Cao, H.F., Du, C.L., Ma, J.Y., Zuo, Y.H., and Zhang, J. (2020). Effect of PIFR-based optimised inhalation therapy in patients recovering from acute exacerbation of chronic obstructive pulmonary disease: protocol of a prospective, multicentre, superiority, randomised controlled trial. BMJ Open, 10(e034804):1–9.

[48] Tattersfield, A.E., Postma, D.S., Barnes, P.J., Svensson, K., Bauer, C.A., O'Byrne, P.M., Löfdahl, C.G., Pauwels, R.A., Ullman, A. (1999). Exacerbations of asthma: a descriptive study of 425 severe exacerbations. Am J Respir Crit Care Med, 160:594–9.

[49] Burkhart, P.V., Rayens, M.K., and Oakley, M.G. (2012). Effect of Peak Flow Monitoring on Child Asthma Quality of Life. J Pediatr Nurs, 27(1):18–25.

[50] Turner, M.O., Taylor, D., Bennertt, R., Fitzgerald, J.M. (1998). A Randomized Trial Comparing Peak Expiratory Flow and Symptom Self-management Plans for Patients with Asthma Attending a Primary Care Clinic. American Journal of Respiratory and Critical Care Medicine, 157(2):540–6.
[51] Littenberg, B. (1988). Aminophylline Treatment in Severe, Acute Asthma a Meta-analysis. Journal of the American Medical Association (JAMA), 259(11):1678–84.
[52] Hartnett, B.J.S., Marlin, G.E. (1976). Comparison of oral theophylline and salbutamol by inhalation in asthmatic patients. Br J Clin Pharmacol, 3(4):591–4.
[53] Davies, B., Brooks, G., and Devoy, M. (1998). The efficacy and safety of salmeterol compared to theophylline: meta-analysis of nine controlled studies. Respiratory Medicine, 92(2):256–63.
[54] Dawson, K.P., Fergusson, D.M. (1982). Effects of oral theophylline and oral salbutamol in the treatment of asthma. Archives of Disease in Childhood, 57:674–6.
[55] Nakano, J., Yano, T., Yamamura, K., Yoshihara, H., Ohbayashi, O., Yamashita, N., and Ohta, K. (2006). Aminophilline suppress the release of chemical mediators in treatment of acute asthma. Respiratory Medicine, 100(3):542–50.
[56] Okour, A.M., Saadeh, R.A., Hijazi, M.H., Khalaileh, H.E.A., and Alfaqih, M.A. (2019). Socioeconomic status, perceptions and obesity among adolescents in Jordan. Pan Afr Med J, 34(148):1–9.
[57] Gradidge, P.J.L., Norris, S.A., Munthali, R. et al. (2018). Influence of socioeconomic status on changes in body size and physical activity in ageing black South African women. Eur Rev Aging Phys Act, 15(6):1–9.
[58] PERMENKES (Peraturan Menteri Kesehatan), Nomor 27 (2014), tentang Petunjuk Teknis Sistem Indonesian Case Base Groups (INA-CBGs), Jakarta, Kementerian Kesehatan Republik Indonesia.
[59] PERMENKES (Peraturan Menteri Kesehatan), Nomor 59 (2014), tentang Standar Tarif Pelayanan Kesehatan Dalam Penyelenggaraan Program Jaminan Kesehatan, Jakarta, Kementerian Kesehatan Republik Indonesia.
[60] Vezina, K., Chauhan, B.F., and Ducharme, F.M. (2014). Inhaled anticholinergics and short-acting beta2-agonists versus short-acting beta2-agonists alone for children with acute asthma in hospital. Cochrane Database Syst Rev, 31(CD010283):1–49.
[61] Lorensia, A., Bahari, F.K. (2020). Cost-Effectiveness Analysis between Salbutamol-Ipratropium Combination with Salbutamol in Asthma Attack. Jurnal Insan Farmasi Indonesia, 3(1):38–49.
[62] Domínguez-Ortega, J., Phillips-Anglés, E., Barranco, P., and Quirce, S. (2015). Cost-effectiveness of asthma therapy: a comprehensive review. J Asthma. 52(6):529–37.
[63] Andrew, A.L., Wong, K.A., Heine, D., Russell, W.S. (2012). A Cost-effectiveness Analysis of Dexamethasone Versus Prednisone in Pediatric Acute Asthma. Academic Emergency Medicine, 19(8):943–8.
[64] Fuseini, H., Newcomb, D.C. (2017). Mechanisms driving gender differences in asthma. Curr Allergy Asthma Rep, 17(3):19.
[65] Yamauchi, K., Ogasawara, M. (2019). The Role of Histamine in the Pathophysiology of Asthma and the Clinical Efficacy of Antihistamines in Asthma Therapy. Int J Mol Sci, 20(1733):1–16.
[66] Church, M.K. (2017). Allergy, Histamine and Antihistamines. Handb Exp Pharmacol, 241:321–31.
[67] Billington, C.K., Ojo, O.O., Penn, R.B., and Ito, S. (2013). cAMP regulation of airway smooth muscle function. Pulm Pharmacol Ther, 26(1):112–20.

Cost-Effectiveness of Length of Stay of Intravenous Aminophylline and Nebulized Salbutamol in Asthma Exacerbations

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DOI: https://doi.org/10.25026/jtpc.v8i1.435

Keywords: asthma, salbutamol, aminophylline, outcome, cost

Abstract

Asthma is a heterogeneous disease which is also one of the major health problems in the world. Uncontrolled asthma symptoms will exacerbate asthma, which is the biggest cause of the patient into the ER. Salbutamol is a bronchodilator that belonged to the short-acting beta-2 agonist (SABA), which is an obligatory choice in the management of asthma exacerbations. Unlike the aminophylline group in Indonesia which is still often used widely and rarely appear in the side effects of its use. The main objective of this study was to evaluate the cost-effectiveness of nebulized salbutamol versus intravenous aminophylline for reduction in asthma symptoms, improvement in lung function, and a long hospital stay. The study involved 57 adults asthma exacerbation patients without complication who received treatment in the ER, were studied by using quasi-experimental methods in this study cost-effectiveness analysis to compare intravenous aminophylline (n:27) versus nebulized salbutamol (n:30) therapy to determine the most cost-effective. Intravenous aminophylline therapy was more cost-effective than nebulized salbutamol in reducing the symptoms of asthma and PEF value improvement. Clinical outcome of the length of hospital stay outcome both had the same effective, and cost analysis results showed intravenous aminophylline (US$5.38) cheaper than nebulized salbutamol (US$5.71). intravenous aminophylline was more effective in reducing asthma symptoms than nebulized salbutamol (Pvalue=0.001). Meanwhile, the average decrease in lung function intravenous aminophylline than nebulized salbutamol, although not significantly different (Pvalue=0.507). Aminophylline therapy was more cost-effective in reducing asthma symptoms and improvement in lung function compared nebulized salbutamol in exacerbations asthma patients. But cost-

effectiveness researchers need to measure substance abuse outcomes in terms of Quality-Adjusted Life Years (QALY), as this will make their findings more relevant to the development of treatment policy.

Downloads

Download data is not yet available.

References

Global Initiative for Asthma (GINA). Global Strategy for Asthma Management & Prevention (Update), USA. 2019.

Bush, A. (2019). Pathophysiological Mechanisms of Asthma. Front Pediatr, 7(68):1–17.

Kementerian Kesehatan. Keputusan Menteri Kesehatan Republik Indonesia, Nomor 312/MENKES/SK/IX/2015, tentang Daftar Obat Essensial 2015, Jakarta, Kementerian Kesehatan Republik Indonesia.

Kementerian Kesehatan. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.02.02/MENKES/523/2015, tentang Formularium Nasional, Jakarta, Kementerian Kesehatan Republik Indonesia.

Travers, A.H., Jones, A.P., Camargo, C.A., Milan, S.J., and Rowe, B.H. (2012). Intravenous beta(2)-agonists versus intravenous aminophylline for acute asthma. Cochrane Database Syst Rev, 12:CD010256.

Roberts, G., Newsom, D., Gomez, K., Raffles, A., Saglani, S., and Begent, J. (2003). Intravenous salbutamol bolus compared with an aminophylline infusion in children with severe asthma: a randomised controlled trial. Thorax, 58:306–10.

Tilley, S.L. (2011). Methylxanthines in asthma. Handb Exp Pharmacol, 200:439?56.

Barnes, P.J. (2010). Theophylline. Pharmaceuticals (Basel), 3(3):725?47.

Lorensia, A., Wahjuningsih, E., Canggih, B., and Lisiska, N. (2011). Pharmacist's Strategies in Treating Asthma Bronchiale Outpatient. Jurnal of Tropical Pharmacy and Chemistry, 1(3):177–91.

Lorensia, A., Wahjuningsih, E., and Supriadi. (2012). Safety of Aminophylline for Asthma Therapy in Delta Surya Hospital at Sidoarjo. Indonesia journal of Clinical Pharmacy, 1(4):154–61.

Lorensia, A., Canggih, B., and Wijaya, R.I. (2013). Analysis of Adverse Drug Reactions in Asthma Patients in a Hospital, Surabaya. Jurnal Farmasi Indonesia, 6(3):142–50.

Lorensia, A., Wahyudi, M., Yudiarso, A., and Kurnia, S.E.D. (2020). Effect of illness perception on improving asthma symptoms with omega-3 fish oil therapy: Pre-post design. Journal of Applied Pharmaceutical Science, 10(6):62–71.

Lorensia, A., Ikawati, Z., Andayani, T.M., Maranatha, D., and Wahjudi, M. (2016). Comparison of Electrolyte Disturbance of Using Intravenous Aminophylline Versus Nebulization Salbutamol for Exacerbation Asthma in Surabaya, Indonesia. International Journal of Pharmaceutical and Clinical Research, 8(4):221–8.

Dalabih, A., Harris, Z.L., Bondi, S.A., and Arnold, D.H. (2012). Contemporary aminophylline use for status asthmaticus in pediatric ICUs. Chest, 141(4):1122–3.

Mahemuti, G., Zhang, H., Li, J., Tieliwaerdi, N., and Ren, L. (2018). Efficacy and side effects of intravenous theophylline in acute asthma: a systematic review and meta-analysis. Drug Des Devel Ther, 12:99?120.

Saint, G.L., Semple, M.G., Sinha, I., and Hawcutt, D.B. (2018). Optimizing the Dosing of Intravenous Theophylline in Acute Severe Asthma in Children. Paediatr Drugs, 20(3):209?14.

Cooney, L., Sinha, I., and Hawcutt, D. (2016). Aminophylline Dosage In Asthma Exacerbations in Children: A Systematic Review. PLoS One, 11(8):e0159965.

Lorensia, A., Ikawati, Z., Andayani, T.M., Maranatha, D., and Wahyudi, M. (2019). CYP1A2 Gene Polymorphism and Theophylline Level in Asthma. The Indonesian Biomedical Journal, 11(1):63–9.

Fenech, A.G., Grech, G. (2011). Pharmacogenetics: Where do we stand?. Journal of the Malta College of Pharmacy Practice, 11:25–33.

Tse, S.M., Tantisira, K., and Weiss, S.T. (2011). The Pharmacogenetics and Pharmacogenomics of Asthma Therapy. Pharmacogenomics Journal, 11(6):383?92.

Uslu, A., Ogus, C., Ozdemir, T., Bilgen, T., Tosun, O., and Keser, I. (2010). The effect of CYP1A2 gene polymorphisms on Theophylline metabolism and chronic obstructive pulmonary disease in Turkish patients. Biochemistry and Molecular Biology reports, 43(8):530?4.

Obase, Y., Shimoda, T., Kawano, T., Saeki, S., Tomari, S.Y., Mitsuta-Izaki, K., Matsuse, H., Kinoshita, M., and Kohno, S. (2003). Polymorphisms in the CYP1A2 gene and theophylline metabolism in patients with asthma. Clinical Pharmacology and Therapeutics, 73(5):468?74.

Roden, D.M., Wilke, R.A., Kroemer, H.K., and Stein, C.M. (2011). Pharmacogenomics: the genetics of variable drug responses. Circulation, 123(15):1661?70.

Sanchez-Ibarra, H.E., Reyes-Cortes, L.M., Jiang, X.L., Luna-Aguirre, C.M., Aguirre-Trevino, D., Morales-Alvarado, I.A.M., Leon-Cachon, R.B., Lavalle-Gonzalez, F., Morcos, F., and Barrera-Saldana, H.A. (2018). Genotypic and Phenotypic Factors Influencing Drug Response in Mexican Patients With Type 2 Diabetes Mellitus. Front Pharmacol, 9(320):1?11.

Queljoe, D.D., Wahjudi, M., Erdiansyah, M., Suryadinata, R.V., and Lorensia, A. (2014). Pilot Study on Genetic Polymorphisms CYP1A2*1F on Asthma Patients and Nonasthma in Indonesia. Indonesia journal of Clinical Pharmacy, 4(1):8?16.

SNPedia. 2016, rs762551. [ONLINE] Available at: https://www.snpedia.com/index.php/Rs762551 [Accessed 12 Desember 2020].

Nunes, C., Pereira, A.M., and Morais-Almeida, M. (2017). Asthma costs and social impact. Asthma Res Pract, 3(1):1?11.

Souiotis, K., Kousoulakou, H., Hillas, G., Bakakos, P., Toumbis, M., Loukides, S., and Vassilakopoulos, T. (2017). Direct and Indirect Costs of Asthma Management in Greece: An Expert Panel Approach. Front. Public Health, 5(67):1?6.

Cookson, R., Mirelman, A.J., Griffin, S., Asaria, M., Dawkins, B., Norheim, O.F., Verguet, S., and Culyer, A. (2017). Using Cost-Effectiveness Analysis to Address Health Equity Concerns. Value Health, 20(2):206–12.

Thomas, R., Chalkidou, K. Cost–effectiveness analysis. 2016. In: Cylus J, Papanicolas I, Smith PC, editors. Health system efficiency: How to make measurement matter for policy and management. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2016. (Health Policy Series, No. 46.) 6. [ONLINE] Available at: https://www.ncbi.nlm.nih.gov/books/NBK436886/. [Accessed 12 Desember 2020].

Savitz, L.A., Savitz, S.T. (2016). Can delivery systems use cost-effectiveness analysis to reduce healthcare costs and improve value?. F1000Res, 5(F1000):1?6.

Chipps, B.E., Foggs, M.B. (2015). Asthma Management and the Allergist: Better Outcomes at Lower Cost. American College of Allergy. [ONLINE] Available at: https://college.acaai.org/sites/default/files/Asthma%20management.pdf. [Accessed 12 Desember 2020].

Lorensia, A., Wijaya, R.I., and Canggih, B. (2013). Cost-Effectiveness Study related to Inpatient Selection of Bronchial Asthma Medication at a Private Hospital in Surabaya. Jurnal Ilmiah Sains & Teknologi, 7(1):56–63.

Singh, A.S., Masuku, M.B. (2014). Sampling Techniques & Determination of Sample Size in Applied Statistics Research: An Overview. International Journal of Economics, Commerce and Management, 2(11):1?22.

National Asthma Council Australia. 2006. Asthma Handbook: Version 2.0 Management Adults. [ONLINE] Available at: https://www.asthmahandbook.org.au/static/files/Australian-Asthma-Handbook-v2.0-Management-%E2%80%93-Adults.pdf. [Accessed 1 Maret 2021].

Fong, N. (2011). Aminophylline/Theophylline: Loading and maintenance dose, NHS Trust: East Lancashire Hospitals. 2011

Barnard, A. (2005). Management of an Acute Asthma Attack, Australian Family Physician, 34(7):531?4.

Luo, Z., Liu, E., Luo, J., Li, S., Zeng, F., Yang, X., and Fu, Z. (2010). Nebulized hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis. Pediatr Int, 52(2):199–202.

Kankaanranta, H., Kauppi, P., Tuomisto, L.E., and Ilmarinen, P. (2016). Emerging Comorbidities in Adult Asthma: Risks, Clinical Associations, and Mechanisms. Mediators of Inflammation, 3690628:1–23.

Veenendaal, M., Westerik, J.A.M., Bemt, L.V.D., Kocks, J.W.H., Bischoff, E.W., and Schermer, T.R. (2019). Age- and sex-specific prevalence of chronic comorbidity in adult patients with asthma: A real-life study. NPJ Prim Care Respir Med, 29(14):1?7.

Mahdavian, M., Power, B.H., Asghari, S., Pike, J.C. (2018). Effects of Comorbidities on Asthma Hospitalization and Mortality Rates: A Systematic Review. Can Respir J, 6460379:1–7.

Lorensia, A., Wahyudi, M., Yudiarso, A., Kurnia, S.E.D. (2020). Effect of illness perception on improving asthma symptoms with omega-3 fish oil therapy: Pre-post design. Journal of Applied Pharmaceutical Science, 10(6):62–71.

Niimi, A. (2011). Cough and Asthma. Curr Respir Med Rev, 7(1):47–54.

Morjaria, J.B., Rigby, A.S., Morice, A.L. (2017). Asthma phenotypes: do cough and wheeze predict exacerbations in persistent asthma?. European Respiratory Journal, 50(1701366):1–9.

Munro, A., Jacobs, M. (2004). Is intravenous aminophylline better than intravenous salbutamol in the treatment of moderate to severe asthma?. Emerg Med J, 21:78?80.

Lorensia, A., Wahjudi, M., Yudiarso, A., Suryadinata, R.V., and Ratnasari, R. (2020). Pilot Study of Lung Function Improvement in Peak Expiratory Flow (PEF) Value Using Fish Oil Containing Omega-3 Therapy in Asthma. Global Medical & Health Communication, 8(3):211–8.

Hua, J., Zhang, W., Cao, H.F., Du, C.L., Ma, J.Y., Zuo, Y.H., and Zhang, J. (2020). Effect of PIFR-based optimised inhalation therapy in patients recovering from acute exacerbation of chronic obstructive pulmonary disease: protocol of a prospective, multicentre, superiority, randomised controlled trial. BMJ Open, 10(e034804):1–9.

Tattersfield, A.E., Postma, D.S., Barnes, P.J., Svensson, K., Bauer, C.A., O'Byrne, P.M., Löfdahl, C.G., Pauwels, R.A., Ullman, A. (1999). Exacerbations of asthma: a descriptive study of 425 severe exacerbations. Am J Respir Crit Care Med, 160:594?9.

Burkhart, P.V., Rayens, M.K., and Oakley, M.G. (2012). Effect of Peak Flow Monitoring on Child Asthma Quality of Life. J Pediatr Nurs, 27(1):18–25.

Turner, M.O., Taylor, D., Bennertt, R., Fitzgerald, J.M. (1998). A Randomized Trial Comparing Peak Expiratory Flow and Symptom Self-management Plans for Patients with Asthma Attending a Primary Care Clinic. American Journal of Respiratory and Critical Care Medicine, 157(2):540?6.

Littenberg, B. (1988). Aminophylline Treatment in Severe, Acute Asthma a Meta-analysis. Journal of the American Medical Association (JAMA), 259(11):1678–84.

Hartnett, B.J.S., Marlin, G.E. (1976). Comparison of oral theophylline and salbutamol by inhalation in asthmatic patients. Br J Clin Pharmacol, 3(4):591–4.

Davies, B., Brooks, G., and Devoy, M. (1998). The efficacy and safety of salmeterol compared to theophylline: meta-analysis of nine controlled studies. Respiratory Medicine, 92(2):256–63.

Dawson, K.P., Fergusson, D.M. (1982). Effects of oral theophylline and oral salbutamol in the treatment of asthma. Archives of Disease in Childhood, 57:674–6.

Nakano, J., Yano, T., Yamamura, K., Yoshihara, H., Ohbayashi, O., Yamashita, N., and Ohta, K. (2006). Aminophilline suppress the release of chemical mediators in treatment of acute asthma. Respiratory Medicine, 100(3):542?50.

Okour, A.M., Saadeh, R.A., Hijazi, M.H., Khalaileh, H.E.A., and Alfaqih, M.A. (2019). Socioeconomic status, perceptions and obesity among adolescents in Jordan. Pan Afr Med J, 34(148):1?9.

Gradidge, P.J.L., Norris, S.A., Munthali, R. et al. (2018). Influence of socioeconomic status on changes in body size and physical activity in ageing black South African women. Eur Rev Aging Phys Act, 15(6):1–9.

PERMENKES (Peraturan Menteri Kesehatan), Nomor 27 (2014), tentang Petunjuk Teknis Sistem Indonesian Case Base Groups (INA-CBGs), Jakarta, Kementerian Kesehatan Republik Indonesia.

PERMENKES (Peraturan Menteri Kesehatan), Nomor 59 (2014), tentang Standar Tarif Pelayanan Kesehatan Dalam Penyelenggaraan Program Jaminan Kesehatan, Jakarta, Kementerian Kesehatan Republik Indonesia.

Vezina, K., Chauhan, B.F., and Ducharme, F.M. (2014). Inhaled anticholinergics and short-acting beta2-agonists versus short-acting beta2-agonists alone for children with acute asthma in hospital. Cochrane Database Syst Rev, 31(CD010283):1?49.

Lorensia, A., Bahari, F.K. (2020). Cost-Effectiveness Analysis between Salbutamol-Ipratropium Combination with Salbutamol in Asthma Attack. Jurnal Insan Farmasi Indonesia, 3(1):38–49.

Domínguez-Ortega, J., Phillips-Anglés, E., Barranco, P., and Quirce, S. (2015). Cost-effectiveness of asthma therapy: a comprehensive review. J Asthma. 52(6):529–37.

Andrew, A.L., Wong, K.A., Heine, D., Russell, W.S. (2012). A Cost-effectiveness Analysis of Dexamethasone Versus Prednisone in Pediatric Acute Asthma. Academic Emergency Medicine, 19(8):943?8.

Fuseini, H., Newcomb, D.C. (2017). Mechanisms driving gender differences in asthma. Curr Allergy Asthma Rep, 17(3):19.

Yamauchi, K., Ogasawara, M. (2019). The Role of Histamine in the Pathophysiology of Asthma and the Clinical Efficacy of Antihistamines in Asthma Therapy. Int J Mol Sci, 20(1733):1?16.

Church, M.K. (2017). Allergy, Histamine and Antihistamines. Handb Exp Pharmacol, 241:321–31.

Billington, C.K., Ojo, O.O., Penn, R.B., and Ito, S. (2013). cAMP regulation of airway smooth muscle function. Pulm Pharmacol Ther, 26(1):112?20.

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- Amelia Lorensia, Endang Wahjuningsih, Benny Canggih, Natalia Lisiska, Pharmacist's Strategies in Treating Asthma Bronchiale Outpatien , Journal of Tropical Pharmacy and Chemistry: Vol. 1 No. 3 (2011): J. Trop. Pharm. Chem.
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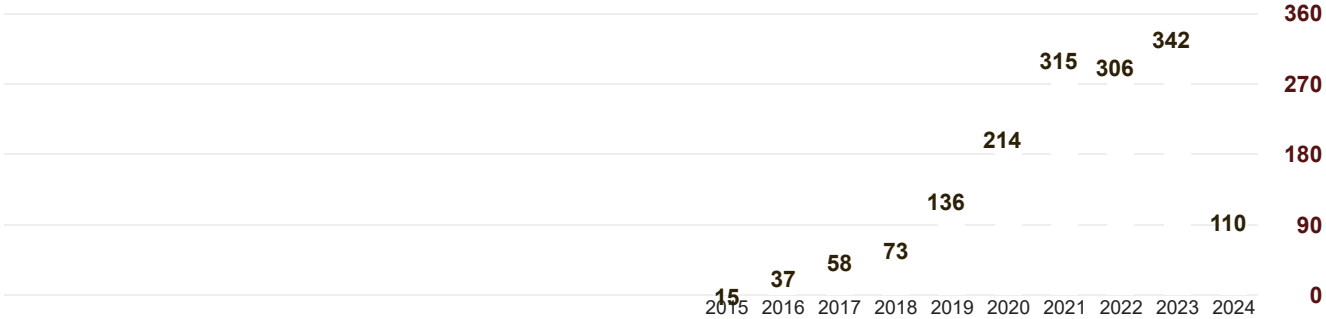

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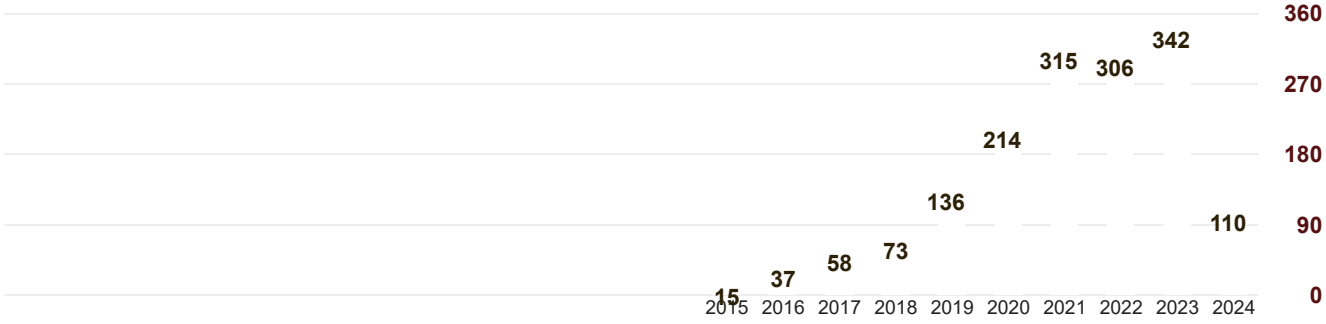

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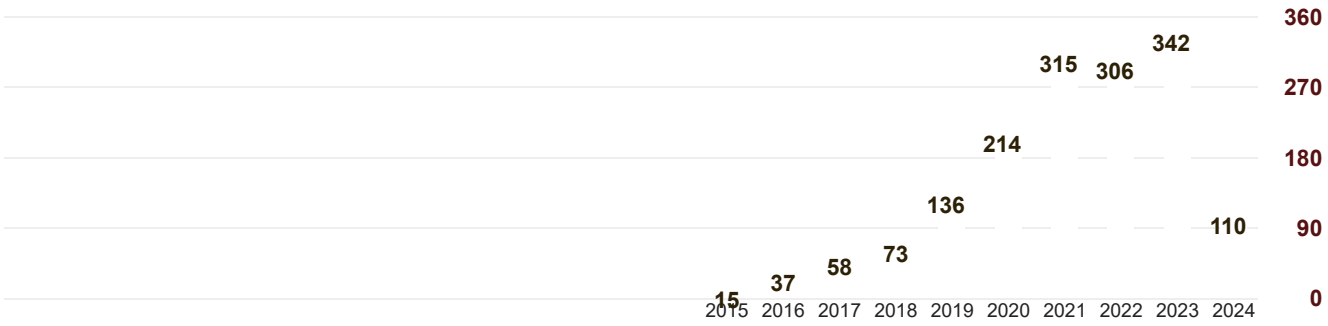

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Ethical Clearance

2019-12-11

Journal of Tropical Pharmacy and Chemistry accreditation

2019-04-16

Current Issue

Vol. 7 No. 2 (2023): J. Trop. Pharm. Chem.

Journal of Tropical Pharmacy and Chemistry (J. Trop. Pharm. Chem) Vol. 7 No. 2 December 2023 is present ten articles from two countries: Indonesia and Ghana.

DOI: https://doi.org/10.25026/jtpc.v7i2

Published: 2023-12-31

From Editor

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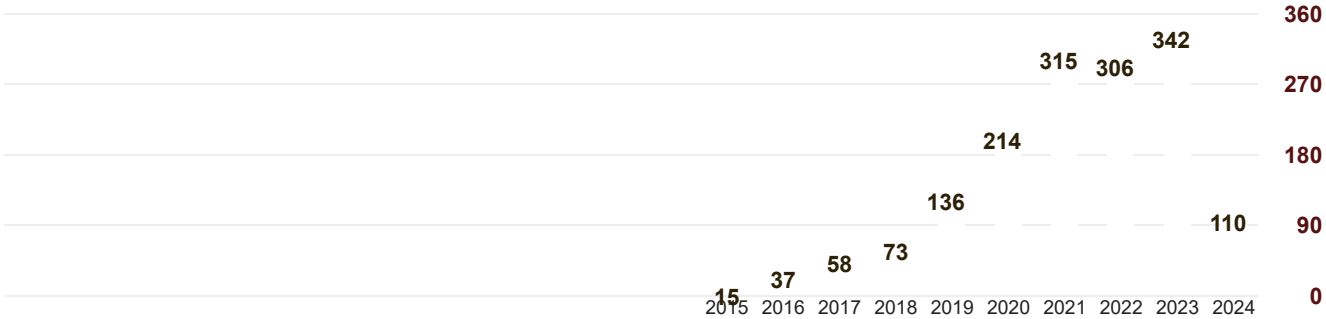

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1. J. Trop. Pharm. Chem.
2. J. Sains. Kes.
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FAKULTAS FARMASI UNIVERSITAS MULAWARMAN
P-ISSN : 20877099 E-ISSN : 24076090 Subject Area : Health, Science, Agriculture, Engineering

0.661538
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by Amelia Lorensia

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Submission ID: 2394422812
File name: inophylline_and_Nebulized_Salbutamol_in_Asthma_Exacerbations.pdf (3.51M)
Word count: 7112
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Cost-Effectiveness of Length of Stay of Intravenous Aminophylline and Nebulized Salbutamol in Asthma Exacerbations

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Abstract

Asthma is a heterogeneous disease which is also one of the major health problems in the world. Uncontrolled asthma symptoms will exacerbate asthma, which is the biggest cause of the patient into the ER. Salbutamol is a bronchodilator that belonged to the short-acting beta-2 agonist (SABA), which is an obligatory choice in the management of asthma exacerbations. Unlike the aminophylline group in Indonesia which is still often used widely and rarely appear in the side effects of its use. The main objective of this study was to evaluate the cost-effectiveness of nebulized salbutamol versus intravenous aminophylline for reduction in asthma symptoms, improvement in lung function, and a long hospital stay. The study involved 57 adults asthma exacerbation patients without complication who received treatment in the ER, were studied by using quasi-experimental methods in this study cost-effectiveness analysis to compare intravenous aminophylline (n:27) versus nebulized salbutamol (n:30) therapy to determine the most cost-effective. Intravenous aminophylline therapy was more cost-effective than nebulized salbutamol in reducing the symptoms of asthma and PEF value improvement. Clinical outcome of the length of hospital stay outcome both had the same effective, and cost analysis results showed intravenous aminophylline (US$5.38) cheaper than nebulized salbutamol (US$5.71). intravenous aminophylline was more effective in reducing asthma symptoms than nebulized salbutamol (Pvalue=0.001). Meanwhile, the average decrease in lung function intravenous aminophylline than nebulized salbutamol, although not significantly different (Pvalue=0.507). Aminophylline therapy was more cost-effective in reducing asthma symptoms and improvement in lung function compared nebulized salbutamol in exacerbations asthma patients. But cost-effectiveness researchers need to measure substance abuse outcomes in terms of Quality-Adjusted Life Years (QALY), as this will make their findings more relevant to the development of treatment policy.

Keywords: asthma, salbutamol, aminophylline, outcome, cost

Received: 19 May 2022 **Accepted**: 02 May 2024

DOI: https://doi.org/10.25026/jtpc.v8i1.435

How to Cite:

Lorensia, A., Ikawati, Z., Andayani, T. M., Maranatha, D., 2024. Cost-Effectiveness of Length of Stay of Intravenous Aminophylline and Nebulized Salbutamol in Asthma Exacerbations. *J. Trop. Pharm. Chem.* **8**(1). 35-47. **DOI**: https://doi.org/10.25026/jtpc.v8i1.435

1 Introduction

Asthma is a heterogeneous disease that can attack from all ages and economic factors, is one of the major health problems in the world [1], Asthma is a chronic inflammatory disorder of the airways, with many cells and cellular elements play a role [1,2]. Worsening asthma symptoms exacerbate asthma acute or sub-acute symptoms and lung function of asthmatic patient status conditions are usually [1]. Salbutamol and aminophylline (theophylline) are used for the treatment of exacerbations asthma [1], including in Indonesia [3,4]. Although salbutamol is the first line of exacerbations asthma [1], previous studies have concluded there is no difference in effectiveness between both of them. A study of randomized controlled trials (RCTs) was identified by Travers et al. [5], not found evidence consistent benefit on intravenous beta-2 agonist or intravenous aminophylline for asthma exacerbations (asthma attacks) [1]. While research by Roberts et al. said there was no difference in the effectiveness of salbutamol and aminophylline the first 2 hours, but aminophylline significantly reduces the length of hospital stay [6]. Small doses of theophylline are known not only can relax airway smooth muscle but also to have anti-inflammatory and immunomodulatory effects, which is the basic theory for the treatment of asthma [7,8]. In Indonesia, the use of aminophylline is still frequently used in the primary therapy of asthma exacerbations in the hospital because it is effective and rarely cause ADR events even when taken in conjunction with other asthma treatment [9,10,11,12]. Even when safety aminophylline compared with salbutamol showed no significant difference between the incidence of hypokalemia and hyponatremia [13]. Although the overseas use of theophylline/aminophylline has been abandoned because it is a drug with a narrow therapeutic range so that a risk of causing ADR [14]. Evidence regarding ADR events of theophylline and aminophylline had a lot of revealed [8,13,15,16,17], so its use abroad has been abandoned.

Differences in effects of aminophylline and salbutamol can be due to different individual characteristics, genetic factors are the main factors that cause a different response to asthma therapy [18,19,20], and drug response can be determined by the relationship between genotype [21,22,23,24]. Indonesian people, especially the Javanese most have gene polymorphism CYP1A2*1F [25]. A genotype at CYP1A2*1F allele are a fast metabolizer, compared with genotype C which is a slower metabolism. Therefore, CYP1A2*1F gene polymorphism (A/A) has a metabolism faster than C/C or C/A, thus causing more lower drug levels [26].

Exacerbations of asthma should receive attention is important because the high risk of causing suffering to patients and their families

as well as increased spending on the health system substantially [27]. The social and economic problems of asthma exacerbations are associated with direct costs (direct costs) of health care use and indirect costs (indirect costs) related to lost productivity [27,28]. Therefore, studies of cost-effectiveness analysis (CEA) to assess the direct costs (direct cost) required (input) and the resulting clinical outcome (output), by comparing the difference in cost (incremental costs) and the different effects (incremental effects) [29,30,31]. In 2003, a study of 401 adult asthma patients showed an annual total cost of illness per person (total per-person annual disease costs) by an average of $4,912. The direct costs by 65% and indirect costs (indirect costs) of approximately 35% of the total costs used in the treatment [32]. In Indonesia, the research conducted by Lorensia et al. [33], Involved patients in this study were 54 Patients, with the total number of problems were 259 cases. The cost of drug-related problems was US$1,983.29. This study demonstrates that effective and rational treatment can influence treatment costs. Therefore, research is needed to consider the selection of drugs in terms of the cost needed in terms of treatment and effectiveness of the drug as a therapeutic outcome.

2 Methods

2.1 Research Design.

The research design was quasi-experimental, so it does not randomize. Each hospital just to get treatment for asthma exacerbations same in all subjects, namely asthma therapy with nebulized salbutamol therapy or intravenous aminophylline.

2.2 Population and Sample.

The population was all patients with exacerbations of asthma in a hospital in Surabaya. Samples research (research subjects) are all patients with asthma exacerbations in all hospitals in Surabaya who meet the inclusion and exclusion criteria of the study. The inclusion criteria are research subjects: (i) Patients aged adults (≥18 years); (ii) Patients are willing to become a subject of research; (iii) The level of mild-moderate asthma exacerbations, because at that level should not be added corticosteroid or other asthma therapies, and patients with severe exacerbations of asthma at a rate of up to life-threatening need additional therapy such as anticholinergics and corticosteroids [1], that could affect the study results. Exclusion criteria research subjects are: (i) Patients who use contraception; (ii) The pregnant patient-lactating; (iii) Patients with chronic renal function impairment; (iv) Patients with chronic liver disease; (v) Patient smoked or quit smoking <2 years; (vi) coffee consumption; and (vii) Patients admitted to getting asthma exacerbation therapy before coming to the emergency room because another therapy/other asthma therapies can affect the outcome of the research is a clinical outcome and ADRs.

Sampling on the subject of the research is consecutive sampling because it is not obtained to frame the subject, so do capture subjects that meet the inclusion and exclusion criteria, who came to the hospital during a certain period. In this study, the great unknown population because the population is experiencing an exacerbation of asthma in a hospital in Surabaya, so it is assumed the general population is not known, based on the formula of Medical Statistics calculating a subject with proportions a subject with [34], then most minimal research subjects each group in this study was 26 people.

2.3 Therapeutic intervention.

Subjects were divided into two groups: the test group (intravenous aminophylline group) and the control group (nebulized salbutamol group). In the intravenous aminophylline group, patients received intravenous aminophylline therapy, slowly with a slow bolus of 6 mg/kg for 20 minutes, followed by infusion (0.9% NaCl) at 5 mcg/kg/hr. Theophylline 1 mg is equivalent to 1:25 mg aminophylline [34,35,36], and the nebulized salbutamol group, patients received nebulized salbutamol therapy 2×5 mg or 2 mL of 0.5% (+2 mL saline) [37,38].

2.4 Outcome.

The outcome used in this study was a reduction in symptoms, lung function improvement (with measurement PEF), and length of hospital stay.

2.5 Cost.

The costs taken into account in the study came from the perspective of the hospital, which was composed of direct costs, such as the cost of medicine, medical measures, the services of medical personnel, and equipment costs related to asthma therapy. Indirect costs and the intangible cost was not counted in this study because it uses a research perspective hospital to be observed during the treatment of asthma patients to get treatment at the hospital.

2.6 Data analysis.

The method of the CEA (Cost-Effectiveness Analysis) will be calculated:

2.6.1 Cost analysis.

Determine the ratio between the cost of the treatment given to the subject of research. Costs were observed originating from the hospital perspective, namely direct costs include nurse service costs, the cost of physician services, the cost of medical equipment, as well as the cost of drugs.

2.6.2 ACER (Average Cost-Effectiveness Ratio).

ACER is the ratio of the cost-effectiveness/benefit (effectiveness) of the treatment given to the subject of research.

The data on the characteristics of the two groups will be tested for homogeneity with chi-square test and if the P value> 0.05 means that the data was no difference between the two groups. Outcomes in the form of number of asthma symptoms (breathness, wheezing, chest tightness, and cough) and improvement in lung function based on peak expiratory flow value (L/Second), were tested on data collection before and after the intervention. Both groups were tested differently by chi-square test and if H0 was rejected when $p<0.05$ and if there wasn't a difference between the two groups.

3 Results and Discussion

3.1 Characteristics of Research Subjects.

The study involved 27 subjects of research on intravenous aminophylline groups and 30 in the nebulized salbutamol group, with a more descriptive can be seen in **Table 1**. Comorbidities/co-morbidities (comorbidities) was a disease that accompanies asthma (exacerbations of asthma), such as hypertension, type 2 diabetes mellitus, etc. Morbidities associated with worsening health, clinical management more complex, and increased health care costs [39,40,41]. Comorbidities experienced by research subjects in the nebulized salbutamol group as gastritis can affect the ADR parameter that causes nausea, vomiting, but in this study, the patients do not experience nausea and vomiting (**Table 1**).

Table 1. Frequency Distribution Baseline Subject Research Aminophylline Intravenous and Nebulized Salbutamol Group

Characters Baseline		Intravenous Aminophylline Group (n=27)		Nebulized Salbutamol Group (n=30)		Homogeneity
Gender	Female	14	(50.85%)	19	(63.33%)	0.176
	Male	13	(48.15%)	11	(36.67%)	
Age (years)	Late adolescence (17-25)	5	(18.52%)	7	(23.33%)	0.075
	Early adult (26-35)	5	(18.52%)	5	(16.67%)	
	Late adult (36-45)	7	(25.93%)	5	(16.67%)	
	Ederly early (46-55)	8	(29.63%)	6	(20.00%)	
	Ederly late (56-65)	2	(7.41%)	6	(20.00%)	
	>65	0	(0.00%)	1	(3.33%)	
	Average	40.11		40.83		
Accompanying diseases	dyslipidemia, type 2 diabetes mellitus	0	(0.00%)	1	(3.33%)	0.000
	dyslipidemia, hyperuricemia	0	(0.00%)	1	(3.33%)	
	type 2 diabetes mellitus, gastritis	0	(0.00%)	1	(3.33%)	
	gastritis	0	(0.00%)	1	(3.33%)	
	none	27	(100.00%)	26	(86.67%)	
Employment	household assistant	10	(37.04%)	10	(33.33%)	0.854
	entrepreneur	9	(33.33%)	10	(33.33%)	
	employee	4	(14.81%)	5	(16.67%)	
	student	4	(14.81%)	4	(13.33%)	
	does not work	0	(0.00%)	1	(3.33%)	

If the P value> 0.05 means that data is no difference between the two groups

3.2 Outcome: Decrease in asthma symptoms.

In Table 2, each of the symptoms experienced by each subject of study was accumulated and assessed a reduced number of symptoms. Then test with Kolmogorov-Smirnov normality, and continued test of independent sample t-test (ratio scale) when the parametric data. No differences in the initial conditions before the patient gets treatment between the two groups, but the groups of intravenous aminophylline were more effective in reducing asthma symptoms experienced by patients (most patients decreased 4 symptoms (55.56%) compared to the nebulized salbutamol group. Symptoms normally generated during exacerbation shortness of breath, the sound when breathing (wheezing), a sense of pressure in the chest. These symptoms occur reversibly and recurrent episodic [1]. Symptoms of shortness of symptom of asthma were the most common. At symptoms of shortness, the initial conditions showed no difference between the two groups and after the therapy showed improvement of symptoms significantly and there is a significant difference after therapy which shows that the group of aminophylline intravenously produces an improvement of symptoms greater than with nebulized salbutamol group. All patients who complained of shortness and tightness disappear before therapy by administration of the intervention in both groups **(Table 2)**.

Table 2. Number of Asthma Symptoms (Breathness, Wheezing, Chest Tightness, and Cough)

Time data collection	Total Symptom	Intravenous Aminophylline Group (n=27)		Nebulized Salbutamol Group (n=30)		Total	P value*
0	1	3	(11.11%)	2	(0.00%)	5	0.570
	2	4	(14.81%)	6	(20.00%)	10	
	3	5	(18.52%)	11	(36.67%)	16	
	4	15	(55.56%)	11	(36.67%)	26	
Average		3.18		3.03		3.10	
1	0	27	(100.00%)	16	(53.33%)	43	0.002
	1	0	(0.00%)	6	(20.00%)	6	
	2	0	(0.00%)	3	(10.00%)	3	
	3	0	(0.00%)	3	(10.00%)	3	
	4	0	(0.00%)	2	(6.67%)	2	
Average		0.00		0.97		0.51	
1-0	+1	0	(0.00%)	1	(3.33%)	1	0.001
	0	0	(0.00%)	2	(6.67%)	2	
	-1	3	(11.11%)	6	(20.00%)	9	
	-2	4	(14.81%)	10	(33.33%)	14	
	-3	5	(18.52%)	7	(23.33%)	12	
	-4	15	(55.56%)	4	(13.33%)	19	
Average $_{1-0}$		-3.19		-2.07		-2.60	
Changes in the value 0 to 1		There is a difference between 0 and 1		There is a difference between 0 and 1			

Total symptom= breathness+wheezing+chet thightness+cough (each symptom rated: 1)
0 = time before the beginning of therapy of asthma exacerbations
1 = time after the initial therapy of asthma exacerbations
1-0 = change / difference after prior therapy with an asthma exacerbation. The "+" means an increase in symptoms of 0 to 1; the sign "-" means to decrease the symptoms of 0 to 1
* if H0 is rejected when p <0.05. Meaning: There isn't a difference between the two groups

In **Table 2**, there was a difference between the initial conditions of the two groups before therapy in wheezing symptoms, but no difference in complaints of wheezing after receiving treatment between the two groups and wheezing conditions largely reduced in the two groups. At symptom distress in the chest and coughing, no differences in initial conditions before the patient gets treatment between the two groups, but the groups of intravenous aminophylline more effectively relieve pressure in the chest and coughing compared nebulized salbutamol group [42]. Symptoms of spontaneous cough were a reflex of the body for their foreign objects to clog or irritate the respiratory tract. Coughing is also

one of the symptoms that appear in asthma exacerbations [43,44], due to bronchoconstriction and inflammation causes blockage of the airways.

Intravenous aminophylline more effective than nebulized salbutamol in addressing the symptoms of shortness, a sense of pressure in the chest, and coughing in the first hour (**Table 2**). Another study by Travers et al. [5], a randomized controlled trial (RCT) using the Cochrane Airways Group Register, comparing intravenous aminophylline and beta-2 agonist administered intravenously in asthma exacerbations was hospitalized. In the RCT, is not found evidence consistent benefit both intravenous beta-2 agonist or aminophylline intravenously to patients with acute asthma. It supports research by Munro dan Jacobs [45], of 71 multiple small research trials that compared the effectiveness of intravenous aminophylline and intravenous salbutamol, found that intravenous salbutamol no better than aminophylline in reducing air obstruction in patients with asthma.

3.3 Outcome: Improvement in lung function.

Comparison of the repair value of PEF between the two groups using the test independent sample t-test (ratio scale), which had previously been tested for normality with the Kolmogorov-Smirnov with a p-value of 0.001 (intravenous aminophylline) and 0.001 (nebulized salbutamol), which means continued with test non-parametric. And after administration of asthma therapy, there was no difference in improvement PEF values between the two group therapy **(Table 3)**.

Table 3. Lung Function Improvements Based on Peak Expiratory Flow Value (L/Second)

Time data collection		Intravenous Aminophylline Group (n=27)	Nebulized Salbutamol Group (n=30)	P value*
0	Average	49.07	24.33	0.233
	SD	82	73	
1	Average	76.48	34.17	0.190
	SD	125	112	
1-0	Average	1.44	1.23	0.507
	SD	50	62	
Changes in the value 0 to 1		0,3463 There is a difference between 0 to 1	0.6873 There is a difference between 0 to 1	

PEF = Peak Ezpiratory Flow
0 = time before the beginning of therapy of asthma exacerbations
1 = time after the initial therapy of asthma exacerbations
1-0 = change/ difference after prior therapy with an asthma exacerbation. The "+" means an increase in symptoms of 0 to 1; the sign "-" means to decrease the symptoms of 0 to 1
* if H0 is rejected when p <0.05. Meaning: There isn't a difference between the two groups

Peak Expiratory Flow (PEF) values predicted peak expiratory rate, a measure of air velocity that can be exhaled lung fastest, after taking a deep breath is expressed in liters per second (L/s). Peak flow meter use rate the PEF. Peak current flow in a patient may indicate changes before a patient experienced an exacerbation [46,47]. Previous studies using PEF value as an asthma therapy clinical outcome had been done by Tattersfield et al. [48], Burkhart et al. [49], dan Turner et al. [50].

In **Table 3**, there was no difference in improvement PEF values between the two group therapy. Other studies that have been done by Littenberg [51], that comparisons between aminophylline therapy with other therapies such as salbutamol, epinephrine, or by other bronchodilators, it was found that there was no difference between aminophylline with the control group. Sensitivity analysis of suspect aminophylline therapy is not effective on its own and more effective when combined with beta-2 agonists. Although studies have been conducted widely, the available research does not provide sufficient evidence to support or reject the use of aminophylline in the treatment of acute severe asthma. Other previous research comparing the two drugs in the treatment of exacerbations of asthma are not yet available, and the reference supporters some studies compared the two drugs in the class or similar, on the condition of chronic

asthma (asthma is stable). As was done by Hartnett dan Marlin [52], comparing theophylline tablets with salbutamol MDI in patients with chronic asthma, salbutamol therapy concluded that further enhance the value of FEV1 after 180 minutes compared to theophylline. However, theophylline showed a longer duration of action and resulted in an increase in FEV1 significantly after 360 minutes, and concluded there was no significant difference to the total effect of the two drugs after 360 minutes. Another study in the form of s conducted by Davies et al. [53], in adult patients with chronic asthma, showed that during the two weeks of treatment, patients receiving salmeterol improve morning PEF value higher than theophylline. The previous study that looked at a combination of both compared to single therapy has also been performed by Dawson dan Fergusson [54], in asthma patients aged children, concluded that the combination therapy salbutamol and theophylline better in enhancing the value of PEF compared single theophylline. In contrast to the results of Nakano et al. [55], which compared aminophylline and nebulized salbutamol, it is known that treatment with aminophylline had the same benefits as nebulized salbutamol therapy in the recovery of lung function.

Measurement of lung function in this study assesses PEF (peak expiratory flow) with a peak flow meter with the same type and brand. The condition of patients who are experiencing an asthma exacerbation also affect the ability of the subject of current research to blow a peak flow meter for such a device would be affected the amount of air inhaled (inspired) and the amount of exhaled air (expiration), while at patients with exacerbations of asthma patients with impaired limitations in expiratory[1]. In addition, other factors that may affect PEF measurements, such as body weight and socioeconomic status [56,57].

Measurement of the best value the patient is not the parameter best value assessment of pulmonary function, because the best value patient should be derived from the value at the time the patient is not experiencing exacerbations of asthma, and the value is used as a benchmark to determine the variability of asthma control the patient with a reference when the value of PEF less than 80% of the value best patient then the patient is at risk for exacerbations of asthma or exacerbations [1]. The PEF value in the study came from the highest value of the peak flow meter blown subject of study which is the best value of the three measurements in the time before getting treatment and the best value of 3 times the measurement at the time after therapy. Then assessing the effectiveness of therapies derived from the improvement, the further the difference then showed a better improvement. One of the parameters of asthma exacerbations effectiveness of therapy is long hospitalization, assuming a more optimal therapy will require further treatment and requires a longer treatment. All the study subjects treated for one day and nothing requiring further treatment or even hospitalization.

A similar study was not found, but one previous study in asthma patients aged children by Roberts et al. [6], comparing intravenous aminophylline with intravenous salbutamol with the method of the randomized double-blind study, in 40 patients with children who have severe asthma exacerbations. This study suggests that the child severe asthma, there was no significant difference in the effectiveness of salbutamol with an IV bolus of aminophylline in the treatment of the first 2 hours, even on the whole, the infusion of aminophylline is superior because it reduces the length of stay in hospital significantly.

Some patients received adjunctive therapy in the form of oxygen, the unit amount of oxygen administered in the hospital is unknown and the cost of providing oxygen in the ER of US$ 1.39 based policies in the hospital where the study, in which oxygen therapy is given to patients with asthma exacerbations if saturation oxygen patients between 90-95% [1].

3.4 Costing.

Data in this study takes into account the cost of direct medical costs than patients without seeing non-medical costs, as it uses the perspective of the hospital. All three hospitals had great pricing standards that vary, therefore, be a limitation of the study that should determine the standard costs used for three different hospitals are. Selection of standard charge was not based on Standard Data research costs are not using System Indonesian

Case Base Groups (INA-CABGs) when appropriate PERMENKES or regulation of health minister No. 27 (2014) in the implementation of Health Insurance in the Social Security System in the Social Security Agency) 2014 according to the letter of the Director of Health Services BPJS No. 3889/III.2/0514 and Circular Letter No. Menkes KF/Menkes/167/III/2014 [58], because at the INA-CBGs use package systems based illnesses suffered by patients fare better medical services and non-medical data so that the costing based on the handling of the diagnosis, which resulted in all therapies have similar costs **(Table 4)**.

In **Table 4**, e-catalog data only includes infusion rates of 500 ml 0.9% NaCl, while used in the study was 0.9% Infusion of NaCl 25 ml and 100 ml are not listed in e-catalogs are reviewed in January 2015 and is not listed also in DPHO-XXXII edition of 2013. the infusion of NaCl was used in the study is the product of PT.Otsuka Indonesia, was based on a hospital policy research site and e-catalogs that use the same PT. Otsuka Indonesia as a provider of goods.

Table 4. Determination of the Costs that are used in Research Per Patient

Groups	Direct Cost		Reference
Intravenous Aminophylline Group	Drugs	Aminophylline injection of 24 mg / ml 10 ml	e-catalog 2014
		Infusion of NaCl 100 ml (Otsu-NS)	Not based on the e-catalog of 2014 because it is not listed in the e-catalog dosage form 100 ml
	Services of medical personnel	Physician services	PERMENKES RI NO 59 (2014) [59]
		Nurses Services *	
		Pharmaceutical care*	
		Medical treatment*	*)
	medical devices	10 mL syringe injection	e-catalog 2014
		adult Infuset	e-catalog 2014
		Alcohol swab (before the injection is done as an antiseptic)	*)
Nebulized Salbutamol Group	Drugs	Ventolin (Salbutamol fluid 0.1%) Packaging: Dus, 4x5 Plastic Bottle @ 2.5 ml	e-catalog 2014
		0.9% saline solution for nebules @ 25 ml (Otsu-NS)	Not based on the e-catalog of 2014 because it is not listed in the e-catalog dosage form 100 ml
		Oxigen	*)
	Services of medical personnel	Physician services	PERMENKES RI NO 59 (2014) [59]
		Services nurses	
		Pharmaceutical care	
	medical devices	Micromise nebulizer	*)
		Alcohol swab	*)

* No details of the volume per patient / per use. Data based on the price at hospital

Table 5. Cost Analysis of Intravenous Aminophylline and Nebulized Salbutamol

Cost (US$)	Intravenous Aminophylline Group (n=27)	Nebulized Salbutamol Group (n=30)
Drugs	2.45	0.97
Medical treatment	0.50	2.32
Physician & nurse services	2.42	2.42
Hospitalization costs	0.00	0.00
TOTAL	5.38	5.71
Independent t-test	P = 0.001 H0 as p <0.05. Meaning: the cost components, no significant differences between nebulized salbutamol group and intravenous aminophylline group Conclusion: Costs that were used in intravenous aminophylline group was significantly greater than in nebulized salbutamol group	

Average cost was used in the intravenous aminophylline group and nebulized salbutamol group in **Table 5**, showed that there are significant differences between the two groups, where the group of nebulized salbutamol greater costs compared with intravenous aminophylline (**Table 5**).

3.5 Cost-Effectiveness Analysis.

Selection of outcome in asthma exacerbations based on parameters improvement of Global Initiative for Asthma [1], and similar previous research in the form of pharmacoeconomics research to treat exacerbations of asthma that has been done by Vezina et al. [60], Lorensia and Bahari [61], Domínguez-Ortega et al. [62], and Andrew et al. [63].

Table 6. Cost-Effectivenes Analysis of Intravenous Aminophylline and Nebulized Salbutamol

Description Calculation CEA		Intravenous Aminophylline Group (n=27)	Nebulized Salbutamol Group (n=30)
Cost (US$)		5.38	5.71
Clinical Outcome:	Average$_{1\text{-}0}$	3.19	2.07
Decrease in asthma symptoms	ACER	24,352.66	39,827.05
Clinical Outcome:	Peak Expiratory Flow (L/second) $_{1\text{-}0}$	1.44	1.23
Improvement in lung function	ACER	53,947.92	67,026.02

1-0 = change/difference after prior therapy with an asthma exacerbation. The "+" means an increase in symptoms of 1-0; the sign "-" means to decrease the symptoms of 1-0

Table 6, showed that testosterone treatment exacerbations of asthma with intravenous aminophylline more cost-effective in reducing the symptoms of asthma compared to nebulized salbutamol and in the improvement of the value of peak expiratory flow compared to nebulized salbutamol. Long hospitalization was not observed for all study subjects hospitalized for 1 hour and no one gets an extension duration of therapy.

Based on tests of homogeneity of the characteristics of the study subjects was known that the characteristic morbidities have significant differences. **Table 1** showed the gender distribution between the two different groups. At the age of children, the prevalence of asthma in boys and girls. Whereas in adulthood, the prevalence of women was more likely to suffer from severe asthma and the onset of asthma is lower than that of men. This was due to an increase in ovarian hormones and testosterone which decrease the airway in asthma. Changes in asthma symptoms during the life phase of an adult woman, including pregnancy and menopause, during sex. hormones change dramatically [1,64].

3.6 Research limitations

3.6.1 Research design.

The research design used in this study was quasi-experimental, where the selection of subjects intervention group was not randomized (random), in contrast to the experimental true.

3.6.2 Hospitals.

Hospital type different affects the severity of the patients who come for treatment. Due to a tiered system of treatment, the hospital is at the top level (tertiary care facilities) have patients who are relatively more complications and more severe illness severity compared to lower health facilities.

3.6.3 Different routes of drug administration.

On the implementation of interventions for intravenous aminophylline, some of the study subjects had difficulty mounting the infusion. This is likely due to an asthma attack increased inflammatory mediators, one of the most influential is the increase in adrenalin and histamine that cause vasoconstriction in the pulmonary circulation and vasoconstriction of the systemic blood vessels [65,66]. Vasoconstriction of the blood vessels and the anxiety level of patients likely to cause difficulties in intravenous injection, whereas patients require immediate attention so that there is some potential research subjects who participated in the study were canceled due to difficulties in the initial injection. The time needed to find a vein in performing the injection also affects the length of the subject of research at the hospital.

While in the treatment of exacerbations of asthma with nebulized salbutamol, treatment preparation easier because the use of nebulized without invasive action. Beta-2 agonist (salbutamol) relaxes smooth muscle of the

airways and inhibits microvascular leakage and improves mucociliary transport by cilia activity or influencing the composition of mucus secretion. Agonists stimulate adenylate cyclase and increase the formation of cAMP in airway tissues. Bronchodilation caused by cAMP. The level of intracellular cAMP can be enhanced with adrenoceptor agonist, which increases the rate of synthesis by adenylate cyclase (AC); or by phosphodiesterase (PDE) inhibitor such as theophylline, which slows the rate of degradation. Bronchoconstriction can be inhibited by a muscarinic antagonist and possibly by an adenosine antagonist [67].

3.6.4 Sampling methods.

This study using consecutive sampling, because not found a subject framework, where previously unknown patients with asthma exacerbations so that researchers should be on stand-by waiting in each hospital. The weakness of this method is that there are several potential research subjects who missed the subject of research, which may be because sometimes researchers can not/ do not immediately come to a place of research, so that prospective research subjects can not be involved in research.

3.6.5 PEF measurement.

The research subjects never see and use a peak flow meter, and no demonstration of recurring due to the condition of patients who require immediate treatment (before therapy), whereas at the time of measurement before getting therapy is the first measurement time for all of the study subjects. Also other factors that could affect the measurement of PEF include gender, height and weight, and socioeconomic status [56,57].

4 Conclusions

Intravenous aminophylline therapy was more cost-effective than nebulized salbutamol in reducing the symptoms of asthma and PEF value improvement. In this study, the characteristics of the respondents in the form of gender (p=0.176), age (p=0.075), and employment (p=0.854) showed no difference between the two groups. Meanwhile, comorbidities (P=0.000) indicated that there were differences between the two groups and could affect the results of the study. Clinical outcome of the length of hospital stay outcome both had the same effective, and cost analysis results showed intravenous aminophylline (US$ 5.38) cheaper than nebulized salbutamol (US$ 5.71). intravenous aminophylline was more effective in reducing asthma symptoms than nebulized salbutamol (Pvalue=0.001). Meanwhile, the average decrease in lung function intravenous aminophylline (1.44) than nebulized salbutamol (1.23), although not significantly different (Pvalue=0.507).

5 Declarations

5.1 Acknowledgments

Funding sources: this research was funded by the Institute of Research and Community Service of the Universitas Surabaya.

5.2 Author Contributions

The names of the authors listed in this journal contributed to this research.

5.3 Funding Statement

This research was not supported by any funding sources.

5.4 Conflicts of Interest

The authors declare no conflict of interest.

5.5 Ethic

Ethical has been approved by the Commission on Health Research Ethics dr. Ramelan Hospital, Surabaya No. 01/EC/KERS/2014.

6 References

[1] Global Initiative for Asthma (GINA). Global Strategy for Asthma Management & Prevention (Update), USA. 2019.
[2] Bush, A. (2019). Pathophysiological Mechanisms of Asthma. Front Pediatr, 7(68):1–17.
[3] Kementerian Kesehatan. Keputusan Menteri Kesehatan Republik Indonesia, Nomor 312/MENKES/SK/IX/2015, tentang Daftar Obat Essensial 2015, Jakarta, Kementerian Kesehatan Republik Indonesia.
[4] Kementerian Kesehatan. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.02.02/MENKES/523/2015, tentang

Formularium Nasional, Jakarta, Kementerian Kesehatan Republik Indonesia.
[5] Travers, A.H., Jones, A.P., Camargo, C.A., Milan, S.J., and Rowe, B.H. (2012). Intravenous beta(2)-agonists versus intravenous aminophylline for acute asthma. Cochrane Database Syst Rev, 12:CD010256.
[6] Roberts, G., Newsom, D., Gomez, K., Raffles, A., Saglani, S., and Begent, J. (2003). Intravenous salbutamol bolus compared with an aminophylline infusion in children with severe asthma: a randomised controlled trial. Thorax, 58:306–10.
[7] Tilley, S.L. (2011). Methylxanthines in asthma. Handb Exp Pharmacol, 200:439–56.
[8] Barnes, P.J. (2010). Theophylline. Pharmaceuticals (Basel), 3(3):725–47.
[9] Lorensia, A., Wahjuningsih, E., Canggih, B., and Lisiska, N. (2011). Pharmacist's Strategies in Treating Asthma Bronchiale Outpatient. Jurnal of Tropical Pharmacy and Chemistry, 1(3):177–91.
[10] Lorensia, A., Wahjuningsih, E., and Supriadi. (2012). Safety of Aminophylline for Asthma Therapy in Delta Surya Hospital at Sidoarjo. Indonesia journal of Clinical Pharmacy, 1(4):154–61.
[11] Lorensia, A., Canggih, B., and Wijaya, R.I. (2013). Analysis of Adverse Drug Reactions in Asthma Patients in a Hospital, Surabaya. Jurnal Farmasi Indonesia, 6(3):142–50.
[12] Lorensia, A., Wahyudi, M., Yudiarso, A., and Kurnia, S.E.D. (2020). Effect of illness perception on improving asthma symptoms with omega-3 fish oil therapy: Pre-post design. Journal of Applied Pharmaceutical Science, 10(6):62–71.
[13] Lorensia, A., Ikawati, Z., Andayani, T.M., Maranatha, D., and Wahjudi, M. (2016). Comparison of Electrolyte Disturbance of Using Intravenous Aminophylline Versus Nebulization Salbutamol for Exacerbation Asthma in Surabaya, Indonesia. International Journal of Pharmaceutical and Clinical Research, 8(4):221–8.
[14] Dalabih, A., Harris, Z.L., Bondi, S.A., and Arnold, D.H. (2012). Contemporary aminophylline use for status asthmaticus in pediatric ICUs. Chest, 141(4):1122–3.
[15] Mahemuti, G., Zhang, H., Li, J., Tieliwaerdi, N., and Ren, L. (2018). Efficacy and side effects of intravenous theophylline in acute asthma: a systematic review and meta-analysis. Drug Des Devel Ther, 12:99–120.
[16] Saint, G.L., Semple, M.G., Sinha, I., and Hawcutt, D.B. (2018). Optimizing the Dosing of Intravenous Theophylline in Acute Severe Asthma in Children. Paediatr Drugs, 20(3):209–14.
[17] Cooney, L., Sinha, I., and Hawcutt, D. (2016). Aminophylline Dosage In Asthma Exacerbations in Children: A Systematic Review. PLoS One, 11(8):e0159965.
[18] Lorensia, A., Ikawati, Z., Andayani, T.M., Maranatha, D., and Wahyudi, M. (2019). CYP1A2 Gene Polymorphism and Theophylline Level in Asthma. The Indonesian Biomedical Journal, 11(1):63–9.
[19] Fenech, A.G., Grech, G. (2011). Pharmacogenetics: Where do we stand?. Journal of the Malta College of Pharmacy Practice, 11:25–33.
[20] Tse, S.M., Tantisira, K., and Weiss, S.T. (2011). The Pharmacogenetics and Pharmacogenomics of Asthma Therapy. Pharmacogenomics Journal, 11(6):383–92.
[21] Uslu, A., Ogus, C., Ozdemir, T., Bilgen, T., Tosun, O., and Keser, I. (2010). The effect of CYP1A2 gene polymorphisms on Theophylline metabolism and chronic obstructive pulmonary disease in Turkish patients. Biochemistry and Molecular Biology reports, 43(8):530–4.
[22] Obase, Y., Shimoda, T., Kawano, T., Saeki, S., Tomari, S.Y., Mitsuta-Izaki, K., Matsuse, H., Kinoshita, M., and Kohno, S. (2003). Polymorphisms in the CYP1A2 gene and theophylline metabolism in patients with asthma. Clinical Pharmacology and Therapeutics, 73(5):468–74.
[23] Roden, D.M., Wilke, R.A., Kroemer, H.K., and Stein, C.M. (2011). Pharmacogenomics: the genetics of variable drug responses. Circulation, 123(15):1661–70.
[24] Sanchez-Ibarra, H.E., Reyes-Cortes, L.M., Jiang, X.L., Luna-Aguirre, C.M., Aguirre-Trevino, D., Morales-Alvarado, I.A.M., Leon-Cachon, R.B., Lavalle-Gonzalez, F., Morcos, F., and Barrera-Saldana, H.A. (2018). Genotypic and Phenotypic Factors Influencing Drug Response in Mexican Patients With Type 2 Diabetes Mellitus. Front Pharmacol, 9(320):1–11.
[25] Queljoe, D.D., Wahjudi, M., Erdiansyah, M., Suryadinata, R.V., and Lorensia, A. (2014). Pilot Study on Genetic Polymorphisms CYP1A2*1F on Asthma Patients and Nonasthma in Indonesia. Indonesia journal of Clinical Pharmacy, 4(1):8–16.
[26] SNPedia. 2016, rs762551. [ONLINE] Available at: https://www.snpedia.com/index.php/Rs762551 [Accessed 12 Desember 2020].
[27] Nunes, C., Pereira, A.M., and Morais-Almeida, M. (2017). Asthma costs and social impact. Asthma Res Pract, 3(1):1–11.

[28] Souiotis, K., Kousoulakou, H., Hillas, G., Bakakos, P., Toumbis, M., Loukides, S., and Vassilakopoulos, T. (2017). Direct and Indirect Costs of Asthma Management in Greece: An Expert Panel Approach. Front. Public Health, 5(67):1–6.

[29] Cookson, R., Mirelman, A.J., Griffin, S., Asaria, M., Dawkins, B., Norheim, O.F., Verguet, S., and Culyer, A. (2017). Using Cost-Effectiveness Analysis to Address Health Equity Concerns. Value Health, 20(2):206–12.

[30] Thomas, R., Chalkidou, K. Cost–effectiveness analysis. 2016. In: Cylus J, Papanicolas I, Smith PC, editors. Health system efficiency: How to make measurement matter for policy and management. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2016. (Health Policy Series, No. 46.) 6. [ONLINE] Available at: https://www.ncbi.nlm.nih.gov/books/NBK436886/. [Accessed 12 Desember 2020].

[31] Savitz, L.A., Savitz, S.T. (2016). Can delivery systems use cost-effectiveness analysis to reduce healthcare costs and improve value?. F1000Res, 5(F1000):1–6.

[32] Chipps, B.E., Foggs, M.B. (2015). Asthma Management and the Allergist: Better Outcomes at Lower Cost. American College of Allergy. [ONLINE] Available at: https://college.acaai.org/sites/default/files/Asthma%20management.pdf. [Accessed 12 Desember 2020].

[33] Lorensia, A., Wijaya, R.I., and Canggih, B. (2013). Cost-Effectiveness Study related to Inpatient Selection of Bronchial Asthma Medication at a Private Hospital in Surabaya. Jurnal Ilmiah Sains & Teknologi, 7(1):56–63.

[34] Singh, A.S., Masuku, M.B. (2014). Sampling Techniques & Determination of Sample Size in Applied Statistics Research: An Overview. International Journal of Economics, Commerce and Management, 2(11):1–22.

[35] National Asthma Council Australia. 2006. Asthma Handbook: Version 2.0 Management Adults. [ONLINE] Available at: https://www.asthmahandbook.org.au/static/files/Australian-Asthma-Handbook-v2.0-Management-%E2%80%93-Adults.pdf. [Accessed 1 Maret 2021].

[36] Fong, N. (2011). Aminophylline/Theophylline: Loading and maintenance dose, NHS Trust: East Lancashire Hospitals. 2011

[37] Barnard, A. (2005). Management of an Acute Asthma Attack, Australian Family Physician, 34(7):531–4.

[38] Luo, Z., Liu, E., Luo, J., Li, S., Zeng, F., Yang, X., and Fu, Z. (2010). Nebulized hypertonic saline/salbutamol solution treatment in hospitalized children with mild to moderate bronchiolitis. Pediatr Int, 52(2):199–202.

[39] Kankaanranta, H., Kauppi, P., Tuomisto, L.E., and Ilmarinen, P. (2016). Emerging Comorbidities in Adult Asthma: Risks, Clinical Associations, and Mechanisms. Mediators of Inflammation, 3690628:1–23.

[40] Veenendaal, M., Westerik, J.A.M., Bemt, L.V.D., Kocks, J.W.H., Bischoff, E.W., and Schermer, T.R. (2019). Age- and sex-specific prevalence of chronic comorbidity in adult patients with asthma: A real-life study. NPJ Prim Care Respir Med, 29(14):1–7.

[41] Mahdavian, M., Power, B.H., Asghari, S., Pike, J.C. (2018). Effects of Comorbidities on Asthma Hospitalization and Mortality Rates: A Systematic Review. Can Respir J, 6460379:1–7.

[42] Lorensia, A., Wahyudi, M., Yudiarso, A., Kurnia, S.E.D. (2020). Effect of illness perception on improving asthma symptoms with omega-3 fish oil therapy: Pre-post design. Journal of Applied Pharmaceutical Science, 10(6):62–71.

[43] Niimi, A. (2011). Cough and Asthma. Curr Respir Med Rev, 7(1):47–54.

[44] Morjaria, J.B., Rigby, A.S., Morice, A.L. (2017). Asthma phenotypes: do cough and wheeze predict exacerbations in persistent asthma?. European Respiratory Journal, 50(1701366):1–9.

[45] Munro, A., Jacobs, M. (2004). Is intravenous aminophylline better than intravenous salbutamol in the treatment of moderate to severe asthma?. Emerg Med J, 21:78–80.

[46] Lorensia, A., Wahjudi, M., Yudiarso, A., Suryadinata, R.V., and Ratnasari, R. (2020). Pilot Study of Lung Function Improvement in Peak Expiratory Flow (PEF) Value Using Fish Oil Containing Omega-3 Therapy in Asthma. Global Medical & Health Communication, 8(3):211–8.

[47] Hua, J., Zhang, W., Cao, H.F., Du, C.L., Ma, J.Y., Zuo, Y.H., and Zhang, J. (2020). Effect of PIFR-based optimised inhalation therapy in patients recovering from acute exacerbation of chronic obstructive pulmonary disease: protocol of a prospective, multicentre, superiority, randomised controlled trial. BMJ Open, 10(e034804):1–9.

[48] Tattersfield, A.E., Postma, D.S., Barnes, P.J., Svensson, K., Bauer, C.A., O'Byrne, P.M., Löfdahl, C.G., Pauwels, R.A., Ullman, A. (1999). Exacerbations of asthma: a descriptive study of 425 severe exacerbations. Am J Respir Crit Care Med, 160:594–9.

[49] Burkhart, P.V., Rayens, M.K., and Oakley, M.G. (2012). Effect of Peak Flow Monitoring on Child Asthma Quality of Life. J Pediatr Nurs, 27(1):18–25.

[50] Turner, M.O., Taylor, D., Bennertt, R., Fitzgerald, J.M. (1998). A Randomized Trial Comparing Peak Expiratory Flow and Symptom Self-management Plans for Patients with Asthma Attending a Primary Care Clinic. American Journal of Respiratory and Critical Care Medicine, 157(2):540–6.
[51] Littenberg, B. (1988). Aminophylline Treatment in Severe, Acute Asthma a Meta-analysis. Journal of the American Medical Association (JAMA), 259(11):1678–84.
[52] Hartnett, B.J.S., Marlin, G.E. (1976). Comparison of oral theophylline and salbutamol by inhalation in asthmatic patients. Br J Clin Pharmacol, 3(4):591–4.
[53] Davies, B., Brooks, G., and Devoy, M. (1998). The efficacy and safety of salmeterol compared to theophylline: meta-analysis of nine controlled studies. Respiratory Medicine, 92(2):256–63.
[54] Dawson, K.P., Fergusson, D.M. (1982). Effects of oral theophylline and oral salbutamol in the treatment of asthma. Archives of Disease in Childhood, 57:674–6.
[55] Nakano, J., Yano, T., Yamamura, K., Yoshihara, H., Ohbayashi, O., Yamashita, N., and Ohta, K. (2006). Aminophilline suppress the release of chemical mediators in treatment of acute asthma. Respiratory Medicine, 100(3):542–50.
[56] Okour, A.M., Saadeh, R.A., Hijazi, M.H., Khalaileh, H.E.A., and Alfaqih, M.A. (2019). Socioeconomic status, perceptions and obesity among adolescents in Jordan. Pan Afr Med J, 34(148):1–9.
[57] Gradidge, P.J.L., Norris, S.A., Munthali, R. et al. (2018). Influence of socioeconomic status on changes in body size and physical activity in ageing black South African women. Eur Rev Aging Phys Act, 15(6):1–9.
[58] PERMENKES (Peraturan Menteri Kesehatan), Nomor 27 (2014), tentang Petunjuk Teknis Sistem Indonesian Case Base Groups (INA-CBGs), Jakarta, Kementerian Kesehatan Republik Indonesia.
[59] PERMENKES (Peraturan Menteri Kesehatan), Nomor 59 (2014), tentang Standar Tarif Pelayanan Kesehatan Dalam Penyelenggaraan Program Jaminan Kesehatan, Jakarta, Kementerian Kesehatan Republik Indonesia.
[60] Vezina, K., Chauhan, B.F., and Ducharme, F.M. (2014). Inhaled anticholinergics and short-acting beta2-agonists versus short-acting beta2-agonists alone for children with acute asthma in hospital. Cochrane Database Syst Rev, 31(CD010283):1–49.
[61] Lorensia, A., Bahari, F.K. (2020). Cost-Effectiveness Analysis between Salbutamol-Ipratropium Combination with Salbutamol in Asthma Attack. Jurnal Insan Farmasi Indonesia, 3(1):38–49.
[62] Domínguez-Ortega, J., Phillips-Anglés, E., Barranco, P., and Quirce, S. (2015). Cost-effectiveness of asthma therapy: a comprehensive review. J Asthma. 52(6):529–37.
[63] Andrew, A.L., Wong, K.A., Heine, D., Russell, W.S. (2012). A Cost-effectiveness Analysis of Dexamethasone Versus Prednisone in Pediatric Acute Asthma. Academic Emergency Medicine, 19(8):943–8.
[64] Fuseini, H., Newcomb, D.C. (2017). Mechanisms driving gender differences in asthma. Curr Allergy Asthma Rep, 17(3):19.
[65] Yamauchi, K., Ogasawara, M. (2019). The Role of Histamine in the Pathophysiology of Asthma and the Clinical Efficacy of Antihistamines in Asthma Therapy. Int J Mol Sci, 20(1733):1–16.
[66] Church, M.K. (2017). Allergy, Histamine and Antihistamines. Handb Exp Pharmacol, 241:321–31.
[67] Billington, C.K., Ojo, O.O., Penn, R.B., and Ito, S. (2013). cAMP regulation of airway smooth muscle function. Pulm Pharmacol Ther, 26(1):112–20.