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ASSESSMENT OF COST EFFECTIVENESS OF DIFFERENT INHALER MEDICATIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Respiratory Medicine

Tamilselvan T*	Professor And Head, Department Of Pharmacy Practice, Nehru College Of Pharmacy, Thrissur, Kerala, India. *Corresponding Author
Alina Bino	Pharm.D Interns, Nehru College of Pharmacy, Thrissur, Kerala, 680588, India.
Anil Varghese	Pharm.D Interns, Nehru College of Pharmacy, Thrissur, Kerala, 680588, India.
Merrina Navin	Pharm.D Interns, Nehru College of Pharmacy, Thrissur, Kerala, 680588, India.
Mrudula Saji	Pharm.D Interns, Nehru College of Pharmacy, Thrissur, Kerala, 680588, India.
Dawn V J	Assistant Professor, Department of Pharmacy Practice, Nehru College of Pharmacy, Thrissur, Kerala, India.
Arya Jayakumar	

ABSTRACT

Chronic Obstructive Pulmonary disease is a chronic disease of the airways characterized by gradual progressive loss of lung function. Advances in inhaled medicines have significantly increased the therapeutic choices for treating disease. Aim of the study was to evaluate the clinical and economic consequences of patients and to find out the most cost-effective drug combination among the different inhaler drug combinations. A retrospective study was conducted among 121 patients seeking treatment from pulmonology department in a tertiary care hospital over a period of six months. Patients with age greater than 18 years who were prescribed with the following drug combinations long acting beta agonist/inhaled corticosteroids, long acting beta agonist/long acting muscarinic antagonist and long acting beta agonist/inhaled corticosteroids/ long acting muscarinic antagonist were included in the study. All the information regarding the study was collected. Patients included in the study were diagnosed with severe or very severe disease. This study demonstrated that patients treated with long acting beta agonist/long acting muscarinic antagonist showed more effectiveness compared to that of long acting beta agonist/inhaled corticosteroids. But while assessing incremental cost effectiveness ratio, long acting beta agonist/inhaled corticosteroids proved to be a cost effective alternative.

KEYWORDS

Chronic Obstructive Pulmonary Disease, Inhalers, Cost Effectiveness, Burden

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is currently one of the world's top three causes of death, with 90% of deaths occurring in low and middle-income nations [1].

COPD is a common, preventable and treatable disease that 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 and influenced by host factors. The primary modifiable risk factor for the development of COPD is cigarette smoking. COPD has a number of risk factors which can be categorized into two - host factors and environmental factors. The interplay of these factors frequently results in the expression of the illness[1].Patients with severe and extremely severe COPD may experience chronic and progressive dyspnoea, productive or unproductive cough, recurrent wheezing, fatigue, weight loss, muscle atrophy, and anorexia.

Spirometry measures the volume of air forcibly exhaled from the point of maximal inspiration (forced vital capacity, FVC) and the volume of air exhaled during the first second of this manoeuvre (forced expiratory volume in one second, FEV1), and the ratio of these two measurements (FEV1/FVC) should be calculated[2].Dyspnoea scale was used to measure shortness of breath and modified COPD Assessment Test (CAT) score was used to evaluate the quality of life of COPD patients[3,4] .

Advances in inhaled medicines have significantly increased the therapeutic choices for treating COPD. With the continued development of revolutionary medical technologies that improve patient outcomes, there has been an increase in interest in determining the comparative cost effectiveness of new pharmaceuticals in order to determine their relative worth [5].

COPD is predicted to cost $32 billion in direct costs and $20.4 billion in indirect costs in the United States. Eighth greatest cause of disability adjusted life years (DALY) lost globally in 2005, but by 2013, it had risen to the fifth most common cause of DALYs lost[1].

Cost effectiveness analysis (CEA) is a type of pharmacoeconomic analysis that compares the relative costs and outcomes (effects) of two or more options. Costs are calculated in monetary terms, while health effects are calculated in natural or physical units. The incremental cost-effectiveness ratio (ICER) is a typical health economics equation that provides a practical method to guide in health intervention decision making. . In ICER, the additional cost and effectiveness obtained from one treatment alternative is compared to the next alternative[6,7].

Education on inhaler use improves breathing technique in some but not all patients, particularly when a "teach-back" method is used[1]. We decided on this particular topic in order to assess the most affordable and cost effective inhaler options available in this rural part of South Indian state, as COPD is the leading cause of death worldwide and it was rather predominantly diagnosed in this healthcare setup.

MATERIALS AND METHODS

The study was conducted at the Pulmonology department of tertiary care teaching hospital, Palakkad. The study was approved by the Institutional Ethics Committee. Prospective observational comparative study was conducted.The duration of the study was 6 months from March to September, 2021. A total of 175 patients were screened and 121 patients with COPD were included in the study.

Study instruments used were patient case notes, laboratory investigation reports, dyspnoea scale , modified COPD assessment test Score. Inclusion criteria included COPD patients of age greater than 18 years, those patients who are prescribed with any of the following drug combinations: Long acting beta agonist (LABA)/ Inhaled corticosteroids (ICS) (Class A), Long acting beta agonist (LABA)/ Long acting muscarinic antagonist(LAMA) (Class B) and Long acting beta agonist (LABA) /Long acting muscarinic antagonist (LAMA) / Inhaled corticosteroids(ICS) [Class C] were included and grouped as Class A, Class B and Class C respectively. Patients who are willing to give their informed consent to participate in the study were included. Patients who are not willing to participate in the study and pregnant women were excluded from this study.

Demographic characteristics such as age, gender, smoking history, allergic history, signs and symptoms, comorbid conditions, dyspnoea scale, management given to them and other relevant information were obtained from patient medical records and patient interview. Baseline

assessment of pulmonary function test such as spirometry (FEV1, FEV1/FVC, and FVC) and modified CAT score were done.

The pharmacoeconomic related direct medical costs were collected from the patient records, medical bills, hospital accounts section, interviewing the patients or patient bystanders. All the information were recorded in a tabulated data and maintained in excel sheets.

Patient counselling was given on proper inhaler technique and smoking cessation. Patient information leaflets were distributed among patients.

Follow up assessment of pulmonary function test such as spirometry (FEV1, FEV1/FVC, and FVC) and modified CAT score was done through telephonic and direct interviews.

Cost effectiveness analysis (CEA) was performed using incremental cost effectiveness ratio (ICER) for comparing the therapeutic alternatives. ICER value measures the economic value of an intervention compared with an alternative.

Statistical Analysis

The data was recorded in a predesigned format and managed in Microsoft excel 2016 and was analysed using statistical program for social sciences (SPSS) version 21.0. Collected data were systematically presented as a frequency distribution table. Descriptive statistics were analysed for demographic parameters.To determine the most effective inhaler class among the given three classes, in terms of FEV1, Analysis of variance (ANOVA) was used. Paired sample "t" test was also used to assess the significant difference between the three different treatment classes. Statistical significance was fixed at $P<0.05$ with confidence interval of 95%.

RESULT

Patient Demographics

A total of 121 COPD patients were recruited during the study period to assess the cost effectiveness of three different combinations of inhaler classes (LABA+ ICS, LABA+LAMA, LABA+LAMA+ICS). Out of 121 patients, 100 male patients and 21 female patients were identified.

Table 1: Patient Demographic Details

Sl No	Demographics	Treatment Regimen		
		Class A (laba+ics)	Class B (laba+lama)	Class C (laba+lama+ Ics)
1.	Gender			
	Male	44	9	47
	Female	11	1	9
2.	Age Groups (Yrs)			
	18-34	4	-	1
	35-54	5	-	4
	55-74	27	9	30
	>74	19	1	21

LABA-Long acting beta agonist, LAMA-Long acting muscarinic antagonist, ICS-Inhaled corticosteroids

Symptoms of COPD Patients

Majority of patients complaints of dyspnea (98.3%).Other manifestations include phlegm (86%), cough (80.1%) and fatigue (68.6%).

Table 2: Difference of COPD Assessment Test score

SL NO	CLASS	INITIAL SCORE	FINAL SCORE	MEAN DIFFERENCE	P VALUE
1.	CLASS A	24.12±5.25	23.12±5.36	1.46 ±1.27	0.002
2.	CLASS B	25.4±4.12	21.1±1.97	4.3±3.62	0.005
3.	CLASS C	26.6±4.28	24.7±5.03	2±1.78	0.000

Table 2 displays that there was significant difference between initial and follow up modified CAT scores. It shows that from finding the mean difference , Class B has maximum effect , Class C has the next maximum effect and class A inhalers have the least effect. ($p<0.05$)

Table 3: Effects of Spirometry

Sl No	Class Of Inhalers	Initial Fev1	Final Fev1	Average Mean Difference	P Value
1.	CLASS A	38.30 ± 11.69	39.38 ± 11.5	1.1 ± 1.34	0.002
2.	CLASS B	37.11±14.59	42.44 ±13.64	4.82 ± 1.87	0.000
3.	CLASS C	38.55 ± 12.86	40.48 ± 12.82	1.75 ± 1.87	0.001

FEV1-Forced expiratory volume in one second

Table 3 reveals that there was significant difference between initial FEV1 and final FEVI values. It is observed that class B inhalers exhibits maximum improvement, class C shows the second maximum improvement whereas class A allows only least improvement.

From table 6 it is evident that there was no significant difference between classes of inhalers in improving the FEV1 ($p>0.05$). It is therefore proven that all the three classes of inhalers provide approximately the same changes in effects.

Table 4: Comparison between Mean of Costs

SL NO	CLASS	COST OF INHALERS (Rs)	TOTAL TREATMENT COST (Rs)	ICER
1.	CLASS A	420.44 ± 156.21	4036.4 ± 2822.36	63.27
2.	CLASS B	892.75 ± 175.2	3539.73 ± 2390.95	1046.69
3.	CLASS C	998.19 ± 256.04	5194.97 ± 3896.39	124.53

ECONOMIC BURDEN

The mean overall cost incurred for a COPD patient during our study period was 4531.55±3372.15. The total treatment cost include medication, laboratory and consultation cost. By calculating ICER, class A was established to be most cost effective combination compared to Class B and Class C. Class A inhalers require only Rs.63.27 extra cost per extra unit of health care effect as compared to class B. But when comparing Class A with Class C inhalers, Class A requires Rs.1046.69 extra cost per extra unit of health effect. Hence Class C was considered to be the least cost effective drug.

DISCUSSION

COPD with its increasing prevalence, morbidity and mortality is faced as the third leading cause of death worldwide[8]. The allocation of devices and its proper use is dependent upon the economic and psychosocial burden which accompanies the disease[9].

An observational prospective study was conducted and 121 patients were analysed during our six month study period. Our results demonstrated a predominance of males (82.6%) over females (17.4%) as shown in table 1. Similar observations were found in the study of Nejc Horvat et al showed COPD to be significantly more common to be in males (67.7%) than females[10]. The prevalence in males is profoundly accredited to smoking and increasing exposure to risk factors such as dust, cold and occupational hazards.

There were 55 patients with grade 3 dyspnoea, 26 patients with grade 4, 19 patients with grade 2, 11 patients with grade 1 and 10 patients with grade 0 dyspnoea according to dyspnoea scale. J C Bestall et al also concluded similar results with majority of patients (34 patients) falling under grade3 dyspnoea scale[11].

Most of the patients are presented with dyspnoea (98.3%), out of which 80.1% manifested as cough and 86% patients produced sputum. Other indications which accompanied the disease incorporates fatigue (68.6%), wheezing, chest tightness and frequent respiratory infections. The cross sectional study on symptom variability depicted by R Kessler et al also shows that breathlessness was the most profound symptom (72.5%) and the most variable symptoms covered were wheezing, cough, phlegm and chest tightness[8].

Our study revealed a significant difference of 4.3±3.62 between initial and final modified CAT scores for class B inhalers, which establishes that class B shows more benefit (table 4). The least effective one was found to be class A inhalers, which was also supported by Tanja Pavlocic et al, where they had a significant difference of 2.3±3.8 between initial and final CAT scores of LABA/LAMA class[12].

Based on our study, there were significant difference between initial and final FEV1 values. Accordingly, LABA/LAMA with an average mean difference of 4.82±1.87 was found to have more benefit while comparing LABA/LAMA/ICS with an average mean difference of 1.75±1.87 class.This was contradicted by Alizaman Sadigov et al, who also benefited mostly from ICS/LABA+LAMA[13] . Our study concluded that there were no significant difference between classes of inhalers for improving FEV1 (p value-0.553>0.5) i.e., all the three inhaler class provide somewhat same benefits. This was evidenced by

Job F M van Boven et al where they too had no significant difference in persistence between users of multiple dose or single dose inhalers (p value 0.99>0.5)[14].LABA/LAMA/ICS was established to be most expensive with a mean total cost of Rs.5194.97±3896.39 as compared to LABA/LAMA which had a mean total cost of Rs. 3539.73±2390.95. This was claimed to be true in a study conducted in the US by Sweta R Palli et al [15].

LABA/LAMA/ICS class of inhalers had the most financial burden which incurred a total cost of Rs.5194.97. The study conducted by Meenakshi Shah et al demonstrated an average annual cost per COPD patients in a government setting was Rs.5654.16 and Rs.35,290.28 in a private setting. The average annual loss of work days per patient was 16.45 days[9]. Therefore COPD has a significant financial burden on society.

Here, LABA/ICS (63.27) provided to be a cost effective option while comparing Class B and C. Whereas, this was contradictory to the study conducted by Melanie Schroeder et al which showed that LABA/LAMA/ICS was a better cost effective option as compared to LABA/ICS with ICER, cost per QALY gained of 642 pounds[16].

CONCLUSION

Most of the patients included in the study were diagnosed with severe or very severe COPD. There is a good general consensus that combined effects of medications of different pharmacological group's amount to a much more convenient strategy in COPD, especially for severe and very severe COPD. In this prospective analysis for assessing the cost effectiveness of different inhaler medications in COPD, we demonstrated that patients treated with LABA/LAMA shows more effectiveness compared to that of LABA/ICS and LABA/LAMA/ICS. But while assessing ICER, LABA/ICS proved to be a cost effective alternative.

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this investigation.

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