Original Article

Study of Drug Utilization Pattern for Acute Exacerbation of Chronic Obstructive Pulmonary Disease in Patients Attending a Government Hospital in Kerala, India

Sajesh Kalkandi Veettil, Kingston Rajiah[1], Suresh Kumar

Departments of Pharmacy Practice, Faculty of Pharmacy, College of Pharmaceutical Sciences, Trivandrum Medical College, Trivandrum, Kerala, [1]Mallige College of Pharmacy, Bengaluru, Karnataka, India

Abstract

Objective: Drug utilization studies are powerful exploratory tools to ascertain the role of drugs in society. This study was conducted to establish the drug utilization pattern and the common adverse drug reactions for the treatment of acute exacerbation of chronic obstructive pulmonary disease (COPD) in one of the government hospitals in Kerala, India. **Methods:** This was a prospective observational study aimed at recognizing the drug utilization pattern for the treatment of acute exacerbation of COPD for 7-day under nonexperimental settings. All information significant to the study was collected from the case records and discussions conducted with the inpatients and bystanders during ward rounds, with the support of a physician. Moreover, daily follow-ups were conducted to assemble data on amendment in therapy, add-on therapy, and clinical improvement until the patient was discharged from the hospital or to an upper limit of 7-day, whichever is earlier. **Results:** All the patients in this study received combination therapy. Among the inhalational β-agonists, salbutamol accounted for 74% use. Parenteral steroids were used in 78% of the patients and all of them received hydrocortisone. Steroid inhalers were used only in 25% of the patients. Anticholinergics were used in 77.5% of patients. Antibiotics were used in 86.7% patients. The main adverse effects noted were dry mouth (15%) and bad taste (10%) and these adverse effects were highly correlated with the use of anticholinergics ($P < 0.05$). **Conclusions:** Despite the use of drugs according to the availability and physician's preference, it was found in the analysis that majority were in accordance with Global Initiative for Chronic Obstructive Lung Disease criteria recommendations.

Keywords: Acute exacerbation, chronic obstructive pulmonary disease, drug utilization

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airflow obstruction that is not fully reversible. The airflow obstruction does not change markedly over several months and is usually progressive in the long-term.[1] Exacerbations are key events in COPD, defined by the presence of worsening symptoms, but also often associated with concurrent deteriorations in pulmonary function and increases in both local and systemic inflammation.[2] COPD is a leading cause of morbidity and mortality worldwide, and results in economic and social burdens that is both substantial and increasing. COPD is the fourth leading cause of death worldwide and is estimated to be the third leading cause of death by 2020.[3] The role of antibiotics in treating mild or moderate exacerbations in patients with acute COPD is unclear.[4] The enormous clinical and economic impact of COPD has prompted the development of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD.[5] This committee has adequately outlined the goals of COPD management that include reduction of disease progression and mortality, relief of symptoms, improvement in exercise tolerance and health status, and prevention of exacerbations and complications. Acute exacerbations of COPD are treated with oxygen (in hypoxemic patients), inhaled β-agonists, inhaled anticholinergics, antibiotics and systemic corticosteroids. Methylxanthine therapy may be considered in patients who do not respond to other bronchodilators. Antibiotic therapy is directed at the most common pathogens, including *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*. Mild to moderate exacerbations of COPD are usually treated with older broad-spectrum antibiotics

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/2249-4863.141622

Address for correspondence: Mr. Sajesh Kalkandi Veettil, Faculty of Pharmacy, College of Pharmaceutical Sciences, Trivandrum Medical College, Trivandrum, Kerala, India.
E-mail: sajesh.vijay@gmail.com

such as doxycycline, trimethoprim-sulfamethoxazole and amoxicillin-clavulanate potassium. Treatment with augmented penicillins, fluoroquinolones, third-generation cephalosporins or aminoglycosides may be considered in patients with more severe exacerbations.[6] International guidelines advocate a 7- to 14-day course of systemic glucocorticoid therapy in acute exacerbations of COPD. However, the optimal dose and duration are unknown.[7] Drug utilization studies are powerful exploratory tools to ascertain the role of drugs in society. These studies create a sound sociomedical and health economic basis for healthcare decision making. COPD is underdiagnosed and repeatedly misdiagnosed, which possibly underwrites to the ongoing upsurges in the occurrence, sickness and death-related with this disease. This is unlucky since COPD cannot be healed, it can be cured efficiently, chiefly through the previous stages of the disease. Evidence-based guidelines (GOLD) established to contribute in the inhibition, diagnosis and controlling of COPD, are offered to health care professionals concerned in learning more about COPD. These guidelines are efficient and reviewed on a consistent basis to replicate recent developments in our understanding of the pathophysiology of and managements available for COPD. However, primary-care physicians have stated a lack of awareness of the essential ideas behind the best management of COPD obtainable in the guidelines.

Methods

The study was conducted during the period of year 2008 from January to June at Trivandrum Medical College and Hospital in Kerala, India which is a tertiary care hospital. This was a prospective observational study aimed at recognizing the drug utilization pattern for the treatment of acute exacerbation of COPD for 7-day under nonexperimental settings. All information significant to the study was collected from the case records and discussions conducted with the inpatients and bystanders during ward rounds, with the support of a physician. Moreover, daily follow-ups were conducted to assemble data on amendment in therapy, add-on therapy, and clinical improvement until the patient was discharged from the hospital or to a upper limit of 7-day, whichever is earlier.[8,9] The adverse drug reactions related to the drugs were monitored and documented in a suitably designed adverse drug reaction documentation form through an interview with the patients. The study was approved by the Human Ethical Committee of the concerned hospital in India. An informed consent form, approved by the Human Ethical Committee, was signed by all patients and this process was in accordance with good clinical practices.

Study sample

A total number of 120 eligible consenting patients were randomly selected by convenience sampling technique for the study. Patients with diagnosis of acute exacerbation of COPD continued treatment as defined by GOLD were randomly selected.[5,9] Exclusion criteria were as follows: Diagnosis of cystic fibrosis, asthma, or severe bronchiectasis, evidence of pneumonia either at presentation or during follow-up.

Statistical analysis

Data were analyzed using computer software, Statistical Package for Social Sciences (SPSS) version 17 by IBM Corporation. Data are expressed in its frequency and percentage. To elucidate the associations and comparison between different parameters, Chi-square test, *t*-test, paired *t*-test, were used.

Results

A total of 120 patients were initially identified and included in the analysis. Demographic and clinical characteristics of the study patients at the time of identification are summarized [Table 1]. Majority of the patients were of a low socioeconomic status according to the modified Kuppuswamy scale.[10] Most of the patients came under Types I and II grade of exacerbation (52.5% and 37.5%, respectively) as per the grading scale for exacerbation of COPD.[11]

All the patients in this study were receiving combination therapy [Table 2]. Among the inhalational β-agonists, salbutamol accounted for 74%, followed by formeterol. Among the oral β-agonist, all of them received salbutamol. Parenteral steroids were used in 72.5% of the patients and all of them received hydrocortisone. Steroid inhalers were used in 25% of patients with all of them receiving budesonide. Methylxanthine was taken by all the patients (100%), in which the most common was deriphylline (hydroxyethyl theophylline), which accounted for about 96% use, followed by aminophylline. Anticholinergics

Table 1: Characteristics of the study population (*n*=120)

Variables	Mean (SD) or percentage
Demographic	
Male sex	87.5
Age (in years)	66 (11)
Socioeconomic status	
Upper middle	7.5
Lower middle	42.5
Upper lower	50
Active smokers	42.5
Smoking index >300 pack-year	94.4
Co-morbid conditions	
Hypertension	30
Diabetes	30
Alcoholism	55.8
Coronary artery disease	10
Tuberculosis	10
Renal disease	5
Hyperlipidemia	2.5
Severity index of lung function test	
FEV_1, percentage of predicted	44.1 (6.2)
FEV_1<40	38.9
FEV_1>40	61.1
Grade of exacerbation	
I	52.5
II	37.5
III	10

FEV_1: Forced expiratory volume in 1 s; SD: Standard deviation

were used in 77.5% of patients in which 90% were ipratropium, followed by tiotropium. Oxygen therapy was used in 82% patients.

Antibiotics were used in 86.7% patients. According to the antibiotic groups, most of the patients came under Group B (62.5%), followed by Group A (17.5%) and Group C (7.5%) where group A indicates mild exacerbation: No risk factors for poor outcome, Group B indicates moderate exacerbation with risk factor (s) for poor outcome and Group C indicates severe exacerbation with risk factors for *Pseudomonas aeruginosa* infection.[12] Drug utilization pattern of antibiotics in this study is given in Tables 3 and 4. Number of drugs including antibiotics used during the study period has been shown in these tables. The adverse effects noted were dry mouth (15%), bad taste (10%), tremor (10%), nausea/vomiting (7.5%), and diarrhea (7.5%). The main adverse effects noted were highly correlated with use of anticholinergics ($P < 0.05$).

Discussion

The age distribution added support to the evidence of the previous studies that only those above 40 years of age were admitted during the period of the study. Regarding the sex wise distribution, majority of the patients were of the male sex which was as high as 87.5%. The females accounted for around 12%. Male to Female ratio was 7:1. This only confirmed the finding of the previous study conducted that males accounted for the majority of the disease burden.[13]

Demographic profile of patients who came under this study revealed that most of them were of a low socioeconomic status according to the modified Kuppuswamy scale.[10] This may be because the hospital in which the study was undertaken was a Government hospital offering free treatment. Another explanation may be that according to the GOLD guideline, people of low socioeconomic status tend to have increased incidence of COPD.[5,14]

Majority of the patients in the present study had co-morbid conditions (n = 93; 77.5%). The most commonly observed co-morbid conditions were alcoholism (55.8%), Type II diabetes mellitus (30%), and hypertension (30%). These findings were almost similar to the result of previous study in which 69.8% patients had co-morbid conditions.[13]

All the patients in this study were receiving combination therapy.[15] All of the patients were receiving methylxanthines out of which 96% were receiving hydroxyethyl theophylline (deriphylline) and the remaining aminophylline. However in the previous studies,[15,16] the use of methylxanthines was minimal. This may be because methylxanthines were one of the most freely available drugs in the hospital in which the study was under taken.

Similarly, all of the patients were receiving either oral or inhalational β-agonists. Among the inhalational β-agonists, salbutamol accounted for 74%, followed by formeterol. Parenteral steroids were used in 72.5% of the patients and all of them received hydrocortisone. Steroid inhalers were used in 25% of patients with all of them receiving budesonide. Anticholinergics were used in 77.5% of patients in which 90% were ipratropium.[15]

Antibiotics were used in 86.7% of patients in this study. This finding was not in accordance with the previous studies,[15,16] which revealed 52% and 99% use, respectively. This may be an indicator of the prevalence of infections among the patients admitted with acute exacerbation of COPD in different demographic areas.

According to the GOLD criteria and Cochrane reviews,[17-20] patients presenting with acute exacerbation of COPD is to be initially managed with β-agonists following which if there is no

Table 2: Drug utilization pattern (n=120)

Pattern	Drugs utilized	Number of times prescribed	Percentage
Prescription pattern	β-agonist (inhaler)	117	97.5
	β-agonist (oral)	67	55.8
	Anticholinergic	93	77.5
	Methylxanthine	120	100.0
	Steroid (parenteral)	87	72.5
	Steroid (inhaler)	30	25.0
	Antibiotics	104	86.7
Number of drugs per prescription	3-4	33	27.5
	5-6	76	63.3
	7	11	9.2

Table 3: Drug utilization pattern of antibiotics (n=120)

Use of antibiotic	Number of times prescribed	Percentage
Type of antibiotics		
Ampicillin	48	40.0
Amoxicillin	6	5.0
Azithromycin	54	45.0
Benzyl penicillin	27	22.5
Cefotaxime	27	22.5
Gentamicin	36	30.0
Ciprofloxacin	9	7.5
Number of antibiotics		
0	15	12.5
1	30	25.0
2	48	40.0
3	27	22.5

Table 4: Drug utilization pattern of antibiotics according to the antibiotic groups (GOLD committee)

Antibiotic used	Group A %	Group B %	Group C %
Ampicillin	0.0	64.0	0.0
Amoxicillin	28.6	0.0	0.0
Azithromycin	71.4	52.0	0.0
Benzyl penicillin	0.0	36.0	0.0
Cefotaxime	0.0	28.0	66.7
Gentamicin	0.0	40.0	66.7
Ciprofloxacin	0.0	0.0	100.0

GOLD: Global initiative for chronic obstructive lung disease

response, then has to be initiated with anticholinergics. The role of methylxanthines is controversial due to the alleged adverse effects. In this study, the use of methylxanthines was found to be high and the usage of anticholinergics was on the lower side. This may be due to the apparent free availability of the methylxanthines and nonavailability of anticholinergics in the hospital of study.

Despite the use of antibiotics according to the availability and physician's preference, it was found in the analysis that majority were in accordance with GOLD criteria recommendations.[5] The GOLD committee had recommended the stratification of patients with acute exacerbation of COPD into three groups, Group A, Group B and Group C for prescribing the antibiotic use. Group A were to be prescribed oral antibiotics of the beta lactams, tetracyclines, macrolides; Group B to receive parenteral or oral antibiotics. Group C were to receive antipseudomonas treatment. It was found in the study that out of the patients coming under Group A, who received oral antibiotics, 71.4% received macrolides and 28.6% received beta lactam, which was in concordance with the GOLD guidelines. Group B received treatment, which was almost similar to the GOLD guidelines. However, the use of gentamicin by 40% of the patients was not in accordance with the guidelines. All of the patients in the Group C were treated with fluoroquinolones in high dose. But they also received cefotaxime (67%) and gentamicin (67%) which was probably for the coverage of other gram positive and Gram-negative organisms.

Despite the rampant use of methylxanthines, the predicted adverse effects of these drugs did not occur in the institution of our study. The main adverse effects noted were dry mouth in approximately 15% of individuals and bad taste (10%). However, these individuals were also receiving anticholinergics, which was a confounding factor. The subsequent main adverse effects were tremor (10%) and nausea/vomiting (7.5%), and their incidence were lower than the previous studies.[18] Tremor might have been due to the use of β-agonists in all these patients. So the predicted adverse effects of methylxanthines according to the Cochrane review and GOLD expert committee did not occur in the population of the study. Diarrhea which was reported by 7.5% patients may be associated with the use of antibiotics, and this was almost similar to the previous study.[20] However, awareness and understanding of COPD need to increase, especially in primary-care settings where the majority of undiagnosed patients with COPD will initially be seen and most of the patient care administered. Health care providers must therefore be committed to disseminating and implementing evidence-based guidelines into their everyday clinical practices if the current trends of increased morbidity and mortality associated with COPD are to be reversed.[21]

Conclusions

Despite the use of drugs according to the availability and physician's preference, it was found in the analysis that majority were in accordance with GOLD criteria recommendations. Even though the treatment prescribed by the physicians was in accordance with the standard treatment guidelines, majority of the patients were not adhering to it. This was because of their financial constraints. Most of the patients were only taking the free medications offered at the hospital, and not buying the drugs, which were unavailable in the hospital. By including these drugs in the central purchase committee list of government, the treatment can be more effective and economy.

Recommendations

The guidelines set forth suggested both viral and bacterial involvement of which the main bacteria were *H. influenzae*, *S. pneumoniae*, and *M. catarrhalis* and other atypical organisms. Studies for the identification of main causative organisms in exacerbation of COPD have not been done in India. Hence, it is a requisite in our institution to send culture and plan treatment according to sensitivity pattern. It's also advisable to find out the microbiological spectrum of COPD exacerbation by various investigational studies, so as to define antibiotic treatment protocols.

References

1. National Institute for Health and Clinical Excellence, chronic obstructive pulmonary disease, management of chronic obstructive pulmonary disease in adults in primary and secondary care (partial update), NICE 2010. Available from: http://www.nice.org.uk/. [Last accessed on 2010 Aug 14].
2. Hurst JR, Wedzicha JA. Management and prevention of chronic obstructive pulmonary disease exacerbations: A state of the art review. BMC Med 2009;7:40.
3. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997;349:1498-504.
4. Boggon R, Hubbard R, Smeeth L, Gulliford M, Cassell J, Eaton S, *et al.* Variability of antibiotic prescribing in patients with chronic obstructive pulmonary disease exacerbations: A cohort study. BMC Pulm Med 2013;13:32.
5. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS, GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med 2001;163:1256-76.
6. Hunter MH, King DE. COPD: Management of acute exacerbations and chronic stable disease. Am Fam Physician 2001;64:603-12.
7. Leuppi JD, Schuetz P, Bingisser R, Bodmer M, Briel M, Drescher T, *et al.* Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: The REDUCE randomized clinical trial. JAMA 2013;309:2223-31.
8. Kong GK, Belman MJ, Weingarten S. Reducing length of stay for patients hospitalized with exacerbation of COPD by using a practice guideline. Chest 1997;111:89-94.
9. Sajesh KV, Salmiah M, Kingston R, Suresh K. Cost of acute exacerbation of COPD in patients attending government hospital in Kerala, India. Int J Pharm Pharm Sci 2012;4:659-61.
10. Mishra D, Singh HP. Kuppuswamy's socioeconomic status scale – A revision. Indian J Pediatr 2003;70:273-4.

11. Fogarty CM, Bettis RB, Griffin TJ, Keyserling CH, Nemeth MA, Tack KJ. Comparison of a 5 day regimen of cefdinir with a 10 day regimen of cefprozil for treatment of acute exacerbations of chronic bronchitis. J Antimicrob Chemother 2000;45:851-8.
12. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease, GOLD 2007. Available from: http://www.goldcopd.org/. [Last accessed on 2013 Jan 24].
13. Mohan A, Premanand R, Reddy LN, Rao MH, Sharma SK, Kamity R, *et al.* Clinical presentation and predictors of outcome in patients with severe acute exacerbation of chronic obstructive pulmonary disease requiring admission to intensive care unit. BMC Pulm Med 2006;6:27.
14. Prescott E, Lange P, Vestbo J. Socioeconomic status, lung function and admission to hospital for COPD: Results from the Copenhagen City Heart Study. Eur Respir J 1999;13:1109-14.
15. Hilleman DE, Dewan N, Malesker M, Friedman M. Pharmacoeconomic evaluation of COPD. Chest 2000;118:1278-85.
16. Miravitlles M, Murio C, Guerrero T, Gisbert R, DAFNE Study Group. Decisiones sobre Antibioticoterapia y Farmacoeconomía en la EPOC. Pharmacoeconomic evaluation of acute exacerbations of chronic bronchitis and COPD. Chest 2002;121:1449-55.
17. McCrory DC, Brown CD. Anti-cholinergic bronchodilators versus beta2-sympathomimetic agents for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2002; (4):CD003900.
18. Barr RG, Rowe BH, Camargo CA. Methylxanthines for exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2003; (2):CD002168.
19. Wood-Baker RR, Gibson PG, Hannay M, Walters EH, Walters JA. Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2005; (1):CD001288.
20. Ram FS, Rodriguez-Roisin R, Granados-Navarrete A, Garcia-Aymerich J, Barnes NC. Antibiotics for exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2006; (2):CD004403.
21. Heffner JE. Using COPD guidelines to improve patient care. Am Fam Physician 2006;73:590-1.

How to cite this article: Veettil SK, Rajiah K, Kumar S. Study of drug utilization pattern for acute exacerbation of chronic obstructive pulmonary disease in patients attending a government hospital in Kerala, India. J Fam Med Primary Care 2014;3:250-4.

Source of Support: Nil. **Conflict of Interest:** None declared.