ORIGINAL ARTICLE

Are Our Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease Adequately Treated? Are We in Line with Gold Guidelines?

Padmaja Udaykumar, Fathima Farangipete

Department of Pharmacology, Fr Muller Medical College, Kankanady, Mangalore, Karnataka, India

ABSTRACT

Background: Adherence to GOLD guidelines is inadequate in the management of acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Evaluating the drug utilization pattern in these patients was the primary objective. **Methods:** We analyzed the prescriptions of hospitalized adult patients with AECOPD excluding those with bronchial asthma, cystic fibrosis and severe bronchiectasis. Anaemic status of these patients was assessed. **Results:** Eighty eligible patients with a mean age ± SD of 65.99 ± 10.7 years were included. Males (65%) outnumbered females. Mean ± SD duration of COPD was 5.9 ± 2.1 yrs. There were 78.75% smokers. Hypertension (n=37, 46.25%) and diabetes (n=25, 31.25%) were the frequent comorbidities. Inhalational drugs were administered to 76 (95%) patients, 72 (90%) received oral while 25 (31.2%) received parenteral medications. B_2-agonist Salbutamol accounted for 74 (97.3%) prescriptions of Inhalational agents, followed by anti-cholinergics (96%), Steroids (61.8%). Among oral medications, β-agonist accounted for 52.7% prescriptions (Terbutaline 97.3%). Antibiotics were prescribed to 66 (82.5%) patients, ceftriaxone 39 (59%) and combination of amoxicillin trihydrate clavulanic acid topped the list. Of parenteral steroids (n=22, 88%) Hydrocortisone (100 mg) was administered to all. Forty eight (61.8%) prescriptions consisted of inhalational steroids (budesonide). Of methylxanthines (67.5%), theophylline was the preferred choice in all. Anti-cholinergics (ipratropium bromide) were prescribed to 91.2% patients. Average number of drugs prescribed was 4.5/patient. There was no statistical significance and relationship between number of drugs, duration of disease, hemoglobin levels, and comorbidities. Conclusion: The treatment protocol for AECOPD in our hospital is in accordance with the current GOLD guidelines. Adherence to GOLD guidelines is feasible in our setup and results appropriate and adequate treatment.

Key words: Steroids, prescriptions, hypertension, bronchiectasis

Correspondence:
Dr Padmaja Udaykumar, MD, Professor and Head,
Department of Pharmacology, Fr Muller Medical College, Kankanady, Mangalore, Karnataka, India.
E-mail: padmajaudaykumar@gmail.com

Access this article online
Website: www.jbclinpharm.org
Quick Response Code:

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is associated with significant morbidity, mortality and is the fourth leading cause of death globally. Contributing factors include tobacco smoking, occupational hazards which not only increase the occurrence, but also the severity and disease complications. Apart from this globalization, industrialization too have resulted in increase in the incidence of COPD.[1]

The enormous clinical and economic impact of COPD prompted the development of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD for better disease management.[2,3] 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.[4] This aims to increase the disease awareness, better management and scope is applicable to those involved in all fields of health care. It is being updated periodically and last revised in January 2016.

Pharmacotherapy holds the vital key to the management of COPD patients which consists of maintenance and reliever medications which include systemic, oral and inhalational therapy.[1] Drug utilization audit is a qualitative assurance program to ensure the proper and safe drug utilization. Drug audits and studies have shown low adherence to GOLD guidelines while treating acute exacerbation of COPD resulting in inappropriate therapy.[5] Hence, we evaluated the pattern of pharmacotherapy prescribed in our teaching hospital which is a tertiary care hospital and assessed if it was in line with the current recommended guidelines using GOLD criteria.

MATERIALS AND METHODS

This was an observational, 5th month, prospective, cross-sectional, prescription based analytical study conducted on the hospitalized patients in a tertiary care centre, after the approval from the Institutional Ethics committee. Data was collected after obtaining written informed consent from the prospective patients. The primary objective was to evaluate the drug utilization pattern in acute exacerbation of COPD (AECOPD) patients at our tertiary care hospital.

The prescriptions of hospitalized adult patients (18-85 years) of either sex, diagnosed with AECOPD were considered for analysis. Prescriptions of those with bronchial asthma, cystic fibrosis and severe bronchiectasis were excluded.

Demography, risk factors, co-morbid conditions, duration of disease, prescription pattern which included number of drugs prescribed, route and frequency of administration with special consideration to the frequency of prescription of antibiotics and inhalational therapy were captured on preapproved proforma. Hemoglobin (Hb) status of patients was noted and those with <13 gm% in male, 12 gms% in female were considered anemic as per the WHO classification.[6]

Statistical analysis

Data captured on proforma was transferred to Microsoft Excel worksheets (2007) and analyzed. Result was presented as frequency, percentage, ratio with tables and figures where appropriate. Descriptive statistics was used.

Cite this article as: Udaykumar P, Farangipete F. Are Our Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease Adequately Treated? Are We in Line with Gold Guidelines? J Basic Clin Pharma 2017;8:S116-S120.

RESULTS

Data of 80 eligible patients with AECOPD were included in our study. Mean age ± SD of patients was 65.99 ± 10.7 years (41-90 years). Males 52 (65%) outnumbered females 28 (35%) with a ratio of 3.7:2. Thirty two (40%) patients were in 61-70 years, followed by 41-50 years and 51-60 years (n=13 each, 16.25%) [Table 1].

Mean ± SD duration of COPD was 5.9 ± 2.1 yrs (range 4-20 years). There were 78.75% smokers; among smokers 14.2% are female.

Hypertension (n=37, 46.25%) and type 2 diabetes mellitus (DM) (n=25, 31.25%) were the most frequent comorbid conditions followed by corpulmponale and ischemic heart disease (IHD) (n=05, 6.25%).

Mean ± SD Hemoglobin was 12.5 ± 2 gms%. Mean Heamoglobin of male patients was 12.5 ± 2.3 and that of females 12.7 ± 1.3, of these 52 men, 23 (44.23%) and four of the 28 females (5.0%) were anemic.

All patients received combination therapy of inhalational, oral and parenteral respiratory medications [Table 2]. Inhalational drugs were administered to 76 (95%) patients, while 72 (90%) patients received oral and 25 (31.2%) patients received parenteral medications [Table 3].

Among inhalational agents, β-agonist Salbutamol accounted for 74 (97.3%) prescriptions. Other drugs included anticholinergic (n=73, 96%) and Steroids (n=47, 61.8%) [Table 4].

Among oral medications, β-agonists accounted for 38(52.7%) prescriptions of which terbutaline was the most prescribed drug (n=37, 97.3%) [Table 4].

Antibiotics were prescribed to 66 (82.5%), patients with ceftriaxone 39 (59%) and combination of amoxicillin tri-hydrate and clavulanic acid being frequently prescribed [Table 4].

Parenteral steroids were used in 22 (88%) patients and all of them received hydrocortisone (100 mg). Forty eight (61.8%) patients were prescribed steroid inhalers and budesonide was prescribed to all these patients.

Of methylxanthine prescriptions (n=54, 67.5%), combination of theophylline and etophylline was prescribed to all these patients. Anti-cholinergic agnet (ipratropium bromide) was prescribed to 73 (91.2%) patients [Table 5].

Average number of drugs prescribed was 4.5./patient with a range of 2-9/patient. Greater number (n=66, 82.5%) patients received 4-6 drugs/patient; this group had more number of patients with anemia (n=20) and associated comorbidities (n=47) [Table 6]. There was no statistical significance or positive association between the number of drugs prescribed, duration COPD, anemia and associated comorbidities either individually or combined (p>0.05).

Twelve (15%) patients required admission to intensive care unit (ICU). Of 12, ten had comorbid conditions such as hypertension (n=5, 13.5%), diabetes mellitus (n=6, 24%), and anaemia (n=7, 25.9%), and >60 years (n=11). Treatment offered to all our patients was in accordance with GOLD guidelines in terms of drugs prescribed and dosage [Figure 1].

Table 1: Age Distribution Among study population

Age (years)	n (%)
41-50	13 (16.25%)
51-60	13 (16.25%)
61-70	32 (40%)
71-80	12 (15%)
>80	10 (12.5%)

Table 2: Comorbid conditions in the study population

Comorbidites	n (%)
Hypertension	37 (46.25)
Diabetes Mellitus	25 (31.25)
Alcohol Dependence Syndrome	01
Chronic Kidney Disease	01
Benign Prostatic hyperplasia	02
Ischaemic heart disease	05
Dyslipidemia	01
Corpulmonale	05
Pulmonary tuberculosis (treated)	01
Atrial Fibrillation	01

Table 3: Prescription Pattern of respiratory drugs

Drugs	n (%)
Oral	72 (90%)
Beta agonist	38 (52.7%)
Methylxanthines	49 (68%)
Steroids	10 (13.8%)
Inhalation	76 (95%)
Beta agonist	74 (97.3%)
Steroids	47 (61.8)
Anticholinergics	73 (96%)
Intravenous	25 (31.25%)
Steroids	22 (88%)
Methylxanthiness	10 (12.5%)
Beta agonist(Salmeterol)	1 (1.2%)

Table 4: Antibiotic prescription pattern

Antibiotics (n-66)	n (%)
AmoxicillinTrihydrate +Clavulanate	20 (30.3%)
Ceftriaxone	39 (59%)
Cefoperazone	3(4.5%)
Cefixime	4 (6%)
Piperacillin +Tazobactum	6 (9%)
Levofloxacin	8 (12.1%)
Azithromycin	3(4.5%)

DISCUSSION

GOLD guidelines were introduced to bring better patient care and therapeutic outcome in the initial outset while reduction of morbidity and mortality in the long run and is followed in many countries.[7-9] However, there have been reports that these guidelines were not followed adequately in the therapy.[10-16] even in the developed countries.[17] Adherence to guideline was better among respiratory physicians compared to others.[18] Non-adherence to guidelines result in inappropriate therapy[7] particularly in early stages wherein steroid usage is rampant. To obtain optimum therapeutic outcome with minimal adverse effects, to minimize over-prescription of drugs, it is recommended to adhere to GOLD guidelines.[19] As over prescription is frequent in clinical practice, particularly in exacerbations,[10] we conducted this study to observe the extent to which these guidelines were followed in our institution.

Table 5: Drug prescription pattern

Drugs	n (%)
Beta agonist	
Inhaler	74 (97.3%)
Oral	38 (52.7%)
Anticholinegics	73 (91.2%)
Methylxanthines	54 (67.5%)
Steroid	
Inhaler	47 (61.8%)
Parenteral	22 (88%)
Antibiotics	66 (82.5%)

Table 6: Correlation of number of prescription to duration of disease, anemia and associated comorbidities

Drugs / prescription	No of patients	Number of patients (Duration of disease)	Patients with Anemia	Associated co-morbidities
2-3	08 (10.0%)	08(5-9 years)	3	5
		02 (1-4years)		
4-6	66 (82.5%)	60 (5-9 years)	20	47
		04 (>9years)		
>6	06 (7.5%)	5(5-9 years)	4	4
		1(>9years)		

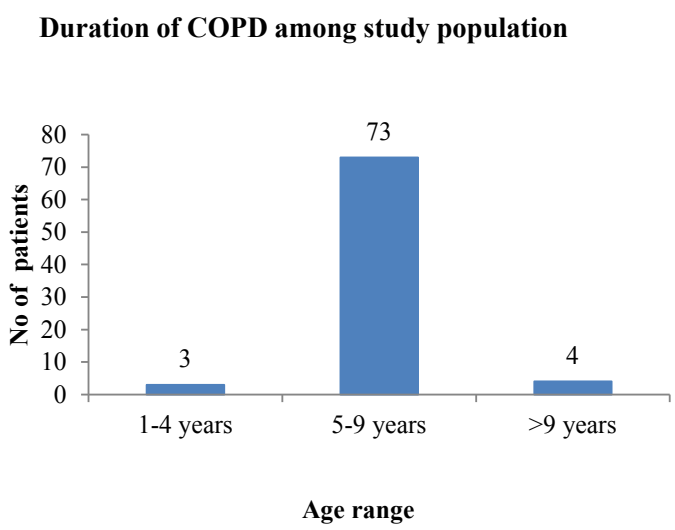

Figure 1: Duration of COPD among study population

We enrolled 80 patients in this study, though comparatively less to derive any concrete conclusion. This is due to our criteria to include only hospitalized patients. We did not include those who received only emergency treatment or on outpatient basis. We had greater number of men than females which could be attributed to tobacco smoking of long duration which is most common. Though our inclusion criteria for age was >18 years, none of our patient was <40 years. The mean age of our patient was 65.9 years, and 32 (40%) patients were in 61-70 years. Our reports are in support of the previous reports that have accounted male sex and patients between 61-70 years of age group were maximum.[20] Available data the prevalence rates of COPD ranges from 2-22% in men and 1.2-19% in women.[2]

Average duration of COPD in our patients was 5.9 years, with a range of 4-20 years. We noted tobacco smoking as the risk factor; of 80 patients, 63 patients were smokers which included former smokers and current smokers. This is in support of the report by Unni *et al.* in which smoking was the strong risk factor.[20] There was no history of smoking in 17 patients in our study, of which majority were females. Of 28 female patients, only nine were smokers. This could be attributable to the regional cultural aspect where smoking in females is considered a taboo; however, some women from rural background still smoke who contributed to the subset of female smokers in our study.

Comorbidities determine the need and duration of hospital stay in COPD patients. Significant number of patients (n=56, 70%) had comorbidities. We noted hypertension (n=37, 46.25%) as the most frequent associated illness followed by Type 2DM (n=25, 31.25%); Cor-pulmonale (n=5, 8.9%), IHD (n=5, 8.9%) were less frequent illnesses. In contrast to our findings, Veettil *et al.*[4] reported comorbidities in greater number of (77.5%) of the COPD patients, of which alcoholism (55.8%) was the most frequent followed by type 2DM (30%) and hypertension (30%). We had only one patient with alcohol dependency syndrome.

We did not find any significant association between disease duration and hemoglobin status. However, 44.0% of men were anemic compared to 5.0% females. This could be attributed to the smoking in men, which causes anemia.

Seventy two (90%) of our patients were on multidrug therapy during hospital stay. This prescribing trend is in accordance with GOLD guidelines and may be attributed to the goals of COPD therapy to minimize symptoms to prevent recurrent exacerbations to reduce the need for hospitalization and to maintain near normal pulmonary function. According to the GOLD guideline, oxygen is administered for the management of hypoxia. Bronchodilators are the mainstay in the therapy of which short acting β_2-agonists either alone or in combination with anti-cholinergics are preferred. Methyl-xanthines are the second line therapy, prescribed to selective cases whose therapeutic response to bronchodilators is insufficient. In addition, systemic corticosteroids are added to hasten the recovery and shorten the recovery time; prednisolone 40 mg/day for 5 days is recommended by the guideline. Appropriate antibiotics to control the infection and adjuvant therapy may also be required in few. Latter depends on the general condition of the patient and treatment may include maintaining adequate fluid and electrolyte balance; use of diuretics, anticoagulants is recommended as appropriate along with the treatment of existing comorbidities.[21]

β-agonists (bronchodilators) are the main stay in the therapy as outlined by GOLD guidelines. In our study, 97.3% patients received inhalationalβ agonist while 39 were prescribed oral beta agonist. Our finding are in concordance with GOLD guidelines, which recommends inhaled short acting β_2 agonist with or without short acting anticholinergic agent as the preferred bronchodilator for treatment of exacerbations. These drugs are the first choice in therapy as they rapidly improve respiratory symptoms during an exacerbation.[1] Long acting β_2 agonist, inhaled corticosteroids and anti-cholinergics reduce the exacerbation rate,[5] hence, the preferred combination in these patients.

Anti-cholinergics are prescribed in COPD to maintain the bronchodilation. Reports favor the early administration of anti-cholinergics as it has shown to reduce exacerbation rate, and improve the time taken for first exacerbation supporting its recommendation in guidelines.[22] In our study, ipratropium bromide was prescribed to 96% patients. Veettil *et al.*[4] observed that anti-cholinergics were prescribed to 77.5% of their patients in which were ipratropium bromide was the preferred drug (90%).

Glucocorticoidesare administered to control life threatening symptoms of acute exacerbation of COPD and Parenteral route are preferred for the initial treatment while inhalation during the later stages for

the advantages it offers such as rapid onset of action, action at the site and less systemic effects. Parenteral steroids were used in 27.5% patients and all of them received Hydrocortisoneas per the hospital treatment protocol. Inhaler steroids used in 60% patients with all of them received Budesonide. In contrast, Veettil *et al.*[4] reported that 72.5% of patients received parenteral steroids (hydrocortisone) while 25% received inhaler budesonide. As per GOLD guidelines steroids and antibiotics can shorten recovery time, improve lung function and arterial hypoxemia and reduce the risk of early relapse, treatment failure and length of hospital stay.[1] Of Methylxanthines (67.5%), theophylline+etophylline combination was the commonly prescribed drug and is similar to previous report from our country.[4]

It has been suggested that, hospitalized patients should receive intravenous treatment with anti-pseudomonal penicillin, third generation Cephalosporin, Macrolides or Flourquinolones as determined by bacterial resistance.[1] López-Campos *et al.* in their audit reported that those patients who met GOLD guidelines were most likely to receive antibiotic therapy and with radiological evidence of COPD; but they also noted that there was overuse of antibiotics as it was prescribed to those who did not warrant it.[23] In our study Ceftriaxone (n=35) was the most commonly prescribed antibiotic, followed by AmoxicillinTrihydrate+Clavulanate (n=20), Levofloxacin(n=8), Piperacillin+Tazobactum (n=6). Unni *et al.*[20] found Levofloxacin was the most commonly prescribed antibiotic followed by Cefoperazone+Sulbactum (40.5%) and Ceftriaxone. Veettil *et al.*[4] found that antibiotics were used nearly 87% patients with Azithromycin being the most frequently used antibiotic followed by Ampicillin, Gentamicin.

Inappropriateness in the treatment has been reported. Corticosteroids alone or in combination with bronchodilators, mostly administered by inhalation were the preferred drugs which in accordance with GOLD guidelines. Corrado *et al.* noted that inappropriate treatment was given to larger proportion (62.1%) patients, consisted of under prescription (37.9%) and over prescription (62.1%).[10] Sarc *et al.* noted unsatisfactory implementation of GOLD guideline calling for adequate adherence.[24] Similar observations were made by Seaman *et al.*[25] Treatment protocol of acute exacerbation of COPD in followed our patients was in accordance with GOLD guidelines and we found no deviation in any patient. Adherence to GOLD guidelines is appropriate in our setup which is a tertiary care teaching institution indicating that our physicians are well aware of and following these guidelines.

Limitation of the study being we included only acute exacerbation cases, and did only the prescription analysis. We did not capture the therapeutic outcome, and comparing the outcome with those who did not follow GOLD guideline would have been confirmatory. Moreover, number of patients was also less as we included only hospitalized patients as it was easy to collect data. We did not assess the adherence to non-pharmacological measures which was found to be less in other study.[18] Despite these limitations, we conclude that our data suggests that our patients were treated appropriately and adequately, in accordance with GOLD guidelines for COPD. This fact supports the observations made by Tang *et al.*[18]

CONCLUSION

The treatment protocol for acute exacerbation of COPD in our institution is in accordance with the current GOLD guideline. Bronchodilators, glucocorticoids and antibiotics were the mainstay of pharmacotherapy. Adherence to GOLD guidelines is feasible in our setup and results appropriate and adequate treatment.

Source of support/funding

None.

Conflict of interest

None.

Acknowledgement

Authors would like to thank patients who consented to this study. Authors acknowledge the Management of Fr Muller Medical College for their support during the conduct of the study. We appreciate the assistance of Dr Latha in editing and proof reading. We acknowledge Dr Navya for assisting in statistical analysis.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease; 2014. (Gold guidelines) Available from: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2014_Jan23.pdf [Last Accessed on 30 Aug 2016].
2. Jindal SK. Emergence of chronic obstructive pulmonary disease as an epidemic in India. Indian J Med Res 2006;124:619-30.
3. 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.
4. Veettil S, Rajiah K, Kumar S. Study of Drug Utilisation Pattern for Acute Exacerbation ofChronic Obstructive Pulmonary Disease in Patients Attending a Government Hospital in Kerala, India. Journal of Family Med 2014;3:250-4.
5. Jochmann A, Scherr A, Jochmann DC, Miedinger D, Török SS, Chhajed PN, *et al.* Impact of adherence to the GOLD guidelines on symptom prevalence, lung function decline and exacerbation rate in the Swiss COPD cohort. Swiss Med Wkly 2012;142:w13567.
6. Blanc B, Finch CA, Hallberg L. Nutritional anemia's. Report of a WHO Scientific Group. WHO Tech Rep Ser 1968;405:1-40.
7. Gunen H, Yilmaz M, Aktas O, Ergun P, Ortakoylu MG, Demir A, *et al.* Categorization of COPD patients in Turkey via GOLD 2013 strategy document: ALPHABET study. Int J Chron Obstruct Pulmon Dis 2015;10:2485-94.
8. Davis KJ, Landis SH, Oh YM, Mannino DM, Han MK, van der Molen T, *et al.* Continuing to Confront COPD International Physician Survey: physician knowledge and application of COPD management guidelines in 12 countries. Int J Chron Obstruct Pulmon Dis 2014;10:39-55.
9. Decramer M, Brusselle G, Buffels J, Corhay JL, De Backer W, Degryse JM, *et al.* COPD awareness survey: do Belgian pulmonary physicians comply with the GOLD guidelines 2010? ActaClin Belg 2013;68:325-40.
10. Corrado A, Rossi A. How far is real life from COPD therapy guidelines? An Italian observational study. Respir Med 2012;106:989-97.
11. Barrecheguren M, Monteagudo M, Ferrer J, Borrell E, Llor C, Esquinas C. *et al.* Treatment patterns in COPD patients newly diagnosed in primary care. A population-based study. Respir Med 2016;111:47-53.
12. Visentin E, Nieri D, Vagaggini B, Peruzzi E, Paggiaro P. An observation of prescription behaviors and adherence to guidelines in patients with COPD: real world data from October 2012 to September 2014. Curr Med Res Opin 2016;32:1493-502.
13. Sen E, GucluSZ, Kibar I, Ocal U, Yilmaz V, Celik O, *et al.* Adherence to GOLD guideline treatment recommendations among pulmonologists in Turkey. Int J Chron Obstruct Pulmon Dis 2015;10:2657-63.
14. Masoompour SM, Mohammadi A, Mahdaviazad H. Adherence to the Global Initiative for Chronic Obstructive Lung Disease guidelines for management of COPD: a hospital-based study. ClinRespir J 2016;10:298-302.
15. Mülleneisen NK. The new GOLD standard recommendation is not implemented in everyday life. Pneumologie 2013;67:241-2.
16. Maio S, Baldacci S, Martini F, Cerrai S, Sarno G, Borbotti M, *et al.* COPD management according to old and new GOLD guidelines: an observational study with Italian general practitioners. Curr Med Res Opin 2014;30:1033-42.
17. Price D, West D, Brusselle G, Gruffydd-Jones K4, Jones R5, Miravitlles M, *et al.* Management of COPD in the UK primary-care setting: an analysis of real-life prescribing patterns. Int J Chron Obstruct Pulmon Dis 2014;9:889-904.
18. Tang CY, Taylor NF, McDonald CF, Blackstock FC. Level of adherence to the GOLD strategy document for management of patients admitted to hospital with an acute exacerbation of COPD. Respirology 2014;19:1191-7.
19. Brusselle G, Price D, Gruffydd-Jones K, Miravitlles M, Keininger DL, *et al.* The inevitable drift to triple therapy in COPD: an analysis of prescribing pathways in the UK. Int J Chron Obstruct Pulmon Dis 2015;10:2207-17.
20. Unni A, Jayaprakash AK, Yadukrishna Mc, Uma Devi P. Drug utilization pattern in chronic obstructive pulmonary disease inpatients at a tertiary care hospital. International J Pharmacy and Pharmaceutical Sciences 2007; 7. Available from: http://innovareacademics.in/journals/index.php/ijpps/article/view/8166 [Last accessed 30 August 2016].

21. GOLD 2016 COPD. Guidelines: http://www.goldcopd.org/guidelines-global-strategy-for-diagnosis-management.html [Last Accessed 17 October 2016].

22. Buhl R, Welte T, Vogelmeier C, Gillissen A, Voshaar T, Kögler H, *et al.* Early treatment of COPD with tiotropium. Pneumologie 2012;66:589-95.

23. López-Campos JL, Hartl S, Pozo-Rodriguez F, Roberts CM. European COPD Audit team. Antibiotic Prescription for COPD Exacerbations Admitted to Hospital: European COPD Audit. PLoS ONE 2015;10:e0124374.

24. Sarc I, Jeric T, Ziherl K, Suskovic S, Kosnik M, Anker SD, *et al.* Adherence to treatment guidelines and long-term survival in hospitalized patients with chronic obstructive pulmonary disease. J Eval Clin Pract 2011;17:737-43.

25. Seaman J, Leonard AC, Panos RJ. Health care utilization history, GOLD guidelines, and respiratory medication prescriptions in patients with COPD. Int J Chron Obstruct Pulmon Dis 2010;5:89-97.