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Evaluation of Bronchodilator Prescription in Chronic Obstruction Pulmonary Disease Patients

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Abstract
Background: Chronic Obstructive Pulmonary Disease (COPD) is an irreversible, progressive chronic lung disease.
Aims: Evaluate the implementation of pharmacological therapy with bronchodilators in COPD patients at the Nursing Facility, Dr. Soehadi Prijonegoro Hospital, for the period January–December 2022, and compare it with the standard treatment of the Global Initiative for Chronic Obstructive Lung Disease (GOLD).
Methods: This study is a non-experimental descriptive study that is conducted retrospectively by looking at medical record data. Sampling is done using purposive sampling techniques, and there are 48 samples used based on the calculation of the Slovin formula. The data analysis included the accuracy of the use of bronchodilator drugs, the dosage precision of bronchodilator use, and the evaluation of prescriptions for bronchodilators compared to the 2022 GOLD standard.
Results: The results of the study showed that as much as 53% of patients were treated with single methylation parenterally, or β2 agonists, or antimuscarinics; 17% used multiple bronchodilator therapy with β2 combination Agonists; 12% used β2/corticosteroid combination therapy inhaler; and 17% used Agonis β2/anti-muscarin combination in nebulizer.
Conclusion: Bronchodilator prescriptions in COPD patients are 100% correct, 58.11% of the doses are correct, and the frequency of use of the drug is in line with the 2022 GOLD standard.

Keywords: COPD, GOLD, Exacerbation, Bronchodilator

Introduction

According to forecasts, Chronic Obstructive Pulmonary Disease (COPD) will soon overtake heart disease as the third biggest cause of mortality globally as its incidence continues to climb. Millions of people around the world are affected by COPD, and incidence is rising, particularly in nations with high smoking rates and limited access to healthcare [1]. Chronic obstructive pulmonary disease is a lung disease in which there is a decrease in lung function over time, a progressive decline in quality of life that cannot be completely cured. The World Health Organization (WHO) estimates that COPD is the most common cause of death in the world, including Indonesia [2, 3].

Implementation of COPD pharmacological therapy is carried out using various groups of drugs, namely bronchodilators, antibiotics, anti-inflammatory drugs, and mucolytics. The group of bronchodilator drugs can be administered in single and double doses in the form of preparations inhaler, nebulizer, oral, and injection. Properly implemented pharmacological therapy can reduce symptoms, risks, and rates of relapse, thereby improving the health status, health tolerance, and quality of life of patients [4, 5].

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) is a programme that aims to produce management recommendations for diagnosis, evaluation, and treatment of COPD based on the best information provided by the GOLD [6, 7] Scientific Committee, GOLD is an international reference in the management of COPD treatment, not except as a standard pattern for prescribing COPD pharmacological therapy. Research related to the evaluation of the prescription of bronchodilators in COPD patients with GOLD as a comparison has never been done in the Sragen district, especially by dr. Soehadi Prijonegoro Hospital, Research related to the evaluation of prescription in COPD patients that was previously conducted was the assessment of therapeutic results using the COPD Assessment Test (CAT) [8].

Research was carried out on the prescription of bronchodilators to COPD patients in the dr. Soehadi Prijonegoro Hospital period January-December 2022 is expected to be an evaluation of the prescription of bronchodilators with GOLD in 2022 as a

comparison and international reference of COPD management so that it can reduce the frequency of exacerbating COPD patients. In addition to previous studies, the study aims to analyse the accuracy of the use of bronchodilator drugs, the dosage precision of bronchodilator use, and the evaluation of the prescribing bronchodilators compared to the 2022 GOLD standard.

Method

Research Plan

This research is included in the type of non-experimental research carried out in a retrospective manner, i.e., with the collection of medical records of patients treated with COPD in the dr. Soehadi Prijonegoro Hospital period of January-December 2022 with the ethical licence number 107/Etik-CRSSP/IV/2023 through the Research Ethics Committee. Sampling is carried out by the purposive sampling method, with a total of 48 patients as a sample of the study, with the criteria of COPD patients aged ≥45 years who do not have the disease accompanying. Patients performed inpatient care in dr. Soehadi Prijonegoro Hospital in January–December 2022. COPD patients used oral bronchodilators, inhalations, and combinations.

Collection of Data

The collection of data included data on the use of bronchodilator drugs, namely methylsantin, agonis β2, antimuscarinics, in combination with ICS (inhalation corticosteroid), oral preparations, injections, and inhalations, and doses of bronchodilatory drugs. Patient characteristic data include age, gender, length of hospitalisation, and state of residence of the patient.

Data Analysis

Data analysis is carried out using Microsoft Excel 2019 and is statistically descriptive to present the results in the form of a percentage distribution of each variable. Patient characteristics data, the accuracy of the drug use, and the dosage of the use of bronchodilator drugs compared with the 2022 GOLD standard are shown in the form of a percentage distribution.

Result and Discussion

The characteristics of the research topic, as well as the results of any univariate, bivariate, and multivariate analyses, are described in the results section. Data collection for one month at dr. Soehadi Prijonegoro Hospital that 48 patients received bronchodilator therapy. Characteristic data of the subjects of the study are presented in Table 1, including age, gender, length of hospitalisation, and patient home status. Table 1 shows that the percentage of patients with an age of >60 years is the highest (70%) between the age range of 45–55 years (14%), and 56-60 years (15%), with the percent of patients based on gender being 67% male and 33% female. This is proof from a study conducted by Hanga *et al*. (2018) [8], that the likelihood of having COPD is increased in people over 40 [9]. The lungs and airways can change as we age naturally, making them more vulnerable to injury from prolonged exposure to risk factors like smoking and air pollution. Men are more likely than women to get COPD. The inherent differences in the structure and function of the lungs between the sexes and greater rates of smoking in males are thought to be the causes of these inequalities [10, 11].

The result of the distribution of the most long-term treatment percentage was 6-10 days at 53%. According to Dong *et al*. (2021) [11], the length of hospitalisation for COPD patients is roughly 10 days of treatment time, with various long variations of treatment depending on the condition, severity, and comorbidity of the patient [12]. It is based on indications of the patient's return home, i.e., reduced or missing pain, can carry out mobilisation, improve clinical conditions and other examinations, treat accompanying diseases, and understand the use of drugs [13]. The percentage of patients who returned home fully recovered was 91%. The average duration of treatment for patients who recovered is 6–10 days. Patients with advanced COPD or those who have additional difficulties may need more intense care, such as long-term oxygen therapy, lung rehabilitation, and surgery [14,15]. Seeing the large percentage of patients who have recovered indicates that the implementation of treatment therapy in PPOC patients has been quite effective. The percentage of patients who returned on their own request was 9%.

Table 1: Demographic Characteristics of COPD Patients

	n=48	%
Age (year)		
45-55	7	15
56-60	7	15
>60	34	71
Sex		
Male	32	67
Female	16	33
LoS (day)		
≤ 5	15	31
6-10	25	53
>10	8	16
Situation Home		
Helaed Home	44	91
Own Request	4	9

*LoS: Length of Stay

Profile of Use of Bronchodilators

The profile of the use of bronchodilators in COPD patients includes the group of bronchodilators, the name of the drug, and the type of preparation. In detail, the profile of the use of bronchodilators can be seen in Table 2. According to research at dr. Soehadi Prijonegoro Hospital, from the medical records of COPD patients in the period January-December 2022, there were three groups of bronchodilator drugs prescribed to the subject, namely β2 agonists, methylsantin, antimuscarinics, and combinations in inhalation as well as in nebulizers. Table 2, shows that the most commonly used bronchodilator is a combination of β2-agonists: corticosteroids in nebulizers, with a frequency of use of 41 samples (29%). The drug can be used as needed to loosen the airway when an attack occurs, as the drug can work quickly with a duration of action of 4-6 hours to reduce symptoms [16].

Table 2: Precision Profile of Bronchodilators

Types of Bronchodilators	Number of Uses	%	Compliance with Standard
Agonis β2 a. Berotec MDI®	6	4	precisely
Combination Agonist β2: Metilsantin a. Salbutamol: Theophylline b. Terbutalin: Theophylline c. Salbutamol: Aminophyllin	 8 15 2	 6 11 1	precisely
Antimuscarinic a. Spiriva Respimat®	13	9	precisely
Methylsantin a. Aminofilin injection	12	9	precisely
Combination Agonist β2: corticosteroid in the inhaler a. Seretide Discus® b. Symbicort®	 10 9	 8 7	precisely
Combination Agonist β2: corticosteroid in the nebulizer a. Ventolin®: Pulmicort®	41	29	precisely
Combination Agonist β2: antimuscarinic in the nebulizer a. Combivent® b. Meprovent®	 9 13	 7 9	precisely
Total	138	100	

*Compliance of drug delivery with the GOLD standard by 2022

Evaluation of Bronchodilator Use

The use of medicines may be said to be unreasonable or inappropriate when the risks that are more likely to occur are not balanced with the benefits of the patient's accurate use of the medicines. The details of the use of bronchodilator drugs can be seen in Table 2, which shows the results are already 100% accurate in accordance with the GOLD standard of 2022 and the General Clinical Practice Assembly of Lung and Respiratory Diseases of 2021. Based on the medical records of COPD patients at the dr. Soehadi Prijonegoro Hospital, the study subjects received more than one drug or obtained a combination of bronchodilator drugs either by oral preparation, injection, inhalation, or nebulizer. The medication given to the patient is in accordance with the dr. Soehadi Prijonegoro Hospital Edition 2022.

Dose accuracy assessment is the appropriateness of the administration of bronchodilator doses that is more emphasised based on the estimate and frequency of administration of the drug, which is then compared to the GOLD standard in 2022. Based on Table 3, the dosage of bronchodilator drugs in COPD patients of 58.11% is already in line with the GOLD standard by 2022 or can be said to be the exact dosage. The dose accuracy of 41.66% is said to not meet the GOLD standard by 2022 as drug dosing and fertility use tend to be less than the standard or underdose.

Bronchodilator is the first-line medication in the management of therapy in PPOC patients. According to research at dr. Soehadi Prijonegoro Hospital from the medical records of COPD patients in the period January–December 2022, there were three groups of bronchodilator drugs prescribed to the subject, namely β2 agonists, methylsantin, antimuscarinics, and combinations in inhalation as well as in nebulizers [17]. The most commonly used bronchodilator is a combination of β2: Corticosteroid agonists in nebulizers. The combination of β2: Corticosteroid agonists and β2:antimuscarinic agonists in nebulizers used in the nebulizer is a short-acting β2-agonist (SABA) and a short-acting muscarin antagonist (SAMA) [18]. The combination with the group of corticosteroids used is already in line with what is recommended by the GOLD update 2022, among other inhaled corticoids and nebulizers such as beklometason, flukatisone, and budesonides.

One of the principles of rational drug therapy is the choice of the right medication. It can be understood that the medication used is effective, safe, economical, and according to the condition of the patient. Precisely the medication for COPD patients is the suitability of the administration of medicines, in particular the group of bronchodilators, in patients with COPD with the GOLD standard update in 2022. The use of bronchodilators is aimed at the primary symptomatic treatment of COPD patients, given individually or in combination. This medication can be used to loosen the airway when an attack occurs, prevent recurrences, and reduce the symptoms that arise. In accordance with the 2022 GOLD update, the use of β2 agonists (fast and long-acting), antimuscarinics (fast action and long action), or a combination of β2-agonists with anti-muscarin and methylsanthin for the pharmacological therapy of COPD patients is strongly recommended [19, 20].

The combination of β2 agonists and antimuscarinics gives the improvement effect of FEV1 and its comparative symptoms given individually. Combined bronchodilator therapy is more effective in relaxing bronchial muscles, maximising the bronchodilatation effect in the treatment of COPD patients, and reducing side effects than increasing single-dose therapy [21]. The use of antimuscarinics with β2 inhalation agonists can provide a good effect on short-term attacks or recurrences. Antimuscarins have the effect of increasing the β2 bronchodilation agonist's rapid action in dealing with recurrent attacks, improving lung function, and significantly reducing the risk of hospitalisation. This is because antimuscarins have a slower effect than β2 agonists, even though they are given simultaneously [22]. Oral β2 agonist combination bronchodilator with methylsantin may be administered to COPD patients, but intravenous administration of methylsantin (injection preparation) such as theophylline and aminofiline is considered second-line therapy, associated with side effects on lung function that are still inconsistent [23].

According to the results in Table 3, drug dosage and fertility use tend to be less than the standard, or underdose. Inaccuracies in the given dose may occur because the assessment of the dose accuracy is based on the dose of the regime given in accordance with the established literature, [24] whereas in the evaluation of this study, the dosage was accurately calculated using the GOLD reference standard of 2022. The administration of aminofilin or theophyllin doses to subjects that were still less than the standard, according to PDPI (2016), was used as a maintenance dose.(12) This is in accordance with the study of Zulkarni, *et al*. (2019) [2], which shows that methylsantin, which is no longer the first line, is still widely used because the group can improve the work of the lungs [2].

Table 3: Precision Profile of Dosage of Bronchodilators

Bronchodilators	Name and Type of Medication	Not suitable	Suitable
		n (%)	n (%)
Methylsantin	Theophyllin (oral)	3 (2,04)	18 (11,62)
	Aminophyllin (oral)	0 (0)	2 (1,36)
	Aminophyllin (injection)	0 (0)	12 (8,19)
Agonist β2	Terbutalin (oral)	1 (0,68)	13 (8,89)
	Salbutamol (oral)	1 (0,68)	9 (6,13)
	Salbutamol Ventolin® (Nebules)	33 (22,58)	0 (0)
	Phenoterol Berotec (MDI)	5 (3,41)	1 (0,68)
Antimuscarinic	Tiotropium Spiritual Respiration (SMI)	12 (8,21)	0 (0)
Combination of antimuscarins / agonist β2	Ipratropium /Salbutamol - Combivent (Nebules) - Meprovent (Nebules)	 9 (6,15) 10 (6,84)	 0 (0) 0 (0)
Combination of β2 agonists and corticosteroids	Salmeterol/Flucatisone Seretide Discus (MDI)	10 (6,84)	0 (0)
	Budesonide/ Formoterol Symbicort 160/4,5 mcg (DPI)	1 (0,68)	7 (4,79)
Total	12	85 (58,11)	62 (41,66)

n: number of uses

%: the percentage calculated from the use of each group divided by the total use multiplied by 100%

The most widely used treatment for COPD is a β2 agonist, which is the first choice because the relieving effect on the lungs is highly expected when exacerbations occur [23]. Donation of β2 agonists to research subjects at dr. Soehadi Prijonegoro Hospital through three routes of administration: oral, nebulizer, and inhalation. Agonis β2 received by COPD patients is salbutamol (0, 5 mg; 0,75 mg; 1 mg; and 2 mg) and terbutaline (0,75 mg, 1 mg, and 2,5 mg) with varying frequencies of use. Administration of terbutalin 0.75 mg and 1 mg with a frequency of three times a day is not the correct dosage as standard, and administration of Salbutamol 0.5 mg; 0.75 mg, 2 mg, 2 mg, 2 times per day, and 1 mg, three times daily, also has not been said to be the correct dose as standard. This is an assessment that is adapted to the actual condition of the patient. In the treatment of chronic obstructive pulmonary disease, it has been demonstrated that the maintenance dose of oral bronchodilator combination 2 agonists with methylsantin is effective (COPD). The addition of methylsantin to 2 agonists widens the airways and enhances long-term lung function, lowering shortness of breath symptoms and enhancing the quality of life for COPD patients [25].

The use of Ventolin® nebules as a β2 agonist that acts 22.58% faster with a dose of 1 ampoule every 6 hours, 8 hours, or 12 hours is already in line with the GOLD standard in 2022. The inhalation of the β2 agonist given to the study subjects was phenoterol bromide (Berotec MDI). The dose given varies, the preparation of 100 mcg is given 3 times a day in 2 sprays, whereas the preparation of 200 mcg given 3 times a day in 1-2 sprays is already in line with the standard dose of GOLD in 2022. By 2022, the administration of antimuscarinic thyotropium bromide in the form of a soft mist inhaler with a dose of 2.5 mcg once a day in 2 sprays will be completely accurate to the GOLD standard. Tiotropium given over a long period of time has been shown to reduce the frequency of exacerbations [26]. In addition, thiotropium also improves symptoms and health status and increases the effectiveness of lung rehabilitation [27].

The combination of nebulizers administered to the study subjects was antimuscarinic ipratropium bromide (0.52 mg) and β2 agonist salbutamol (3.01 mg). The dose given varies from 1 ampoule of nebula every 8 or 12 hours, and the dose will be fully in accordance with the GOLD standard by 2022. The combination of antimuscarinic and β2 agonists in the nebulizer can be used to cope with acute exacerbations but is not recommended for long-term use. Using a combination of rapid-acting bronchodilators regularly and when necessary will improve FEV1 and symptoms [16, 28]. A total 7.52% of the dosage and frequency of use of salmeterol/ flukatisone or formoterol/ budesonide inhalation combination medications will already be in line with the GOLD standard by 2022, and there are still 4.79% that are not in line [29, 30]. Regular use of inhaled corticosteroid monotherapy is not recommended because inhaled corticosteroids have the ability to inhibit the local immune response in the airways, prolonged use of them is linked to an increased risk of respiratory infections, including pneumonia. A decrease in bone mineral density and an increased risk of osteoporosis have also been linked to long-term usage of inhaled corticosteroids in COPD patients [21, 31-33].

Conclusion

Patterns of use of bronchodilators in COPD patients in the dr. Soehadi Prijonegoro Hospital period January-December 2022, which is the exact medication of 100% in accordance with the GOLD standard of 2022, and the dosage accuracy and frequency of the drug use of 41.66% are not

appropriate, as much as 58.11% according to the gold standard of 2022. The inaccuracies of the given dose are affected by the differences in the given regimen, so the dose is adjusted to the related literature already established.

Declarations

The ethical licence number 107/Etik-CRSSP/IV/2023 through the Research Ethics Committee.

Conflict of Interest

The authors have no conflict of interest in anything in this research.

Authors' Contribution

M. Fiqri Zulpadly conceptualized the study, created the methodology, wrote original draft, and reviewed; Najla Anisah Qumairoh wrote and edited the manuscript.

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