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RESEARCH ARTICLE

Therapy pattern of bronchodilators in chronic obstructive pulmonary disease (COPD) patients with acute exacerbations

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Abstract

Background: Acute exacerbation of chronic obstructive pulmonary disease (COPD) is a worsening condition of acute respiratory symptoms caused by microbial infection, increased air pollution, and fatigue. **Objective:** This study determines the pattern of bronchodilators in patients with acute exacerbations of COPD. **Method:** This study was observational, using the health medical records of patients with COPD at the Universitas Airlangga Hospital, Surabaya. It was conducted between January-December 2019 on male patients who received bronchodilator therapy until discharge and were from age 40 and older. **Result**: A total of 48 patients met the inclusion criteria. The most commonly used bronchodilator therapy for inpatients was the combination of ipratropium bromide/salbutamol sulfate 0.5 mg/2.5 mg through inhalation in 63.64%. The most frequently used bronchodilator for discharge was salbutamol sulfate 2-4 mg orally in 87.50%. **Conclusion:** Therapy for acute exacerbation of COPD using a combination of ipratropium bromide/salbutamol sulfate as a preventive therapy is in line with the GOLD guidelines.

Introduction

Chronic respiratory diseases are chronic diseases of the airways and other parts of the lung, including Chronic Obstructive Pulmonary Disease (COPD) which is one of the most common. COPD is a common and treatable disease characterised by progressive airflow limitation and tissue destruction. Acute exacerbation of COPD is defined as a worsening condition of acute respiratory symptoms characterised by exceeding baseline changes in dyspnea, cough, or sputum that results in additional therapy (Criner *et al*. 2015; Brown & Braman, 2020). The Global Initiative Guidelines for Chronic Obstructive Lung Disease (GOLD) recommended that bronchodilators are the mainstay for the treatment of COPD through inhalation or oral administration. Regarding the effectiveness and safety profile, inhaled bronchodilators are preferred to oral bronchodilators. Long-acting bronchodilators are more comfortable and more effective than short-acting bronchodilators (Antus, 2013; Dong *et al*., 2015). A combination of bronchodilators such as Short-Acting Muscarinic Antagonist (SAMA) and Short-Acting β2-Agonist (SABA) is more effective than a single dose of SABA or SAMA in the first treatment of acute exacerbation of COPD patients. A combination of SABA and SAMA could fix lung function, control exacerbation, and lower hospitalisation rates (Cushen *et al*., 2016). Besides, the combination of Long-Acting β2-Agonis (LABA) and Long-Acting Muscarinic Antagonist (LAMA) bronchodilators is recommended for COPD as maintenance therapy to prevent acute exacerbations in COPD patients (Aaron *et al*., 2007; GOLD, 2020).

This study was conducted to determine the pattern of bronchodilators in patients with acute exacerbation of chronic obstructive pulmonary disease at the Universitas Airlangga Hospital of Surabaya. Furthermore, this study

contributes to improving pharmaceutical care and the use of different types of bronchodilators for acute exacerbation of chronic obstructive pulmonary disease.

Methods

Design

This study was an observational study using medical records of inpatients with acute exacerbation of COPD until discharge. Patients hospitalised at the Universitas Airlangga Hospital from January–December 2019 who were male and aged over 40 years, and who received bronchodilator therapy for at least one day, were studied. This study was approved by the Ethics Committee of the Universitas Airlangga Hospital with the registered number of ethical approval: 132/KEP/2021. The sample size was determined by the time limited sampling method. The data collected were extracted to identify patient demographics data, and bronchodilator therapy.

Result

A total of 48 patients met the inclusion criteria. Table I shows the characteristics of patients with acute exacerbation of COPD. The most patients were 65-74 years in 17 patients (35.42%). Based on smoking history, the active smokers was 22 patients (45.83%), and ex-smokers 26 patients (54.17%), the most comorbid was pneumonia in 27 patients.

Table I: Patient's characteristics

Characteristics	N (frequency)	%
Age		
45-54 years	2	4.17%
55 - 64 Years	16	33.33%
65 - 74 Years	17	35.42%
> 75 Years	13	27.08%
Smoking history		
Active smoker	22	45.83%
Ex-smoker	26	54.17%
Comorbid		
Ulcus decubitus	1	1.47%
Post stroke	1	1.47%
Osteoarthritis	2	2.94%
Diabetes mellitus	2	2.94%
Post-tuberculosis	4	5.88%
Hyperprostate	4	5.88%
Gastrointestinal disease	5	7.35%
Congestive heart disease	7	10.30%
Hypertension	15	22.06%
Pneumonia	27	39.71%

Note: Each patient can have more than one comorbid

As shown in Table II, 48 patients with acute exacerbations of COPD were administered bronchodilators during their hospital stay until they were discharged from the hospital.

Table II: Pattern of bronchodilators in acute exacerbation of chronic obstructive pulmonary disease (COPD)

Bronchodilators	Route	Dose	Frequency	∑ (%)	Total	%
Inpatient (n=121)						
Ipratropium bromide/Salbutamol sulfate	i.h	0.5/2.5 mg	1x1 2x1 3x1 4x1	21 (17.36) 8 (6.61) 39 (32.23) 9 (7.44)	77	63.63
Procaterol HCl	i.h	30 mcg/0.3 ml	1x1 2x1 3x1 4x1	13 (10.74) 1 (0.83) 15 (12.40) 3 (2.48)	32	26.45
Salbutamol Sulfate	i.h	2.5 mg/2.5 ml	1x1 2x1 3x1	6 (4.96) 1 (0.83) 5 (4.13)	12	9.92
Discharge (n=48)						
Salbutamol sulfate	Oral	2 mg 4 mg	3x1 3x1	32 (66.67) 10 (20.83)	42	87.50
Budesonide/ Formoterol	i.h	160/4.5 mcg	2x1	2 (4.17)	2	4.17
Salmeterol/ Fluticasonepropionate	i.h	50mcg/250 mcg	2x1	2 (4.17)	2	4.17
Indacentrol	i.h	300 mcg	1x1	1 (2.08)	1	2.08
Tiotropiumbromide	i.h	2.5 mcg	1x2	1 (2.08)	1	2.08

i.h : Inhalation

In Table II, The bronchodilator used for inpatients was a combination of ipratropium bromide/salbutamol sulfate 0.5 mg/2.5 mg, through inhalation in 63.64%. The single inhalation bronchodilators were procaterol HCl and salbutamol sulfate prescribed in 26.45%, and 9.92% respectively. For patients discharge, the most used bronchodilator was salbutamol 2-4 mg as a single therapy, prescribed in 87.50%. The combination of LABA and ICS namely salmeterol/fluticasone propionate and budesonide/formoterol prescribed in 4.17%.

Discussion

All of the acute exacerbation of COPD patients involved in this study were male, who meet the inclusion criteria were 48 patients. Based on research conducted by Spannella and authors (2019), COPD patients in America aged 65 years and over had the potential of experiencing recurrent acute exacerbations and required hospitalisation. The risk of death in patients aged 80 was three times that of patients aged 65 and younger. Cigarette smoke can weaken the lung's defense against infection, narrow the airways, cause swelling in the airways and damage the air sacs so that it can be concluded that smoking is a major factor causing COPD (GOLD, 2020; American Lung Association, 2021). COPD patients were accompanied by several comorbidities as a result of inflammation that occurs in the respiratory tract (Bourdet and Williams, 2017). An increase in the amount of mucus and a decrease in mucus clearance make cells susceptible to microbial infections (*S. pneumoniae, H. influenza*). The changes may lead patients with acute exacerbations of COPD to be more susceptible to pneumonia (Trethewey, Hurst, and Turner, 2020).

Bronchodilators are the recommended first-line drug therapy for all COPD patients with acute exacerbation. Bronchodilators are helpful to reduce the narrowing of the bronchial tubes and increase the value of Forced expiratory volume in 1 second (FEV_1) (SBourdet and Williams, 2017). The combination of SABA and SAMA is recommended as the first treatment given to patients with acute exacerbations of COPD because it can improve lungs function, control acute exacerbations, and reduce hospitalisation rates among COPD patients (GOLD, 2020).

The combination of ipratropium bromide/salbutamol sulfate, 0.5/2.5 mg used as a combination of SABA and SAMA, is prescribed especially when a patient experiences worsening breathing or is concerned about recurrent exacerbation while being admitted. The maximum dose of ipratropium bromide/salbutamol sulfate was 0.5/2.5 mg, administered six times a day (GOLD, 2020). In a study conducted by Cushen and authors (2016), the combination of 2.5 mg salbutamol sulfate (SABA) and 0.5 mg ipratropium bromide (SAMA) inhalation is used for patients with acute exacerbation of COPD (Cushen *et al*, 2016). The combination of SABA and SAMA led to improved lung function, as evidenced by a significant increase in post-bronchodilator Forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) ratio while minimising the occurrence of drug side effects. This combination can also reduce morbidity in patients with two synergistic bronchodilators to increase the stability of the respiratory tract (Thomas *et al*., 2017).

Salbutamol sulfate is used as a preventive therapy in discharged patient for controlled exacerbation because of its rapid onset of action. The recommended dosage was three-four times per day, with the maximum daily dose not exceeding 32 mg. The onset of action is three to five minutes and a duration of action of four to six hours, recommended as the first-line drug therapy for acute exacerbations of COPD (GOLD, 2020). The combination of salmeterol/fluticasone propionate and budesonide/formoterol was used based on the patient's previous therapy regimen. Combination of LABA and inhaled corticosteroids (ICS) can be used in patients with a history of recurrent exacerbations of COPD to provide maintenance therapy and prevent further exacerbations (GOLD 2020).

However, one week after discharge, patients are usually recommended to return for a health check-up, and may be prescribed a combination therapy of LABA with or without LAMA or a combination of LABA and ICS for patients with recurring exacerbations (GOLD, 2020).

The inhalation route was the most used route of administration in the management of COPD because it allows for the maximum delivery of medication directly to the target organs while minimising the risk of systemic side effects (Barnes, 2013). The use of bronchodilators was in accordance with the guidelines for the treatment of acute exacerbations of COPD listed in the Global Initiative for Chronic Obstructive Lung Disease guidelines (GOLD, 2020).

Conclusion

The management therapy for acute exacerbations COPD was a combination of ipratropium bromide/salbutamol 0.5/2.5 mg administered inhalation for inpatients. For patients discharge, salbutamol was used as a single therapy. Acute exacerbation of COPD using bronchodilators followed the GOLD guidelines, as a combination or single dose therapy.

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