EVALUATION OF TREATMENT BRONCHODILATORS AND CORTICOSTEROIDS IN COPD INPATIENT IN HOSPITALS DR. MOEWARDI SURAKARTA JANUARY 2016-JUNE 2017

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) is one of the cause of mortality and morbidity in worldwide. This study aims to determine the pattern of treatment of bronchodilators with or without corticosteroids and their effects on changes carbon dioxide pressure in blood (PCO_2) and oxygen pressure in blood (PO_2) in COPD patients of inpatient in RSUD Dr. Moewardi Surakarta January 2016-June 2017. This research is a retrospective descriptive research design, data collecting by tracking medical records patients with 195 samples. The results showed that treatment of COPD patient using single bronchodilator of 30,8%, bronchodilator combination of 57,1%, bronchodilator combination with corticosteroid of 1% and corticosteroid equal to 91,3%. Effect of bronchodilator treatment without corticosteroids on changes in the largest largest PCO_2 change of 14.8%, the smallest change in PCO_2 5.9%, the largest PO_2 change was 19%, the smallest PO_2 change was 5.6%, whereas in patients who received bronchodilator treatment with corticosteroids there was the largest PCO_2 change of 87.4%, the smallest PCO_2 change of 0%, the largest PO_2 change by 75.7%, the smallest change in PO_2 is 0.13%.

Keywords : COPD, bronchodilator, corticosteroid, PCO_2 , PO_2

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the causes of mortality and morbidity in the world. According to the 2018 Global Initiative for Chronic Obstructive Lung Disease (GOLD), COPD is currently the fourth leading cause of death in the world but is projected to be the 3rd leading cause of death by 2020. The incidence of COPD can increase with an increase in the number of smokers because 90% of COPD sufferers are smokers or former smokers. Based on the results of a survey of non-communicable diseases, the Directorate General of PPM and PL in 5 provincial hospitals in Indonesia, namely West Java, Central Java, East Java, Lampung and South Sumatra in 2004, first-rate COPD contributed 35% to morbidity, followed by asthma bronchial by 33%, lung cancer by 30% and others by 2% (PDPI, 2011).

Chronic Obstructive Pulmonary Disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation that is due to airway

and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The classification of airflow limitation severity of COPD can shown based on post-bronchodilator FEV_1 with spirometry test. According to 2018 GOLD to date, there is no conclusive clinical trial evidence that any existing medications for COPD modify the long-term decline in lung function. Bronchodilators are one of the drugs recommended for the treatment of COPD (GOLD, 2018; PDPI, 2011). Combination of a long beta₂-agonist and an inhaled corticosteroid may benefit for patients with persistent exacerbations (GOLD, 2018), but should balance the potential benefits of inhaled steroids in COPD against the potential side effects (Yang, et al., 2012).

Based on data taken from the health profile of the city of Surakarta in 2014, the prevalence of COPD in Dr. Moewardi as many as 578 patients. Research has been done on therapeutic patterns and costs for COPD patients, but evaluations of bronchodilator and corticosteroid treatment have never been carried out. Based on the above problems,

it is necessary to evaluate bronchodilator treatment with or without corticosteroids in COPD patients in the inpatient installation of Dr. Moewardi Surakarta and its effect on changes in carbon dioxide pressure in the blood (PCO₂) and blood oxygen pressure (PO₂) in COPD patients in the inpatient installation of Dr. Moewardi Surakarta.

Methods

This research is a descriptive research. Retrospective data collection was carried out by tracing the treatment records of COPD patients who were hospitalized in Dr. Moewardi Surakarta from January 2016-June 2017. The sample size was determined based on the Slovin formula, obtained 190 patients. Sampling was taken by purposive sampling. Inclusion criteria: inpatient installation patients at Dr. Moewardi Surakarta, patients with COPD diagnosis or from spirometry marked with FEV₁/FVC < 0.70, patients who received

bronchodilator treatment (beta₂-agonist, anticholinergic and methyl xanthine) alone or in combination with or without corticosteroids, and adult patients aged ≥ 18 years. Exclusion criteria: patients with a diagnosis of asthma.

Analysis

Univariate analysis was used to obtain an overview of the frequency distribution and proportion of the variables studied such as age, sex, occupation, smoking history, spirometry, clinical symptoms, comorbidity, treatment, and effects of treatment on changes in PCO₂ and PO₂ levels.

Results and Discussion

Patients characteristics

1. Age

Age distribution of COPD patients in the inpatient installation of Dr. Moewardi Surakarta in January 2016-June 2017 is shown in table

Table 1. Age distribution of patients

Age	n = 195	
	n	%
18 – 44 years	5	2,6
45 – 54 years	8	4,1
55 – 64 years	50	25,6
65 – 74 years	76	39
> 75 years	56	28,7
Amount	195	100

n: number of patients

Based on the results of the study found patients in the age range of 18-44 years as many as 5 people (2.6%), aged 45-54 years obtained as many as 8 people (4.1%), aged 55-64 years 50 people (25.6%), age 65-74 years 76 people (39%) and age > 75 years 56 people (28.7%). From these data it can be seen that the greatest prevalence of COPD occurs in the age range 65-74 years which reaches 39% of the total sample. Based on GOLD (2018), airway obstruction is more common at the age of over 40 years and the highest is at the age of over 60 years. This is in line with research conducted by Permatasari (2016) most COPD patients in the age range 55-64 years (56.2%), also supported by Naser's study (2016) the largest COPD age group in the age range of 60 years and over is as much as 55%. Decreased lung function will be accelerated in people who continue to smoke after more than 45 years of age (Suradi, 2007).

The maximum function of the respiratory system is reached at the age of 20-25 years, after which there is a progressive decrease in lung capacity in connection with aging. Physiological changes in COPD are responsible for progressive abnormalities in elderly patients. But many anatomical and physiological changes in COPD also appear in the

lungs of elderly patients who do not smoke. This shows that the aging process is a factor that contributes to the incidence of COPD (Hanania, et al., 2010).

1. Gender

Distribution of COPD patients in the inpatient installation of Dr. Moewardi Surakarta in January 2016-June 2017 based on gender shown in table 2. Based on the results of the study, COPD patients with male gender showed greater numbers than women. Gender plays a role in determining whether a person is more susceptible to COPD or not. From the results of this study obtained the number of male patients as many as 170 people (87.2%) and the female sex as many as 25 people (12.8%). Judging from the aspect of risk factors for smoking habits, patients with male gender have a higher risk of developing COPD. Based on Riskesdas (2010) the prevalence of male smokers in Indonesia is 16 times higher than women. This is supported by the results of Permatasari's (2016) study of male patients dominating COPD (96.9%).

Table 2. Gender distribution of patients

Gender	n = 195	
	N	%
Male	170	87,2
Female	25	12,8
Amount	195	100

n: number of patients

2. Job

In table 3 shows the job of COPD patients in the inpatient installation of Dr. Moewardi Surakarta from January 2016-June 2017.

There were 25 COPD patients who has complete job data. The most occupations of COPD patients are farmers and retirees with a proportion of 24% each. Data on the work of carpenters and pedicab drivers shows that each proportion is 8%. In the data of work no job (housewives) it is stated that they use firewood for cooking. A cross-sectional observational study showed that self-reported exposure to workplace dust and fumes in men and women is associated with airflow obstruction, respiratory symptoms, more emphysema, and gas trapping similarly in men and women (Marchetti, et al., 2014).

According to Oemiati (2013) one of the risk factors for COPD is exposure of particles from smoking, indoor pollution, outdoor pollution and pollution in the workplace. Indoor pollution such as cooking with biomass materials with poor kitchen ventilation such as exposed to wood fuel or fuel oil smoke is estimated to contribute up to 35% (Reilly, 2008). WHO reports that indoor pollution is responsible for the deaths of 1.6 million people each year (WHO, 2008). Outdoor pollution such as combustion smoke, factory or mining materials. Pollution in the workplace such as organic dust, textile industry, iron and steel industry, wood industry, paint or ink manufacturing chemicals, is estimated at 19% (Di Pede, 2002).

Tabel 3. Characteristics of COPD patients

Job	n = 25	
	n	%
Farmer	6	24
Carpenter	2	8
Pedicab driver	2	8
Retired	6	24
No job	4	16
Entrepreneur	5	20
Amount	25	100

n: number of patients with complete job data

3. Smoking history

Distribution of smoking history of COPD patients in the inpatient installation of

Dr. Moewardi Surakarta from January 2016-June 2017 is shown in table 4.

Table 4. Distribution of patient smoking history

Smoking history	n = 111	
	n	%
Active smokers	75	67,6
Ex-smokers	11	9,9
Non-smokers	25	22,5
Amount	111	100

n: number of patients with complete smoking history data

Based on the results of the study obtained 111 medical records of patients who contain smoking history. From these data can be calculated patients with a history of active smokers as many as 75 people (67.6%), ex-

smokers 11 people (9.9%), non-smokers 25 people (22.5%). The relationship between cigarettes and COPD is a dose response relationship, which is seen from the length of smoking habits and the number of cigarettes

consumed every day it will risk greater disease (PDPI, 2011). The results of this study are in line with the research conducted by Naser (2016) history smoking COPD patients occupy the largest percentage. According to the 2011 National Socio-Economic Survey (SUSENAS) data, 67.4% of adult men in Indonesia are active smokers (BPS, 2011).

Spirometry Test Value and Clinical Symptoms of COPD Patients

Spirometry test value shows the severity of COPD which is divided into mild, moderate,

heavy and very severe. The degree of severity of COPD patients is determined based on $FEV_1/FVC < 70\%$ which means that there is an obstruction using a spirometer (GOLD, 2018). Clinical symptoms of COPD patients consist of shortness of breath, coughing with phlegm, coughing without phlegm, and wheezing.

1. Spirometry test value

Table 5 shows the distribution of the severity of COPD patients in the inpatient installation of Dr. Moewardi Surakarta from January 2016-June 2017.

Severity	Value of Spirometry Test	n = 34	
		n	%
Mild	$FEV_1/FVC < 70\%$	10	29,4
	$FEV_1 \geq 80\%$ predicted		
Moderate	$FEV_1/FVC < 70\%$	22	64,7
	$50\% \leq FEV_1 < 80\%$ predicted		
Severe	$FEV_1/FVC < 70\%$	2	5,9
	$30\% \leq FEV_1 < 50\%$ predicted		
Very severe	$FEV_1/FVC < 70\%$	0	0
	$FEV_1 < 30\%$ predicted		
Amount		34	100

n : number of patients with complete spirometry test data

There were 34 patients who had complete spirometry test data from 195 COPD patients. Based on the results of the study showed that patients who experienced mild obstruction were 10 people (29.4%), moderate obstruction 22 people (64.7%) and those with severe obstruction 2 people (5.9%), and no patients who experienced very severe obstruction. The classification of severity of COPD can be used to determine the treatment of appropriate COPD patients (PDPI, 2011). In

line with the research conducted by Permatasari (2016) at Dr. RSUD Soetomo Surabaya, the greatest severity of COPD patients is in moderate obstruction by 50%.

2. Clinical symptoms

In table 6 shows the distribution of clinical symptoms of COPD patients in the inpatient installation of Dr. Moewardi Surakarta from January 2016 - June 2017.

Table 6. Distribution of comorbidities of COPD patients

Comorbidities	n = 171	
	n	%
Cardiovascular disease	81	47,4 %
Respiratory disease	59	34,5 %
Others	31	18,1 %
Amount	171	100

n: number of patients with comorbidity

A total of 81 patients (47.4%) COPD had comorbid cardiovascular disease which included Heart Failure Hypertension (HHF), Congestive Heart Failure (CHF), Old Myocardial Infarction (OMI), arrhythmia, cardiomegaly, Acute Decompensated Heart Failure (ADHF), hypertension and stroke. In addition to cardiovascular disease, respiratory diseases such as pneumonia, tuberculosis, lung cancer, laryngeal cancer and asthma are found in

the proportion of 34.5%. In other comorbidities, there were 18.1% of diseases such as diabetes mellitus and gastritis.

Cardiovascular disease can be increased due to systemic inflammation caused by COPD which includes atherosclerosis, ventricular dysfunction, systemic heart disease, stroke, hypertension, chronic heart failure, sudden cardiac death (Sin DD, et al., 2006). Vanfletern et al. (2013) reported the largest five percentages

of comorbidity in COPD were hyperglycemia (54%), atherosclerosis (53%), hypertension (48%), dyslipidemia (36%) and osteoporosis (31%). The role of systemic inflammation is very important in the pathogenesis of comorbidities in COPD. Various risk factors for COPD (such as smoking and old age) as well as components of the metabolic syndrome (dyslipidemia, obesity and hypertension) using a systemic

inflammatory pathway can cause various comorbidities (Kulsum, 2016).

Bronchodilator and Corticosteroid Treatment

In table 7 shows the distribution of treatment proportions of COPD patients in the inpatient installation of Dr. Moewardi Surakarta from January 2016-June 2017.

Table 7. Distribution of the proportion of treatment for COPD patients

Treatment	n	%
Single bronchodilator	60	17 %
Bronchodilator combination	113	32 %
Bronchodilator with corticosteroids	2	0,6 %
Corticosteroids	178	50,4 %
Amount	353	100

n : amount of treatment

The treatment distribution of COPD patients here is separated based on the use of a single bronchodilator, combination bronchodilator, bronchodilator and corticosteroids, and corticosteroids. Based on the results of the study showed that patients get one or more treatment therapies. The most proportion of treatment for COPD patients is corticosteroid use in the form of injection of 50.4%. The most commonly used corticosteroid is methyl prednisolone through an injection form. Corticosteroids are used when an acute exacerbation occurs which serves to suppress inflammation that occurs either in oral form or intravenous injection (PDPI, 2011). According to Senior and Anthonisen (1998) that in COPD patients have improved pulmonary function after the use of anti-inflammatory methyl prednisolone corticosteroids.

In combination treatment therapy, the proportion of use was 115 patients. The drug used was a combination of fenoterol (berotec): ipratropium (atrovent) in 105 patients and a combination of salbutamol: ipratropium (combivent) in 8 patients. These two combinations of bronchodilators are a combination of the Short-acting beta₂-agonist (SABA) group: Short-acting anticholinergic agent (SAMA). In addition it is also used a combination of formoterol: budesonide which is a group of Long-acting beta₂-agonists (LABA): corticosteroids in 2 patients. All combinations of these drugs are used through the Nebuliser route. Nebulizer can be used to treat acute

exacerbations. Besides that the use of combination drugs is simpler and makes it easier for sufferers (PDPI, 2011).

For the treatment of single bronchodilators that are often used are methyl xanthine (aminophylline) and SABA (salbutamol) via injection routes (drip) with a proportion of use of 17%. Injection or drip forms can be used to treat acute exacerbations (PDPI, 2011).

Effects of Treatment on Changes in Levels of PCO₂ and PO₂

Based on the results of the study obtained 51 COPD patients who underwent blood gas analysis, 2 patients received bronchodilator treatment without corticosteroids and 49 patients received bronchodilator treatment with corticosteroids.

1. Bronchodilator treatment without corticosteroids

Bronchodilators that are intended in this study are anticholinergics, beta₂ agonists and methyl xanthine, while those without corticosteroids mean that patients do not get corticosteroid treatment either in the form of injection, inhalation or oral during blood gas analysis.

In table 8 can be seen the largest and smallest percentage changes in levels of PCO₂ and PO₂ in bronchodilator treatment without corticosteroids in COPD patients.

Table 8. The largest and smallest percentage changes in PCO₂ and PO₂ levels in bronchodilator treatment without corticosteroids

Level	Changes	Pre	Post	%
PCO ₂ (mmHg)	Largest	62	54	14,8 %
	Smallest	49,8	47	5,9 %
PO ₂ (mmHg)	Largest	96,4	119	19 %
	Smallest	136	144	5,6 %

Based on the results of this study, the highest change in PCO₂ levels was 14.8% from 62 mmHg to 54 mmHg, while the smallest was 5.9% from 49.8 mmHg to 47 mmHg. The biggest change in PO₂ level was 19% from 96.4 mmHg to 119 mmHg, while the smallest was 5.6% from 136 mmHg to 144 mmHg. The therapeutic treatment obtained by this patient is

a combination of fenoterod bronchodilator: ipatropium by nebulizer.

2. Bronchodilator treatment with corticosteroids

The percentage change in PCO₂ and PO₂ levels in bronchodilator treatment with corticosteroids can be seen in table 9.

Table 9. The largest and smallest percentage changes in PCO₂ and PO₂ levels in bronchodilator treatment with corticosteroids

Level	Changes	Pre	Post	%
PCO ₂ (mmHg)	Largest	77,6	41,4	87,4 %
	Smallest	32	32	0 %
PO ₂ (mmHg)	Largest	88,3	296,3	75,5 %
	Smallest	156,8	157	0,13 %

Based on the results of the study, the largest change in PCO₂ levels was 87.4% from 77.6 mmHg to 41.4 mmHg, the treatment therapy obtained by this patient included a combination of fenoterol nebulizer: ipatropium, aminophylline injection and methyl prednisolone injection. The smallest level of PCO₂ was 0% from 32 mmHg but did not give any changes at the end of the blood gas analysis.

At the highest change in PO₂ levels was 75.5% from 88.3 mmHg to 296.3 mmHg, these patients received treatment therapy which included a combination of fenoterol: ipratropium nebulizer and methyl prednisolone injection. While the smallest PO₂ level is 0.13% from 156.8 mmHg to 157 mmHg.

Research that shows the effect of corticosteroids on changes in PCO₂ and PO₂ levels, as was done by Rodrigues-Roisin (2005), namely in a comparative study the use of budesonide corticosteroid nebulizer with oral prednisone showed a small but significant increase in PO₂ in the prednisone group and a decrease in PCO₂ in both groups.

Based on Senior and Anthonisen (2009) and Rodrigues-Roisin (2005) studies it can be concluded that it was proven that after the use of corticosteroid anti-inflammatory drugs in COPD patients gave improvement in pulmonary function, thus affecting the levels of PCO₂ and PO₂. The results of this study are in accordance with research conducted by Senior and

Anthonisen (2009) and Rodrigues-Roisin (2005), because between the results of bronchodilator treatment with or without corticosteroids can increase levels of PO₂ and reduce levels of PCO₂ in the blood, although the data changes the smallest PCO₂ bronchodilator treatment with corticosteroids showed no changes (0%), but the PO₂ levels showed an increase. Inhaled long acting beta₂-agonists and corticosteroid combination treatment produces better control symptoms and lung function (Calverley, et al., 2003), but should balance the potential benefits of inhaled steroids in COPD against the potential side effects (Yang, et al., 2012).

Conclusion

The results show that Drug use in COPD patients hospitalized for COPD in Dr.Moewardi Hospital, respectively, single bronchodilator by 17%, combination bronchodilator by 32%, combination bronchodilator with corticosteroids by 0.6%, and corticosteroids by 50.4%. There were differences in changes in initial and final PCO₂ levels between patients who received bronchodilator treatment without corticosteroids with patients who received bronchodilator treatment with corticosteroids, in patients who received bronchodilator treatment without corticosteroids there was the largest PCO₂ change of 14.8%, the smallest change in

PCO₂ 5.9%, the largest PO₂ change was 19%, the smallest PO₂ change was 5.6%, whereas in patients who received bronchodilator treatment with corticosteroids there was the largest PCO₂ change of 87.4%, the smallest PCO₂ change of 0%, the largest PO₂ change by 75.7%, the smallest change in PO₂ is 0.13%.

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