DRUG UTILIZATION EVALUATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) requires extensive treatment with multiple drug therapy.Due to its increasing prevalence and complications, it is rapidly becoming one of the world's most serious health issues. It is necessary to treat the disease at the earliest with proper monitoring and evaluation of the therapy to prevent further progression and associated complications. Drug utilization evaluation is mainly used to understand the drug use pattern; use of irrational drugs; intervention to improve drug use andcontinuous quality improvement. Hence the present study was undertaken to understand the prescription pattern of patients diagnosed with COPD in a teaching hospital of South India.A total of 100 patients diagnosed with COPD was included in the study. The severity level of COPD was analysed using Modified Medical Research Council Questionnaire (mMRC) scale and the medications prescribed for treating were analyzed using GOLD treatment guidelines. Most of the patients were admitted with Grade-2 of modified Medical Research Council (mMRC) dyspnoea scale. Corticosteroids (22%) were the most prescribed class of drugs in which inhaled corticosteroids (budesonide and fluticasone) were preferred. The most prescribed combination therapy was salbutamol with ipratropium bromide. The majority of patients was treated with multiple drug therapy, in which combination of corticosteroids, β2 agonists, methylxanthines and anticholinergics along with antibiotics were used. Independent of socioeconomic status, poor health literacy is associated with greater COPD severity.

***Key Words:** Chronic Obstructive Pulmonary Disease, Drug Utilization Pattern, Prescription pattern*

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) has become a major public health concern of today. Due to the high prevalence, morbidity and mortality of COPD, it is rapidly becoming a significant health issue creating powerful challenges in future [1]. COPD is characterised by airflow obstruction which is not completely reversible. The airflow flow obstruction remains unchanged for several years but, in the long term it worsens as it progresses. COPD encompasses two serious lung diseases –

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emphysema and chronic bronchitis – which result in chronic airway inflammation and progressive loss of lung function, making it difficult to breathe normally [2]. One of the main events in COPD is an exacerbation which is defined as the presence of worsening symptoms along with local and systemic inflammation.

COPD is one of the world's most serious health issues. According to WHO, 65 million people have moderate to severe COPD. COPD usually remains under diagnosed and under treated making it fifth cause of morbidity and mortality in developed world [3]. In 2005, many people died of COPD, which corresponds to 5% of all deaths globally. All the low- and- middle income countries contribute to the 90% of COPD deaths [4].COPD at one time, was more common in men, but because of increased tobacco use among women in high-income countries and the higher risk of exposure to indoor air pollution (such as biomass fuel used for cooking and heating) in low-income countries, the disease now affects men and women almost equally [5,6]. Cigarette smoking, hereditary deficiency of alpha 1-antitrypsin, exposure to tobacco smoke, occupational dust and chemicals are some of the common factors leading to COPD. Dyspnoea, chronic cough with or without sputum and poor exercise tolerance are the symptoms of COPD and in exacerbations, the severityof these symptoms is observed [6,7].

Patient adherence in chronic diseases remains a task, resulting in poor health outcomes and increased healthcare expenditures. Non-adherence to COPD treatment can lead to increased frequency of exacerbations, recurrent hospital admissions and mortality rate. Therefore, educating or counselling the patient regarding their condition, pathology, warning signs and symptoms and adherence to medications can help reduce exacerbations and also is a key element inthe successful COPD treatment [7,8].

COPD is treated with both pharmacological as well as non-pharmacological means. COPD patients tend to have acute exacerbations which are treated with oxygen, β2 agonists, anticholinergics, antibiotics and systemic steroids. Patients with acute exacerbations are commonly prescribed with antibiotics like Azithromycin due to their underlying infection. Prescribing antibiotics have shown an improved respiratory function within COPD patients [7,8,9]

Drug utilization evaluation (DUE) is mainly used to understand the drug use pattern; use of irrational drugs; intervention to improve drug use and continuous quality improvement. Taken together, treatment of COPD mostlyrequire multiple drug therapy with proper monitoring. Here comes the importance of DUE for ensuring appropriateness and quality outcome of the therapy in COPD patients.

METHODOLOGY

In this prospective observational study, we included 100 patients who diagnosed with COPD, admitted in the MVJ Medical College and Research Hospital, Bangalore during a period of 6 months. Patients, aged 18 years and above, diagnosed with COPDand who visited the hospital for acute exacerbation of the disease were included in this study. We excluded patients who were diagnosed with asthma. The human ethical approval was taken before conducting the study. The clinical, demographic and medication data were documented into specifically prepared case report form (CRF). The severity level of COPD was analysed using Modified Medical Research Council Questionnaire (mMRC) scale and the medications prescribed for treating COPD were analyzed using GOLD treatment guidelines.

RESULTS

Demographic details of the study population

A total of 446 drugs was prescribed for the treatment of COPD in 100 prescriptions. Patients were assessed for their socioeconomic status, gender, specific history and literacy about the disease and medication use.

When compared, the prevalence of COPD was 62% in males and 38% in females. Among the study patients, the common age groups were 41-50 years (34%) and 51-60 years (23%).

Going ahead with the social status of the study patients, it was found that from the total study population, 37% of patients were smokers (which included currents and reformed smokers), 32% of patients consumed alcohol and remaining 14% were tobacco users. Among the study, patients who were smokers, 20% were current smokers, whereas 17% of them were reformed smokers.

The literacy status of the study population showed that, 81% of patients were illiterate about their disease and medication use and only 19% of them were found to be literate about the same [Table 2].

As per the socioeconomic status, the study, patients were divided into three grades as follows:

-   Grade I for people in administration

-   Grade II for employees and clerical staff

-   Grade III for gardeners, peons, security guards and drivers

It was found that the prevalence of COPD was higher in Grade III patients (82%), followed by 12% in Grade II and 8% in Grade I [Table 1].

Table 1. Demographic details of the study population

Parameters	%
Gender-wise percentage distribution of study patients	Males: 62% Females: 38%
Age-wise percentage distribution of study patients	31-40yrs: 15% 41-50yrs: 34% 51-60yrs: 23% 61-70yrs: 15% > 70yrs: 13%

Social status of the study patients	Smoking: 37% Alcohol consumption: 32% Tobacco consumption: 14%
Status of patients with smoking history	Current smokers: 20% Reformed smokers: 17%
Literacy status of the study population about the disease/medication	Illiterate: 81% Literate: 19%
Socioeconomic status of the study patients	Grade I: 6% Grade II: 12% Grade III: 82%

To assess the patients with severity of dyspnoea, mMRC grading was used which showed that majority of the patients belonged to Grade 2 (48%), followed by 26% in Grade 3, 18% in Grade 1, 5% in Grade 0 and the remaining 3% in Grade 4.

Drugs used for the management of COPD

It was observed that only 1% of prescriptions showed single drug therapies and the remaining 99% contained multiple drug therapies for COPD. Prescription of more than 3 drugs (79%) was majorly seen within the multiple drug therapies.

For the management of COPD,out of the total number of drugs prescribed, 98 drugs belonged to the class of corticosteroids, including all oral, inhalation and systemic [22.2%], 83 drugs were from the class of methylxanthines [18.8%], 75 drugs from anticholinergics [16.9%], 74 drugs were beta-agonists [16.7%], 49 drugs were antibiotics [11.1%], 39 drugs were mucolytics [8.8%] and the remaining 28 components were oxygen therapy [5.4%], shown in (Table 2).

Table 2. Pharmacological class-wise distribution of drugs prescribed for the management of COPD

Class of drug	Number of drugs prescribed	Percentage (%)
β2-agonists	74	16.7%
Corticosteroids	98	22.2%

Anticholinergics	75	16.9%
Methylxanthines	83	18.8%
Mucolytics	39	8.8%
Antibiotics	53	11.1%
Oxygen therapy	28	5.4%

The Monotherapy prescription pattern was evaluated which showed the following drugs being commonly prescribed. The drugs werederiphylline (13.9%), doxiphylline (13.06%), ciprofloxacin (7.8%), theophylline (6.9%), cefotaxime (5.7%),hydrocortisone (5.3%), levofloxacin (4.9%), ceftriaxone (4.5%), prednisone (3.7%), azithromycin (3.7%) and levosalbutamol (1.2%). Depending upon each patient condition and severity, it was observed that the oral route (40%) is the most common route of administration followed by, inhalation (37%) and parenteral routes (23%).
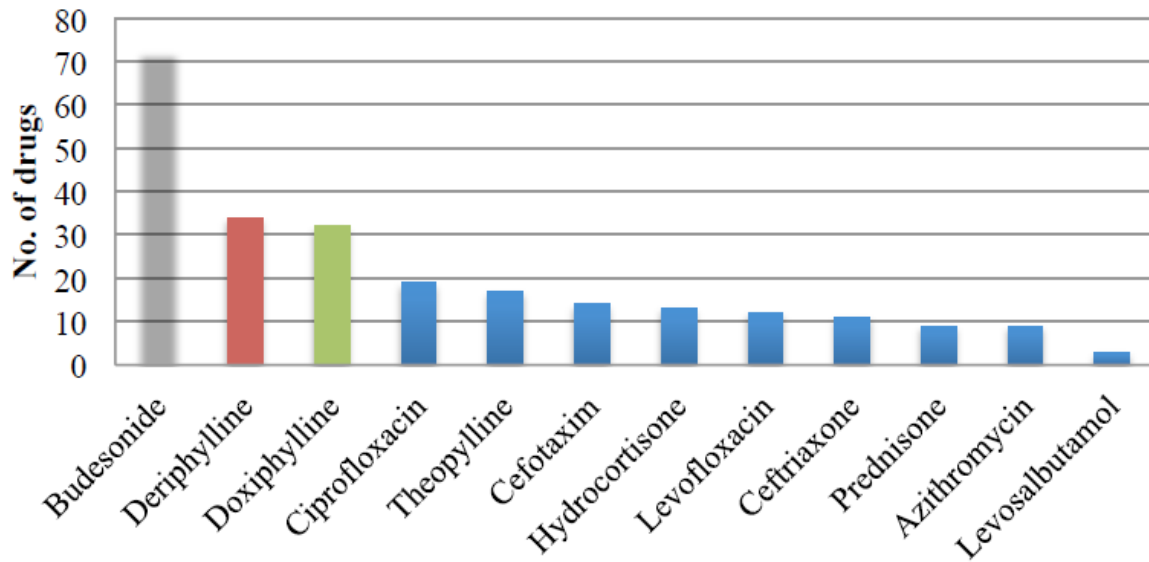

Figure 1: Prescribing pattern of drugs in monotherapy.

In the assessment of combination therapy for COPD, we found that, salbutamol + ipratropium bromide (54.5%) was most commonly prescribed. Also, combinations of dexmethorphan + bromohexine (23.2%), pipercillin + tazobactum (12.1%), amoxicillin + clavulanate (6.1%), ipratropium bromide + fluticasone (3%) and budesonide + formetrol (1%) were used in the combination therapy.
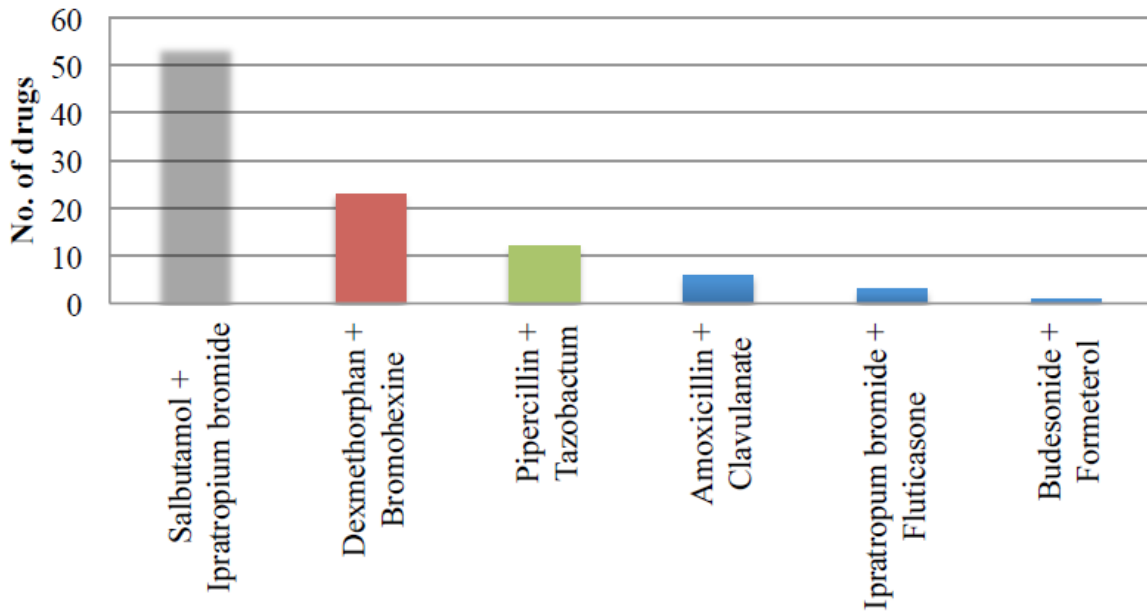
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Figure 2: Prescribing pattern of drugs in combination therapy.

As, COPD patients present acute exacerbations with underlying infection, the antibiotics given for treatment of COPD were also evaluated. It was observed that Ciprofloxacin (22.9%) was the most prescribed antibiotic for COPD followed by Cefotaxim (16.9%), Pipercillin-Tazobactum (14.5%), Levofloxacin (14.5%), Ceftriaxone (13.2%), Azithromycin (10.8%) and Amoxicillin-Clavulanate (7.2%).
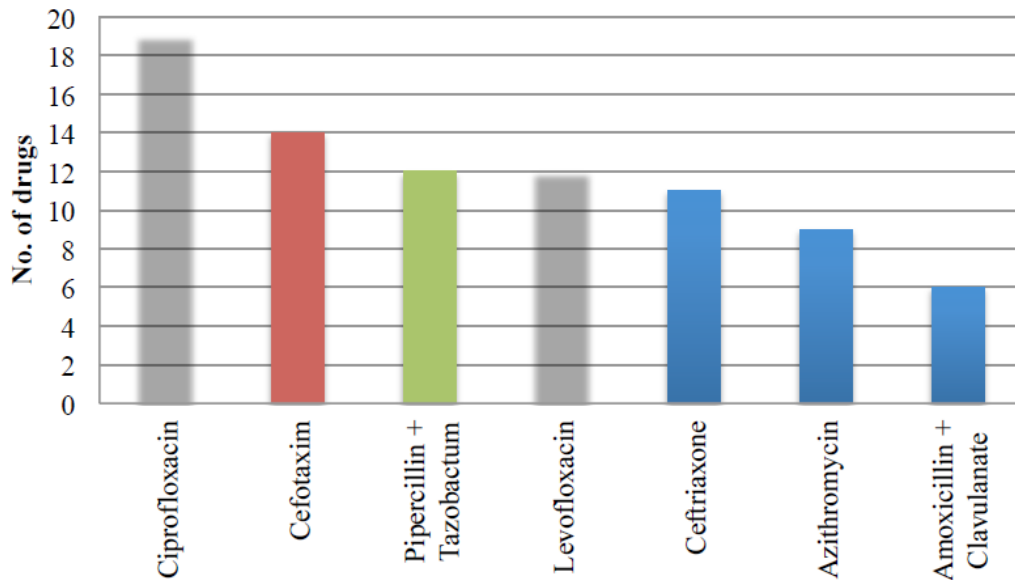
Figure 3: Prescribing pattern of antibiotics.

In the study, 45% of patients presented COPD with co-morbidities in which, hypertension (31.1%) was the most common co-morbidity accompanied by hypertension with type-2 diabetes mellitus (24.4%), anemia (15.6%), type-2 diabetes mellitus (13.3%), asthma (4.4%), varicose veins with gastritis (2.2%), hypertension with metabolic encephalopathy (2.2%), gastritis (2.2%), anemia with hypoprotenemia (2.2%) (Table 3).

Table 3. Types of Co-morbidities with COPD among study patients.

Co-morbidity	No. of prescriptions (N = 100)	Percentage (%)
COPD + HTN	14	31.11
COPD + HTN + T2DM	11	24.4
COPD + Anemia	7	15.5
COPD + T2DM	6	13.3
COPD + Asthma	2	4.4
COPD + Varicose veins + Gastritis	1	2.2
COPD + HTN + Metabolic Encephalopathy	1	2.2
COPD + Gastritis	1	2.2
COPD +Anemia + Hypoprotenemia	1	2.2
COPD + Metabolic encephalopathy	1	2.2

DISCUSSION

Nowadays, an increasing trend has been observed in the incidence of COPD. As this chronic disease requires long-term treatment, irrational use of drugs may be possible that might lead to certain consequences. DUE is an essential part of pharmacoepidemiological studies by which understanding of drug use, according to the guidelines can be assessed knowing the

more common patterns of prescribing. It also aids in elaborating the training programs and adapting the given treatment, according to the current or updated guidelines.

In the present study, the 100 prescriptions that were observed during the study period, the incidence of COPD in male patients was higher compared to female patients (62% vs. 38%). This was similar to the results of a study done by Afonso AS et. al which reported a higher prevalence of COPD in males than in females (3.54 vs. 2.34) [10,11]. Study patients belonging to the age group of 41-50yeras had a high prevalence of COPD. As the age group mentioned falls under the working age group, there can be an increased exposure to environmental pollutants, making it at risk for such population to get affected by COPD.

The demographic details of the patients enrolled in the study revealed that most of them were of low socioeconomic status depending upon the occupation of the patient. This is in accordance with a study by Veettil SK et.al which shows the patients with a low socioeconomic status as a hospital study was conducted in a rural area and also is explainable by the GOLD guidelines which says that people of low socioeconomic status, tend to have a greater risk of developing COPD [12,13]. When screening the study population for their literacy, it was found that 81% of the patients were illiterate about their disease condition and the medicine being prescribed to them. Poor health literacy can pose greater risks for worsening of COPD-status and this finding emerges a need to counsel the patients regarding the disease, the medications, its indication and proper usage[14,15].

In our study, we assessed that out of the 100 prescriptions, 55% of the patientpresented with COPD alone, whereas 45% of patients presented COPD along with certain co-morbidities. Out of the patients with COPD along with co-morbidities, 66.7% of these patients had a single co-morbid condition, while the remaining 33.3% of the patients had 2 or more co-morbid conditions. The most commonly observed comorbid conditionswere hypertension (31.1%). The findings were similar to a study showing common co-morbidities as hypertension, type-2 Diabetes and alcoholism. Due to the increasing age, lifestyle modifications and stress, it can lead to hypertension like co-morbidities which overall affect the heart and respiratory functioning further giving a way for acquiring COPD[15].

The risk factors for COPD make it more challenging for the physicians to treat it and get better patients outcome. As per the survey done in the present study, the common risk factors into focus were smoking, alcoholism and tobacco consumption. Out of the 100 prescriptions reviewed, it was seen that 37% of the patients had smoking status (which includes both current and reformed smokers). Also, the maximum duration of smoking seen in the present study was between 10-20 years. As compared to a similar study, the results of maximum smoking duration were observed to be more than 30 years, which differed from the results of the present study [16].

The most common feature of COPD is dyspnoea which gradually worsens as the disease progresses. According to the modified Medical Research Council (mMRC) scale for dyspnoea, it was observed that 48% of the study patients had Grade-2

dyspnoea.This was different when compared to the mMRC dyspnoea grading of a previous study that showed higher prevalence of patients having Grade 4 dyspnoea (40.38%). This could be because of exposure to outdoor and indoor pollutants that was comparatively lesser in our study [17,18].

Within the observed 100 prescriptions, 79% of the prescriptions contained more than 3 drugs. The prescription of more than 3 drugs for a patient attributed to the possibility of presentation of acute exacerbation of COPD requiring antibiotic and corticosteroid treatment and also a failure of the doctors to prescribe a single effective drug for the same.

Since, COPD requires extensive treatment, different classes of drugs used in the treatment were also assessed in the present study. Among them, corticosteroids were mostly prescribed (21.9%). When compared to the study conducted by Maazuddinl M et.al, our results were not in accordance, as the use of antibiotics was higher in that study (86.7%). This highlights the prevalence of infections in patients admitted for acute exacerbation of COPD in different demographic areas [19].

In acute exacerbations of COPD, underlying infections are always ruled out since they can also aggravate the disease. Treating COPD with antibiotics has shown better respiratory response and hence, they become an essential part of COPD treatment. In our study, it was observed that, Ciprofloxacin was most commonly prescribed antibiotic for management of COPD.

In the course of COPD, alongwith the antibiotics, corticosteroids in the form of inhalations play a major role. Rest showing a slow systemic effect, inhalers show an immediate effect giving the patients rapid relief from dyspnoea.Deriphylline was the most prescribed methylxanthine (13.9%). When observed in other studies, budesonide was most commonly used inhaled corticosteroid for COPD patients. This showed a similarity that, our study also showed high use of budesonide (29.4%) as the inhaled corticosteroid [19,20].

Among the combination therapies, salbutamol with ipratropium bromide was the most preferred combination (54.5%). These findings were similar to results from a previous study where the salbutamol with ipratropium bromide combination was used in 54% of the cases. Salbutamol with ipratropium bromide was mostly preferred in older patients as it prevents cardiovascular complications and also one can avoid high doses of β2 agonist drugs [20,21].

In this study, we were able to analyse the medications prescribed in COPD but, for better patient care in long term there is a need to assess the utilization of the same.

CONCLUSION

Independent of socioeconomic status, poor health literacy is associated with greater COPD severity. As COPD is a challenging issue, medication adherence is the key element for its treatment success. Elderly patients with associated long-term co-

morbidities, also affect COPD, making it more severe and posing a risk for emergency patient evaluation. We could highlight the pattern of drug utilization in COPD, in which mainly corticosteroids, β2 agonists, methylxanthines and anticholinergics along with antibiotics were used for the management. In the final analysis, it was found that the majority of the drugs were in accordance with the GOLD criteria recommendations.

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