



The Effect of Long-Acting Beta-2 Agonist Monotherapy and Long-Acting Anticholinergic Monotherapy to Quality-of-Life in Group B Stable COPD Patients

Tri Setia Negara Sinulingga,¹ Pandiaman Pandia¹ Amira P. Tarigan,¹ Putri Chariani Eyanoe²

¹Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Sumatera Utara/ RSUP H. Adam Malik, Medan, Indonesia

²Department of Community Medicine, Faculty of Medicine, Universitas Sumatera Utara, Indonesia

Abstract

Background: Based on the 2019 Global Initiative for Chronic Obstructive Lung Disease (GOLD), treatment for group B stable COPD patients is a long-acting beta-2 agonist (LABA) or long-acting anticholinergic (LAMA). Some studies experienced that LAMA was better than LABA but the opposite was also found in several studies. COPD patients often experience a decline in physical activity which causes a decrease in quality of life. We aimed to compare the effect of LABA or LAMA on quality of life in group B stable COPD patients.

Methods: This was a study with case series design conducted on 50 COPD patients divided into two groups. The first group consisted of patients who used LABA for at least 3 months. The second group used LAMA for at least 3 months. All subjects filled in the SGRQ. The calculation of SGRQ was carried out using Microsoft Excel Calculator SGRQ.

Results: A total 41 men and 9 women were enrolled in this study. There was no significant difference between the use of indacaterol monotherapy and tiotropium monotherapy on the quality of life although tiotropium showed a better quality of life (76%) than indacaterol monotherapy (64%).

Conclusion: There was no significant difference in the use of indacaterol and tiotropium on the quality of life although in this case tiotropium showed better results ($P=0.538$).

Keywords: COPD, indacaterol, tiotropium, quality of life, SGRQ

Corresponding Author:

Tri Setia Negara Sinulingga |
Department of Pulmonology and
Respiratory Medicine, Faculty of
Medicine, Universitas Sumatera Utara,
RSUP H. Adam Malik, Medan,
Indonesia | trisinulingga@yahoo.com

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is one among a group of non-communicable diseases that is a public health problem in Indonesia. This is due to the increase in life expectancy and the higher exposure to risk factors, such as host factors that are thought to be associated with the incidence of COPD, the increasing number of smokers, especially in the younger age group, as well as indoor and outdoor air pollution and also pollution at work.¹

Currently in Indonesia, COPD is estimated to have 4.8 million patients with a prevalence of around 5.6%. This figure will continue to increase along with the escalating number of smokers because 90% of COPD patients are smokers and ex-smokers.²

In 2011, COPD was listed as the third leading cause of death in the United States, and by 2030 it is estimated that the mortality rate of COPD will intensify to 4.5 million people annually.³ The World Health Organization (WHO) states that by 2030, COPD will be the third leading cause of death in the world.⁴

Shortness of breath causes the patient to be panic, anxious and frustrated, so the patient reduces activity to avoid the difficulty in breathing. Patients will fall into physical deconditioning, which is an adverse condition due to low activity that could affect the musculoskeletal, respiratory, cardiovascular and other systems. This situation causes a decline in functional capacity, so that the quality of life also decreases.⁵ One of the measuring tools used to evaluate the quality of life of COPD patients is the Saint George's Respiratory Questionnaire (SGRQ).

In pharmacological therapy, the drugs most often used for COPD patients are bronchodilators with two types: beta-2 agonists and anticholinergic drugs.⁶ Beta-2 agonists work by relaxing respiratory smooth muscle through stimulation of beta-2 adrenergic receptors that are abundant in airway smooth muscles. Stimulation of beta-2 adrenergic receptors at the cellular level will stimulate G protein to activate adenylate cyclase which converts adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP), resulting in decreased calcium release and changes in membrane potential that cause muscle relaxation. Intracellular cAMP plays a role in regulating respiratory smooth muscle tone, resulting in bronchodilation. In addition, beta-2 agonists, which also stimulate beta-2 adrenergic receptors in the presynaptic parasympathetic ganglia of the airways, inhibit the release of acetylcholine, which is a bronchoconstrictor, inducing bronchodilation.⁷

Anticholinergic or antimuscarinic bronchodilators are non-selective cholinergic muscarinic receptor antagonists that act by blocking parasympathetic acetylcholine. Acetylcholine binds to M1 and M3 and causes smooth muscle contraction via an increase in cyclic guanosine monophosphate (cGMP) or by activation of G protein. This protein then activates phospholipase C to produce inositol triphosphate (IP3), leading to the release of calcium from intracellular stores and activation of myosin light chain kinase which then causes smooth muscle to contract. Anticholinergics block this cascade and reduce smooth muscle tone by reducing intracellular calcium release.⁸

Based on 2019 GOLD, the treatment options for group B stable COPD were long-acting beta-2 agonists (LABA) or long-acting antimuscarinics (LAMA). Examples of LABA are indacaterol and salmeterol while the example of LAMA is tiotropium.³ Data regarding the different effects of LABA or LAMA bronchodilators on quality of life in group B stable COPD patients in Indonesia are still very limited. With this background, we were interested in conducting a study on the effect of indacaterol monotherapy versus tiotropium monotherapy on quality of life in

group B stable COPD patients.

METHODS

This was a descriptive study with a case series design from April 2019 to June 2019, at the outpatient clinic of H. Adam Malik Hospital Medan and the Education Hospital of Universitas Sumatra Utara, Medan.

All study subjects were group B stable COPD patients who had received indacaterol or tiotropium for at least the past 3 months. Patients were then interviewed and an informed consent was given for the study; then, the patients were asked to complete the SGRQ under the direction of the researcher. The SGRQ contains 50 questions, consisting of symptom domains on questions 1-8, activity domains on questions 11-17 and 36-44, and impact domains on questions 9,10, 18-35 and 45-50. The calculation of the score is a total processing of 50 statements where each alternative answer to the respondent on the SGRQ has a weight.⁸ Furthermore, the total score is calculated using the standard Microsoft Excel "Calculator SGRQ" software.

The Health Research Ethics Committee approved the research procedure. Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS), where the value of $P < 0.05$ was considered significant.

RESULTS

In this study, the majority of subjects were male, users of indacaterol (86%) and tiotropium (88%), mostly in age range of 60-69 years, where in this age range, users of indacaterol were 13 people (52%) and tiotropium were 11 people (44%). Most of the subjects were Batak ethnic with 14 indacaterol users (56%) and 17 tiotropium users (68%). All study subjects had a smoking history with severe Brinkman index, consisted of 21 indacaterol users (84%) and 14 tiotropium users (56%). Most subjects taking indacaterol and tiotropium were in the obesity criteria. The characteristics of the study subjects can be seen in Table 1.

Table 2 below indicates that the use of tiotropium monotherapy resulted in a better quality of life (76%) than indacaterol monotherapy (64%).

Table 1. Characteristics of Research Subjects

Characteristics	Indacaterol		Tiotropium	
	N	%	N	%
Age				
40–49 years	5	20.0	4	18.0
50–59 years	5	20.0	6	24.0
60–69 years	13	52.0	11	44.0
≥70 years	2	8.0	4	18.0
Gender				
Men	19	86.0	22	88.0
Women	6	24.0	3	12.0
Occupation				
Civil Servant	4	18.0	3	12.0
Retired	8	32.0	3	12.0
Farmer	5	20.0	4	18.0
Self-employed	8	32.0	15	60.0
Brinkman Index				
Mild	0	0	3	3.0
Medium	4	16.0	8	32.0
Severe	21	84.0	14	56.0
Ethnic group				
Batakese	14	56.0	17	68.0
Javanese	6	24.0	4	18.0
Etc.	5	20.0	4	18.0
Body mass index				
Underweight	1	4.0	1	4.0
Normoweight	3	12.0	7	28.0
Overweight	10	40.0	8	32.0
Obese	11	44.0	9	36.0

Statistical tests using chi-square test revealed no significant difference between indacaterol and tiotropium ($P>0.05$). In this case, the tiotropium group showed a higher value. This pointed out that many factors affect the quality of life of COPD patients other than indacaterol and tiotropium treatment, such as age, gender, healthy lifestyle, etc.

Table 2. Overview of Research Subjects' Quality of Life

Quality of Life	Indacaterol		Tiotropium		P
	N	%	N	%	
Good	16	64.0	19	76.0	0.538*
Bad	9	36.0	6	24.0	
Total	25	100.0	25	100	

Note: *chi-square

Details per domain could not be displayed because the calculation of the SGRQ score was done with the Microsoft excel SGRQ calculator tool which exhibited the overall live score.

DISCUSSION

In this study, the majority of the subjects were male. This is in line with the actual conditions that we could observe: men are the most common patients with COPD. The high prevalence of COPD in males is related to the fact that the prevalence of smoking is 16 times higher in males (65.9%) than females (4.2%).⁹

The majority of subjects were aged 60-69 years where in this age group, 13 people (52%) were indacaterol users and 11 people (44%) were tiotropium users. This is identical to a study conducted at the H Adam Malik Hospital, which pointed out that the mean age of COPD patients was 61.4 years.¹⁰ Age is associated with changes in lung structure and function that may intensify the pathogenesis of COPD, which can escalate the incidence of COPD in the elderly.¹¹

Most subjects were Batak ethnic, where in this ethnicity, 14 people were indacaterol users (56%) and 17 were tiotropium users (68%). This is related to the culture of the Batak tribe, where cigarettes are used in several traditional events, and also the custom of the Batak tribe to smoke even from a young age.¹²

All study subjects had smoking history, and among these smokers with severe Brinkman index, 21 people used indacaterol (84%) and 14 used tiotropium (56%). This follows a related study in which most subjects had severe Brinkman index (68.9%).¹³

Cigarette smoke is a very high oxidant that can cause inflammation in the lungs and airways. The correlation between smoking and COPD is a dose-response relationship; the more the number of cigarettes smoked and the longer the smoking habit, the higher the risk of suffering from COPD.²

This study also assessed the quality of life of COPD patients who used indacaterol and tiotropium monotherapy as assessed by the SGRQ. The SGRQ is one of the measuring tools used to assess the quality of life of COPD patients that has been recognized in the medical field. The SGRQ contains 3 components, namely symptoms, activities and

impacts.

From the component of symptoms and impacts there were no significant differences between indacaterol dan tiotropium. Based on the activities component, tiotropium users had less activity limitations than indacaterol. Thus, on the overall score we obtained that the use of tiotropium monotherapy showed a better quality of life (76%) than indacaterol monotherapy (64%). After the statistical test, the difference between the two did not show any significance ($P>0.05$).

Different results were obtained by Buhl et al. in 2011 among 1477 patients with moderate and severe COPD who underwent a blind trial of once-daily dose of indacaterol and tiotropium for 12 weeks. The study revealed similar improvements in FEV₁ values on indacaterol and tiotropium groups after 12 weeks of treatment, with statistical tests proving indacaterol not inferior to tiotropium.

However, the reasons for these differences are still being investigated until now. Indacaterol and tiotropium may have different effects on overall lung volume, despite the similarity of FVC results. It would be interesting to compare the effects on inspiratory capacity. The two drugs have distinct bronchodilator effects on the small airways, possibly due to regional variations in the distribution of muscarinic and adrenergic receptors of the airways. This is what causes the difference in non-bronchodilator effects on pulmonary ventilation and pulmonary hemodynamics.

Another opinion suggests that the parasympathetic nervous system is a major component of airway smooth muscle tone and there is evidence proving that the cholinergic system is increased in COPD.^{14–16} Therefore, COPD is recommended to be treated with anticholinergic drugs rather than beta-2 agonists.^{15,16}

LIMITATION

Limitation of this study is writer could not rule out other factors that affect the quality of life of COPD patient such as age, gender, healthy lifestyle, etc.

CONCLUSION

In this study, tiotropium monotherapy showed a better quality of life than indacaterol monotherapy, but this difference was not statistically significant.

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CONFLICT OF INTEREST

None.

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