Drug utilization study and Clinical Pharmacist Interventions in Asthma and Chronic Obstructive Pulmonary Disease (COPD) Patients of a Tertiary Care Hospital

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Abstract

A prospective and observational study was carried out over a period of six months in medicine department of a tertiary care hospital. A total of 72 and 150 Asthma and COPD patients respectively were monitored and assessed for different parameters. In the present study males were the predominant in asthma and COPD patients, the main risk factor involved in these diseases were active and passive smoking of tobacco. The risk of the disease increases with increased age in the present study. Polypharmacy and antibiotic therapy is inevitable in the present diseases due to multiple factor involved. The important classes of drugs prescribed were xanthenes derivatives, β-agonists, steroids, Leuco-triene inhibitors and mucoloytics. Patient education was provided for Asthma and COPD patients through GINA (Asthma) and GOLD (COPD) guidelines in order to improve the patient's quality of life. The concept of patient education is well established in developed countries, but yet to be implemented successfully in developing country like India where Pharmacy practice/ Pharm.D programmes is still under developmental stage.

Keywords

Asthma, COPD, Drug utilization, KAP, Patient education.

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INTRODUCTION:

Drugs play an important role in improving human health and promoting well-being. However, to produce the desired effect, they have to be safe, efficacious and have to be used rationally. Drug/Medicine Utilization Evaluations is defined as an ongoing and systematic process designed to maintain the appropriate and effective use of

medications *JCAHO* (1994). Enough number of people is suffered from Asthma and COPD, hence it becomes very essential to spread a thorough awareness among the patients in relation to disease and its medication.

The drug utilization evaluation among the asthmatic and COPD patients will provide a powerful tool in order to find depth of awareness among patients. The technique for drug utilization review (DUR) can provide a useful means of determining whether drug use is appropriate in the treatment of individual patients (Carruthers,1997). Nowadays there is increase in the incidence of chronic diseases such as bronchial asthma (BA) and chronic obstructive pulmonary disease (COPD) (Sujata Sapkota *et.al*, 2011). In India asthma is known to be one of the major causes of morbidity and mortality, comprising about 3-11% of adults and 3-5% of pediatric population (Patel Pinal D *et.al,* 2012). Similarly the prevalence rates of COPD ranges from 2 to 22 % in men and 1.2 to 19 % in women (Surinder K. Jindal, 2006). Globally asthma disease is one the most common chronic disease and currently affects approximately 300 million people in the world. It is a chronic inflammatory disorder of the lung airways characterized and determined by increased responsiveness of tracheobronchial tree to a multiple stimuli (McFadden ER, 2001). The prevalence of asthma has risen in affluent countries over the 30 years but now appears to have stabilized, with approximately 10-20% of adults and 15% of children affected by the serious asthma disease (Longo LD, Kasper LD, Jameson LJ, *et.al*.2012). According to WHO, 65 million people have moderate to severe chronic obstructive pulmonary disease (COPD). More than 3 million people died of COPD in 2005, which corresponds to 5% of all deaths globally. It is known that almost 90% of COPD deaths occur in low- and middle-income countries. At one time, COPD 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. By 2020 it is estimated that COPD become third leading cause of death worldwide according to *NICE* (2010) Guidelines.

OBJECTIVES:
- Evaluation of drug therapy in the treatment of Asthma and COPD patients.
- To emphasize the role of clinical pharmacist in the prevention of Asthma and COPD.
- To assess the patient education through KAP questionnaire.

MATERIALS AND METHODS:
Study design and settings
It was a hospital based prospective observational and indirect interventional study in Asthma and COPD patients. Study was carried out at in-patient department of medicine for a period of six month at Shri.B.M.Patil medical college hospital and research Center, Vijayapur. The patients were enrolled in the study as per the inclusion and exclusion criteria.

Inclusion criteria:
Patients diagnosed with asthma and COPD were included.
Both the genders, who are aged 18 years and above.

Exclusion criteria:
OPD patients are excluded.
Pregnant women's with asthma are excluded from the study.

Source of data:
The study is based on the data collected from the in-patient case files (including patient's specific information, laboratory investigations and drug therapy) who are receiving treatment in the hospital at the time of the study.

Statistical analysis:
The number of patients and percentage of data were calculated with the help of regular Microsoft excel 2007 sheet and P value was determined using SPSS 17th Version software by applying the McNemers Chi-square test. The sample size was calculated by the following formula with the help of statistician.

$$n = \frac{Z^2 \times p \times q}{d^2}$$

Where, n=sample size Z = Standard deviation, p= Proportion of the population having characteristics, q=1-p, d=degree of precision.

RESULTS:

Gender wise categorization of patients enrolled in the study:

Asthma: Out of 72 subjects enrolled for the study, 42 (58.33%) were male and 30 (41.66%) were female, as described in Table I. *COPD:* Out of 150 subjects enrolled for the study, 116 (77.3%) were male and 34 (22.6%) were female, as described in Table II.

Table I - Gender wise categorization of Asthma subjects enrolled in the study.

Gender	No. of patients	Percentage (%)
Male	42	58.33%
Female	30	41.66%

Table II - Gender wise categorization of COPD subjects enrolled in the study.

Gender	No. of patients	Percentage%
Male	116	77.3%
Female	34	22.6%

Distribution of age groups with Asthma and COPD:

Asthma: Out of the total number of subjects enrolled, maximum number of patients found were elderly patients 61-70 years of age 36.11%, followed by age groups of 51-60 years comprising about 22.22%; 71-90 years of age 22.22% and 41-50 years of age 6.94%; 21-30 years of age 6.94%; with the least percentage of age group 31-40 years comprising about 5.55% of subjects enrolled in the study. The prevalence of asthma was with the age group of 61-70 years, as described in Table III. *COPD:* Out of total number of subjects enrolled, maximum number of patients found were elderly patients 61-70 years of age 37.3%, followed by age groups of 71-90 years comprising about 26.6%; 51-60 years of age 21.3% and 41-50 years of age 9.3%: 31-40 years of age 3.3%; with the least percentage of age group 20-30 years comprising 2.0% subjects enrolled in the study. The prevalence of COPD was with the age group of 61 to 70 years, as described in Table IV.

Table III - Distribution of asthma patients with age group.

Age group (In years)	No. of patients	Percentage (%)
21-30	05	6.94%
31-40	04	5.55%
41-50	05	6.94%
51-60	16	22.22%
61-70	26	36.11%
71-90	16	22.22%

Table IV - Distribution of COPD patients with age group.

Age groups	No. of patients	Percentage (%)
21-30	03	2.0%
31-40	05	3.3%
41-50	14	9.3%
51-60	32	21.3%
61-70	56	37.3%
71-90	40	26.6%

Patient distribution based on risk factors:

Asthma: Out of total number of subjects enrolled in the study, maximum numbers of patients found are from tobacco chewing and smoking 32 (44.44%) followed by air pollution 25 (34.72%) and the least are without habits 15 (20.83%). The prevalence of asthma was with tobacco smoking 32 (44.44%), as described in Table V. *COPD:* Out of total number patients enrolled in the study, maximum numbers of patients found are from smoking 92 (61.3%), smoking exposures 35 (23.3 %), and others 23 (15.3%). The prevalence of COPD was with smoking 92 (61.3%), as described in Table VI.

Table V - Distribution of asthma patients based on risk factors.

Habits	No. of patients	Percentage (%)
Tobacco smoking	32	44.44%
Air pollution	25	34.72%
Others	15	20.83%

Table VI - Distribution of COPD patients based on risk factors.

Habits	No. Of patients	Percentage (%)
Smoking	92	61.3%
Smoking exposures	35	23.3%
Others	23	15.3%

Distribution of drugs prescribed in Asthma and COPD according to route of administration:

Asthma: Out of total number of drugs, maximum number of drugs prescribed are with oral route 170 (45.6%), inhalation route 121 (32.5%) and the least are with parenteral 82 (22%), as described in Table VII. *COPD:* Out of total number of drugs, maximum number of drugs are prescribed with oral route 294 (44.5%), inhalation route 256 (38.7%) and the least are with parenteral route 110 (16.6%), as described in Table VIII.

Table VII - Distribution of drugs prescribed in Asthma according to route of administration.

Route	No. of drugs	Percentage (%)
Oral	170	45.6%
Inhalation	121	32.5%
Parenteral	82	22.0%

Table VIII - Distribution of drugs prescribed in COPD according to route of administration.

Route	No. of drugs	Percentage (%)
Oral	294	44.5%
Inhalation	256	38.7%
Parenteral	110	16.6%

Patient distribution based on drug therapy regimen:

Asthma: Out of 72 patients, majority of them 42 (58.33%) received multiple drug therapy (>4 drugs) followed by 4 drugs 22 (30.55%), 3 drug 6 (8.33%) and 2 drugs 2 (2.77%), as described in Table IX. *COPD:* Out of 150 patients, majority of them 104 (70.6%) received multiple drug therapy (>4 drugs) followed by 4 drugs 41 (27.3%), 3 drugs (2%), as described in Table X.

Table IX - Distribution of asthma patients based on drug therapy regimen.

Multiple drug therapy	No. Of patients	Percentage (%)
>4 drugs	42	58.33%
4 drugs	22	30.55%
3 drugs	06	8.33%
2 drugs	02	2.77%
1 drugs	00	00%

Table X - Distribution of COPD patients based on drug therapy regimen.

Multiple drug therapy	No. of patients	Percentage (%)
>4 drugs	104	70.6%
4 drugs	041	27.3%
3 drugs	005	3.3%
2 drugs	000	0.0%
1 drug	000	00%

Patient distribution based on fixed dose combination:

Asthma: Majority of the patients were prescribed with salbutamol +Ipratropium bromide 59 (81.94%) followed by budesonide + formetrol 13 (18.05%), as described in Table XI. *COPD:* Majority of the patients were prescribed with salbutamol + Ipratropium bromide 125 (83.33%) followed by budesonide + formetrol 25 (16.66%), as described in Table XII.

Table XI - Distribution of asthma patients based on fixed dose combination.

Fixed dose combination	No. of patients	Percentage (%)
Salbutamol + Ipratropium bromide	59	81.94%
Budesonide + formetrol	13	18.05%

Table XII - Distribution of COPD patients based on fixed dose combination.

Fixed dose combination	No. of patients	Percentage (%)
Salbutamol + Ipratropium bromide	125	83.33%
Budesonide + formetrol	25	16.66%

Patient distribution based on antibiotics prescribed:

Asthma: Among the antibiotics, levofloxacin 34 (47.22%) were prescribed mostly followed by Ceftriaxone 7 (9.72%), ofloxacin 5 (6.94%), cefoperazone sodium 5 (6.94%), Azithromycin 3 (4.16%), amoxicillin + calvulinic acid 3 (4.16%), cefixime 3 (4.16%), piperacillin + tazobactum 3 (4.16%) and the least prescribed are amikacin 3 (4.16%), cefotaxim 2 (2.77%), amoxicillin 2 (2.77%), as described in Table XIII. *COPD:* Among the antibiotics, levofloxacin 59 (39.3%) were prescribed mostly followed by Ceftriaxone 36(24%), piperacillin + tazobactum 15 (10%) cefixime 8 (5.3%) cefoperazone 6 (4%) amoxicilline+calvulinic acid 4 (2.66%), cefotaxime 4 (2.66%), gentamicin 4 (2.66%), amikacin 4 (2.66%), ampicillin 4 (2.66%), levocitrizine 3 (2%) azithromycin 3 (2%), as described in Table XIV.

Table XIII - Distribution of asthma patients based on antibiotics prescribed.

Name of the drug	No. of patients	Percentage (%)
Levofloxacin	34	47.22%
Ceftriaxone	7	9.72%
Ofloxacin	5	6.94%
Cefaperazone Sodium	5	6.94%
Azithromycin	3	4.16%
Amoxicillin+calvulinicacid	3	4.16%
Cefixime	3	4.16%
Piperacillin+tazobactum	3	4.16%
Amikacin	3	4.16%
Cefotaxim	2	2.77%
Amoxicillin	2	2.77%
Kanamycin	2	2.77%

Table XIV - Distribution of COPD patients based on antibiotics prescribed.

Name of the drug	No. of patients	Percentage%
Levofloxacin	57	39.3%
Ceftriaxone	36	24.0%
Piperacillin+tazobactum	15	10.0%
Cefixime	8	5.3%
Cefaperazone	6	4.0%
Amoxicillin+ Calvulinic acid	4	2.66%
Cefotaxim	4	2.66%
Gentamicin	4	2.66%
Amikacin	4	2.66%

Ampicillin	4	2.66%
Levocitrizine	3	2.0%
Azithromycin	3	2.0%

Distribution of drugs based on category:

Asthma: Among the anti asthmatics methyl xanthines 55 (76.38%) were most frequently prescribed followed by corticosteroids 50 (69.4%), short acting β_2 agonist 31 (43.05%), antihistamines 12 (16.6%), Leukotriene receptor antagonist 9 (12.5%), mucolytics 7(9.72%), as described in Table XV. *COPD:* Among the COPD drugs methylxanthines 139 (92.6%) were mostly prescribed followed by corticosteroids 135 (90%), mucolytics 12 (8%), as described in Table XVI.

Table XV- Commonly prescribed class of drugs for Asthma.

Anti asthmatics	No. of drugs	Percentage (%)
Methyl xanthenes	55	76.38%
Corticosteroids	50	69.44%
Short acting β_2 agonist	31	43.05%
Antihistamines	12	16.66%
Leukotriene receptor antagonist	9	12.50%
Mucolytics	7	9.72%

Table XVI - Commonly prescribed class of drugs for COPD.

Drugs for COPD	No. of drugs	Percentage%
Methyxanthines	139	92.6%
Corticosteroids	135	90.0%
Mucolytics	12	8%

Patient Education through KAP Questionnaires: KAP Questionnaires data for Asthma and COPD were described in Table XVII and Table XVIII respectively.

Table XVII - KAP questionnaires for Asthma.

Sr.No.	QUESTIONNAIRES	Before Education		After Education		Total No. of patients	Mc Nemers chi square test
		Yes	No	Yes	No		
1	Do you know what asthma is?	25 (34.72%)	47 (65.27%)	41 (56.94%)	31 (43.05%)	72	P=0.001*
2	Do you know what are the triggering factors of asthma are?	20 (27.77%)	52 (72.22%)	37 (51.38%)	35 (48.61%)	72	P=0.001*
3	Are you coming for regular check up?	28 (38.88%)	44 (61.11%)	41 (56.94%)	31 (43.05%)	72	P=0.001*
4	Are you taking the medications for asthma properly?	30 (41.66%)	42 (58.33%)	40 (55.55%)	32 (44.44%)	72	P=0.003*
5	Do you know how to use inhalers?	21 (29.16%)	51 (70.83%)	49 (68.05%)	23 (31.94%)	72	P=0.001
6	If you are prescribed with medicines for a month then are you taking the medicines at exact time?	32 (44.44%)	40 (55.55%)	42 (58.33%)	30 (41.66%)	72	P=0.115 NS
7	Do you know complication of Missing dose?	30 (41.66%)	42 (58.33%)	40 (55.55%)	32 (44.44%)	72	P=0.003*

Sr.No.	QUESTIONNAIRES	Before Education		After Education		Total No. of patients	Mc Nemers chi square test
		Yes	No	Yes	No		
8	Has a doctor or other healthcare professional ever taught you what to do during an asthma attack or episode?	30 (41.66%)	42 (58.33%)	39 (54.16%)	33 (45.83%)	72	P=0.003*
9	Do you know benefits of life Style modifications?	35 (48.61%)	37 (51.38%)	40 (55.55%)	32 (44.44%)	72	P=0.145 NS
10	Are you following dietary restrictions?	25 (34.72%)	47 (65.27%)	42 (58.33%)	30 (41.66%)	72	P=0.005*

Note: *: Indicates significant difference and NS: Indicates No significant difference

Table XVIII - KAP questionnaires for COPD.

Sr.No.	QUESTIONNAIRES	Before Education		After Education		Total No. of patients	Mc Nemer's chi square test
		YES	NO	YES	NO		
1	Do you know what COPD?	51 (34.00%)	99 (66.00%)	87 (58.00%)	63 (42.00%)	150	P=0.001*
2	Do you know what the triggering factors of COPD are?	45 (30.00%)	105 (70.00%)	73 (48.66%)	77 (51.33%)	150	P=0.001*
3	Are you coming for regular check up?	62 (41.33%)	88 (58.66%)	88 (58.66%)	62 (51.33%)	150	P=0.001*
4	Are you taking COPD medications properly?	60 (40.00%)	90 (60.00%)	95 (63.33%)	55 (36.66%)	150	P=0.001*
5	Do you know how to use inhalers?	45 (30.00%)	105 (70.00%)	70 (46.66%)	80 (53.33%)	150	P=0.0033*
6	If you are prescribed with medicines for a month then are you taking the medicines at exact time?	43 (26.66%)	107 (71.33%)	71 (47.33%)	79 (52.66%)	150	P=0.004*
7	Do you know complication of Missing dose?	62 (41.33%)	88 (58.66%)	88 (58.66%)	62 (51.33%)	150	P=0.033*
8	Do you know smoking exacerbates COPD?	50 (33.33%)	100 (66.66%)	75 (50.00%)	75 (50.00%)	150	P=0.001*
9	Do you know benefits of life Style modifications?	33 (22.00%)	117 (78.00%)	59 (39.33%)	91 (60.66%)	150	P=0.012*
10	Are you following dietary restrictions?	70 (46.66%)	80 (53.33%)	89 (59.33%)	61 (40.66%)	150	P=0.001*

Note: *: Indicates significant difference and NS: Indicates No significant difference.

DISCUSSION:

Bronchial Asthma and COPD were seen as the leading cause of morbidity and mortality in India. We carried out a prospective observational study to assess the monitoring and evaluation of drug utilization in asthma and COPD patients in tertiary care hospital. Drug utilization evaluation is the mainstay for the rational use of drugs. In many countries including India safe and effective use of drug is gaining more concern because inappropriate use and prescribing of drugs leads to complication in the health care system for delivering efficacious provisions. Guidelines for rational prescribing practices are put forth to improve the standards of prescribing.

The present study shows that out of 72 asthma patients 42 (58.33%) were male and 30 (41.66%) were female. Then present study revealed that asthma was more prevalent in males than in females. This is synonymous with the study conducted in Andhra Pradesh by Languluri Reddenna *et.al* (2013). Out of 150 COPD patients 116 (77.3%) were male and 34 (22.6%) were female. Then present study revealed that COPD was more prevalent in males than in females. This is in accordance with Sharon Sunil *et.al* (2015)

We found that the greatest number of patients were in the age group of 61-70 years i.e. 26 (36.11%) and 56 (37.3%) in asthma and COPD respectively. Age may be the risk factor for development of Asthma and COPD. Other risk factor which may triggers the disease were tobacco smoking 32 (44.44%), air pollution 25 (34.72%) and others 15 (20.83%) Studies done by Gupta PR and Mangal DK (2006) also conclude the same. Risk factors for COPD were smoking 92 (61.3%) smoking exposures 35 (23.3%) and others 23 (15.3%). It reveals that the major causing factor for asthma was dust 27 (38.5%) and COPD was smoking 92 (61.3%). This is in accordance with Sharon Sunil *et.al* (2015).

The route of administration of anti-asthmatics is concerned it was observed that in present study that oral route was the mostly preferred route (45.60%) followed by inhalation (32.5%) and parenteral route (22.00%).These results were in par with the studies conducted by Shimpi R.D *et.al* (2012), this diversity may be depend on the prescribing habits of a doctor and need of a patient.

The inhalation route of drug administration causes a high local concentration in to the lungs with a low systemic delivery, significantly improves the therapeutic effectiveness and minimizes the systemic side effect. According to the standard guidelines of asthma, inhalation therapy should be the first choice, but only 32.5% patients at the time of study used inhalers this could be because of patient's side, the level of acceptance is low apart from patient's non-compliance and coordination associated with use of inhaler. However this will require more of patient's education and knowledge convincing by the treating physician or by the clinical pharmacist on importance of inhalation therapy.

The study showed that in COPD patients most preferred route of administration was oral 294 (44.5%) followed by inhalation 256 (38.7%) and parenteral 110 (16.6%). This is not in accordance with the study conducted by Maqusood M *et.al*. (2016)

All patients were on multiple drug therapy, may be because in asthma and COPD mostly require more than one drug to control the symptoms; hence, combination therapy is often required to treat the disease.

In the present study majority of asthma patients 42 (58.33%) received multiple drug therapy (>4drugs) followed by 4 drugs 22 (30.55%) and 3 drugs 6 (8.33%) and 2 drugs (2.77%).This is analogous with the study done by Patel Pinal D *et.al* (2012). In the same way out of 150 COPD patients, majority of them 104 (70.6%) received multiple drug therapy (>4 drugs) followed by 4 drugs 41 (27.3%), 3 drugs (2%).

Present study shows that both asthma and COPD patients were also prescribed with fixed dose combinations. Among them Salbutamol with ipratropium bromide was the most frequently prescribed combination in both asthma 59 (81.94%) and COPD 125 (83.33%). Because these drugs works by opening air passages to the lungs and relaxing the muscles in the walls of the small airways in the lungs. This is in accordance with the Michael Babita *et. al*. (2016)

Present study shows that in asthma patients levofloxacin 34 (47.22%) was mostly prescribed antibiotic followed by Ceftriaxone 7(9.72%), and ofloxacin 5 (6.94%), cefoperazone sodium 5(6.94%), Azithromycin 3(4.28%), amoxicillin + calvulinic acid 3 (4.16%), cefixime 3 (4.16%), piperacillin + tazobactum 3 (4.16%) and the least prescribed are amikacin 3 (4.16%), cefotaxim 2 (2.77%), amoxicillin 2 (2.77%).This is in accordance with the Michael Babita *et. al*. (2016) Similarly in COPD patients also levofloxacin 59 (39.3%) was mostly prescribed antibiotic followed by Ceftriaxone 36 (24%), piperacillin + tazobactum 15 (10%) cefixime 8 (5.3%) cefoperazone 6 (4%) amoxicilline+calvulinic acid 4 (2.66%), cefotaxime 4 (2.66%), gentamicin 4 (2.66%), amikacin 4 (2.66%), ampicillin 4 (2.66%), levocitrizine 3 (2%) azithromycin 3 (2%).

Among the anti-asthmatics methyl xanthines 55 (76.38%) were most frequently prescribed followed by corticosteroids 50 (69.4%), short acting β_2 agonist 31 (43.05%), antihistamines 12 (16.6%) leukotriene receptor antagonist 9 (12.5%) mucolytics 7 (9.72%).Studies of Arumugam et al and Kumar et al also showed similar trends (Carruthers AA 1997, Anil K, Tiwari HK *et.al* 2004) Among the COPD drugs Methyxanthines 139 (92.6%) were mostly prescribed followed by corticosteroids 135 (90%), mucolytics 12 (8%). Probably due to their low cost.

In the usual practice, patients receive a general counseling from the physicians or their assistants. Apart from these, a patient education material recommended by the GINA and GOLD which is available as patient guide was used in educating the patients.

Patient education was given to patients. The following subjects were dealt in educating the patients i.e. nature of asthma and COPD disease, causative factors and preventive measures, needed lifestyle changes for asthma and COPD patients, medications usage, and method of using peak flow meters for monitoring lung functions.

The KAP questionnaire is a comprehensive, easily understandable and easy to interpret questionnaire that allows clinicians, clinical pharmacists and other health care professionals to measure the changes in asthmatic and COPD patients experience as a result of patient education.

Present study shows that most patients' knowledge about disease, preventive measures and risk factors improved after educating whereas few elderly were not able to improve their quality of life due to poor remembering capacity and the patient education provided was effective and results were in better therapeutic outcome. Many patients also conveyed their thankfulness for providing patient education which improved their quality of life and knowledge about disease.

CONCLUSION:

Drug utilization in asthma and COPD were evaluated in patients who were admitted to a General medicine ward. Apart from physicians, pharmacists can also play a role in correct prescribing practice. In our study we found that the incidence of both Asthma and COPD were more common in males when compared to females. Majority of patients were prescribed with multiple drug therapy out of which oral route was the most preferred one. Patient education found to have significant influence on improvement in the knowledge, attitude and practice of asthma and COPD towards its management. Greater understanding of illness and a change in attitude and practice of medicine would result in better therapeutic outcome. The concept of patient education is well established in developed countries, but yet to be initiated in developing country like India. Provision of patient education by the clinical pharmacist was well received and encouraged by the patients and medical fraternity. Thus along with the pharmacological treatment, patient education is also an important aspect of treatment for asthma and COPD. Till today the curative rate of asthma and COPD is a global challenge, therefore the better understanding of etiopathogenesis and novel approach of drug therapy regimen may improve the quality of life of a patient.

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