

PENGARUH PEMBERIAN MONOTERAPI INDACATEROL DAN TIOTROPIUM TERHADAP KUALITAS HIDUP PADA PASIEN PENYAKIT PARU OBSTRUKTIF KRONIK STABIL GRUP B

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Abstrak

Latar belakang: Berdasarkan Global Initiative for Chronic Obstructive Lung (GOLD) 2019, terapi pilihan untuk Penyakit Paru Obstruktif Kronik (PPOK) stabil grup B adalah agonis beta-2 kerja panjang (LABA) atau antikolinergik kerja panjang (LAMA). Beberapa studi menunjukkan LAMA lebih baik daripada LABA tetapi sebaliknya juga ditemukan hasil berbeda dalam beberapa studi. Pasien PPOK sering mengalami penurunan aktivitas fisik yang menyebabkan penurunan kualitas hidup. Penelitian ini bertujuan untuk membandingkan efek monoterapi indacaterol atau monoterapi tiotropium terhadap kualitas hidup pada pasien Penyakit Paru Obstruktif Kronik (PPOK) stabil grup B.

Metode: Ini adalah studi desain seri kasus yang dilakukan pada 50 pasien COPD dibagi menjadi dua kelompok. Kelompok pertama adalah pasien yang menggunakan indacaterol selama minimal 3 bulan, kelompok kedua adalah tiotropium selama minimal 3 bulan. Semua subjek dianamnesa dan diminta mengisi kuesioner SGRQ. Perhitungan kuesioner SGRQ dilakukan dengan Microsoft Excel Calculator SGRQ.

Hasil: Total 41 pria dan 9 wanita terdaftar dalam penelitian ini. Berdasarkan penelitian ini ditemukan bahwa penggunaan monoterapi tiotropium menunjukkan kualitas hidup yang lebih baik (76%) dibandingkan monoterapi indacaterol (64%). Namun setelah dilakukan uji statistik tidak ada perbedaan signifikan penggunaan monoterapi tiotropium dibandingkan monoterapi indacaterol ($p=0,538$).

Kesimpulan: Tidak terdapat perbedaan yang bermakna pada penggunaan monoterapi indacaterol dan monoterapi tiotropium terhadap kualitas hidup pasien PPOK stabil grup B ($p=0.538$).

Kata kunci: COPD, indacaterol, tiotropium, kualitas hidup, SGRQ

THE EFFECT OF MONOTHERAPY LONG-ACTING BETA-2 AGONIST AND MONOTHERAPY LONG-ACTING ANTICHOLINERGIC TO QUALITY OF LIFE STABLE COPD PATIENTS GROUP B

Abstract

Background: Based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2019, treatment for stable Chronic Obstructive Pulmonary Disease (COPD) patients group B is long-acting beta-2 agonist (LABA) or long-acting anticholinergic (LAMA). Some studies experience LAMA is better than LABA but the opposite is also found in several studies. COPD patients often experience decrease 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 stable COPD patients group B.

Methods: This was a case series design study conducted on 50 COPD patients divided into two groups. The first group is patients who use LABA for a minimum of 3 months, the second group is LAMA for a minimum of 3 months. All subjects filled in the SGRQ questionnaire. The calculation of the SGRQ questionnaire is done with Microsoft Excel Calculator SGRQ.

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

Conclusion: There is no significant difference in the use of indacaterol and tiotropium to quality of life although in this case tiotropium shows better results ($p=0.538$).

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

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is one of a group of non-communicable diseases that is a public health problem in Indonesia. This is due to the increasing 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 young age group, as well as indoor and outdoor air pollution and at work.¹

Currently, in Indonesia, it is estimated that there are 4.8 million patients with a prevalence of around 5.6%. This figure will continue to increase with the increasing number of smokers because 90% of COPD patients are smokers and former 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 death rate from COPD will increase to 4.5 million people each year.³ The World Health Organization (WHO) states that in 2030, COPD will be the third leading worldwide cause of death.⁴

Shortness of breath caused the patient to panic, and become anxious and frustrated, so the patient reduced activity to avoid shortness of breath. The patient will fall into physical deconditioning, namely, an adverse condition due to low activity and can affect the musculoskeletal, respiratory, cardiovascular and other systems. This situation causes the functional capacity to decrease, so the quality of life also decreases.⁵ One of the measuring tools used to measure 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. The types of bronchodilators that are often used in the treatment of COPD are beta 2 agonists and anticholinergic drugs.⁶

Beta 2 agonists work by relaxing respiratory smooth muscle through stimulating beta 2 adrenergic receptors that are abundant in airway smooth muscle. Anticholinergic or antimuscarinic bronchodilators are non-selective cholinergic muscarinic receptor antagonists that work by

blocking acetylcholine in the parasympathetic nervous system, causing bronchodilation.⁷

Based on GOLD 2019, the treatment options for group B stable COPD are long-acting beta-2 agonists (LABA) or long-acting antimuscarinics (LAMA). Examples of long-acting beta-2 agonists are indacaterol and salmeterol. An example of a long-acting antimuscarinic drug is tiotropium.

Data regarding the different effects of giving LABA or LAMA bronchodilators on quality of life in patients with stable COPD group B in Indonesia are still very limited. Against this background, researchers are interested in conducting a study on the effect of indacaterol monotherapy versus tiotropium on quality of life in group B stable COPD patients.

METHOD

This research is a descriptive study with a case series design carried out over 4 months, from April 2019 to June 2019, at the Outpatient Polyclinic of H. Adam Malik Hospital Medan and the Education Hospital of the University of North Sumatra Medan.

All study subjects were group B stable COPD patients who had received indacaterol or tiotropium for at least the past 3 months. After that, an anamnesis was taken, and informed consent was given to the study; then, the patient was asked to fill out the Saint George's Respiratory Questionnaire (SGRQ) under the direction of the researcher. The SGRQ questionnaire 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 respondent's score is the total processing of 50 statements in which each alternative answer to the respondent on the SGRQ has its weight.⁸ Furthermore, the total score of the respondents 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 chi-square test using the Statistical Package for Social Sciences (SPSS), where the p-value < 0.05 was significant.

RESULTS

In this study, the majority of subjects were male, both users of indacaterol (86%) and tiotropium (88%), with the majority aged 60-69 years, where users of indacaterol were 13 people (52%) and tiotropium were 11 people (44%). The majority of the subjects were Batak ethnic with 14 indacaterol users

(56%) and 17% tiotropium users (68%). All study subjects had a smoking history with an average of severe Brinkman index, where indacaterol users were among 21 people (84%) and tiotropium among 14 people (56%). This study found that most subjects using indacaterol and tiotropium were included in the obesity criteria. The characteristics of the research subjects can be seen in Table 1

Table.1 Characteristics of Research Subjects

			Indacaterol		Tiotropium	
Demographic Characteristics			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
Job	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	Light		0	0	3	3.0
	Medium		4	16.0	8	32.0
	Heavy		21	84.0	14	56.0
Ethnic Group	Batak		14	56.0	17	68.0
	Jawa		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

Meanwhile, table 2 below shows that the use of tiotropium monotherapy showed a better quality of life (76%) than indacaterol monotherapy (64%).

Statistical tests using the chi-square test showed no significant difference between indacaterol and tiotropium users ($p > 0.05$). In this

case, the tiotropium group showed a higher value. This indicates that many factors affect the quality of life of COPD patients other than indacaterol and tiotropium treatment.

DISCUSSION

In this study, the majority of the subjects were male. This is in line with conditions in the field, which state that men are the largest number of people with COPD. The high prevalence of COPD in males is related to the fact that the prevalence of smokers is

Table.2 Overview of Research Subjects' Quality of Life

Quality of Life	Indacaterol		Tiotropium		p-value
	N	%	N	%	
Good	16	64.0	19	76.0	0.538*
Bad	9	36.0	6	24.0	*chi-square
Total	25	100.0	25	100	

16 times higher in males (65.9%) than females (4.2%).⁹

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

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

All study subjects had a smoking history, and the average number of subjects with a severe Brinkman index was 21 people (84%) and tiotropium users (56%). This follows a related study where most subjects had a severe Brinkman index (68.9%).¹³ Cigarette smoke is a very high oxidant that can cause inflammation in the lungs and airways. The relationship 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 questionnaire. Saint George's Respiratory Questionnaire (SGRQ) is one of the measuring tools used to assess the quality of life of COPD patients that have been recognized in the medical world. This study found 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 in 1477 patients with moderate and severe COPD who conducted a blind trial of once-daily doses of indacaterol and tiotropium for 12 weeks. The study showed similar improvements in indacaterol

and tiotropium in FEV₁ values after 12 weeks of treatment, with statistical tests proving indacaterol not inferior to tiotropium.

However, the reasons for these differences are still being researched until now. Indacaterol and tiotropium may have a different effect 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 from the airways. This is what causes different non-bronchodilator effects on pulmonary ventilation and pulmonary hemodynamics.

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

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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