ASSESSMENT OF DRUG USAGE PATTERN IN PATIENTS OF ASTHMA: A CROSS-SECTIONAL STUDY IN A TERTIARY CARE TEACHING HOSPITAL IN EASTERN INDIA

Respiratory Medicine

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ABSTRACT

Background: In India, asthma imposes a substantial burden; though the disease still remains under-recognized, underestimated and under-treated in masses. With a global need of promoting rational drug use in healthcare, drug utilization pattern studies could provide feedback to prescribers and help in fostering rational drug usage. The present study was planned to study the drug utilization pattern in patients of asthma in a tertiary care set-up in eastern India and to evaluate it with respect to GINA guidelines.

Materials and Methods: The study was carried out over a period of one year where cases with confirmed diagnosis of asthma, who gave informed consent to participate were included. Drug usage pattern was determined in the light of drugs prescribed, mean drugs per prescription, percentage of drugs prescribed in generic name and having conformation to national essential drug list. Percentage of inhalational, injectable, fixed dose combination and antibiotics per prescription were noted. Data were checked for completeness and statistically analysed.

Results: The present study included 370 participants. A total of 1514 drugs were prescribed, with 4.09 drugs per prescription. 12.55% of drugs prescribed were from national essential drug list. A total of 1031 anti-asthma drugs were prescribed with 2.8 anti-asthma drugs per prescription. Among the various classes of anti-asthma drugs, maximum prescribed were inhalational corticosteroids, followed by long acting inhalational beta 2 agonist and anti-leukotriene drugs. 96.5% of total patients were on inhalational drugs, with budesonide and formoterol being majorly prescribed.

Conclusion: The usage pattern as assessed in our study was in conformation to GINA guidelines. Guidelines like GINA have enlightened physicians about the rational prescribing in asthmatic patients.

KEYWORDS

Asthma, Drug Usage Pattern, Essential Drugs, GINA

INTRODUCTION

The last few decades have seen a rise in the prevalence of all allergic diseases, including asthma; asthma is a common chronic disease that affects the quality of life of patients and has a significant economic impact. Nowadays global warming, environmental pollution and natural disasters like earthquake, landslides, supercyclones aid the increase number of asthmatic patients. Around 235 million people are living with asthma. Over 80% of asthma-related deaths occur in low- and lower-middle income countries.^[1] In India, asthma imposes a substantial burden; though there is a paucity of appropriate epidemiological data to determine prevalence for asthma or the allergic asthma. The burden of rhinitis and asthma in Indian population is presently estimated more than one billion. But despite imposing substantial burden both diseases still remains under-recognized, underestimated and under-treated, in India. Besides focusing in the unmet needs in asthma treatment, the Global Asthma Physician and Patient Survey also revealed that there exists a direct relationship between the quality of physician-patient communication, the level of treatment side effects and the extent of patient compliance, highlighting a clear need for improved patient-focused care in asthma. Patients with severe persistent asthma who are inadequately controlled despite Global Initiative for Asthma (GINA)^[2] step IV therapy, are a challenging population with significant unmet medical need. Several reasons have been quoted for this non-maintenance of therapeutic effects, such as patient non-adherence, poor inhalation, lack of response to pharmacotherapy, presence of co-morbid diseases, triggers such as respiratory infections (particularly viral), indoor allergens and

environmental exposures. This subset of patients, who experience frequent exacerbations requiring emergency department visits or hospitalizations, may benefit from novel therapies like anti immunoglobulin-E (IgE) antibodies, cytokine modulators and allergen immunotherapy; designed to target specific mechanisms underlying airway inflammation.^[3] Through a coordinated worldwide effort, GINA 2019 aims to increase awareness regarding asthma among health professionals, public health authorities and the community at large, and also aims to improve its prevention and management. The global strategy for asthma management and prevention has been extensively revised to provide a comprehensive and integrated approach to asthma management that can be adapted for local conditions and for individual patients.^[2]

Asthma is one of the commonest chronic diseases in India, also very much prevalent in the states of eastern India. Most of asthmatic patients are relieved from the symptoms by anti-inflammatory drugs, bronchodilators and concurrent use of antileukotrienes drugs. Despite varied therapeutic options being currently available, a vast majority of asthma patients with moderate to severe persistent asthma continue to experience symptoms even after therapy with inhaled or systemic corticosteroids.^[4] These patients require frequent/planned/unplanned medical attention and seek care in emergency departments and other urgent care facilities. With a global need of promoting rational drug use in healthcare, drug utilization pattern studies could provide feedback to prescribers and help in fostering rational drug usage. In this background the present study was planned to study the drug utilization

pattern in cases of asthma and to evaluate it with respect to GINA guidelines.

MATERIALS AND METHODS

The present observational cross sectional study was carried out in a tertiary care hospital in eastern India over a period of one year where data were collected from general medicine wards and outpatient department of general medicine and chest medicine. Cases with confirmed diagnosis of asthma, who gave informed consent to participate in the study, were included.

Drug usage pattern was determined in the light of drugs prescribed, mean drugs per prescription, percentage of drugs prescribed in generic name and having conformation to national essential drug list. Percentage of inhalational, injectable, fixed dose combination and antibiotics per prescription were noted. Cost per prescription per day was calculated. Determinants of drug usage were age, sex, pregnancy, lactation, occupation, comorbidities, addiction history, stages of asthma, findings of pulmonary function test and non pharmacological advices, if any. Data were checked for completeness and statistically analysed.

RESULTS

The present study included 370 participants, with male: female ratio being 2.7:1. Maximum patients belonged to the age group (41 – 50yr) followed by (21 – 30yr) & (31 – 40yr). (Table 1) 7% of females were pregnant while 3% were lactating. Among 370 patients 213 patients (57.6%) had no addiction history. 42.1% were smokers, while 1.08% were addicted to alcohol.

Patients were interviewed for associated comorbidities, where diabetes was highest (13.6%), followed by hypertension (12.9%), allergic rhinitis (12.2%), hypothyroidism (0.9%) and COPD (0.8%). Assessing the stages of asthma, mild asthma was observed in 47.2%, moderate in 36% and severe in 16.77% patients. Only 95 prescriptions (26%) were containing PFT standing.

Total numbers of drugs prescribed were 1514. So numbers of drugs per prescription were 4.09. Total number of fixed dose combination (FDC) drugs prescribed was 508, with 1.37 FDCs being prescribed per prescription. 0.13% of all drugs were prescribed in generic name. A total of 12.55% of prescribed drugs (n=190) were from National List of Essential Medicine 2015^[5]. Numbers of essential medicines prescribed per prescription were 0.51. Regarding prescribing anti microbial agents (AMA), 99 patients were prescribed to single or fixed drug combination of AMA. 8.70% of total prescribed drugs were AMA, with majority prescriptions being azithromycin and moxifloxacin. 7.3% of total prescriptions received injectable drugs, with maximum prescribing being pantoprazole (33%) followed by ceftriaxone (27%), ondansetron (27%), amoxycillin+clavulanic acid (7.2%) and hydrocortisone (5.8%). (Table 2)

Total numbers of anti asthmatic drugs in the study population were 1031 (68% of total prescribed drugs). Drugs prescribed for asthma per prescription were 2.8 in number. Among the various classes of anti-asthma drugs, maximum prescribed were inhalational corticosteroids, followed by long acting inhalational beta 2 agonist and anti-leukotriene drugs. (Figure 1) 2.04% of total prescribed drugs were systemic corticosteroids. Systemic corticosteroids were prescribed among 31 patients, with 26 of them receiving oral deflazacort and 5 cases receiving inj hydrocortisone. Numbers of inhalational drugs used per prescription were 2.36. 96.5% of total patients were on inhalational drugs, with budesonide and formoterol being majorly prescribed. Inhalation drugs were delivered via dry powder inhaler in 69.5% patients followed by metered dose inhaler with spacer in 16.3%, metered dose inhaler in 6.7% and nebulisers in 7.5%. All patients presented with acute severe asthma were inhaling drugs via nebulisers. Minimum cost per prescription per day was 11 INR, while maximum cost per prescription per day was 130 INR. Mean cost per prescription per day was 63.38±35.591 INR.

Only 7 patients were receiving monotherapy (1.9%). Drugs used for monotherapy was montelukast. Total number of drugs prescribed to pregnant ladies was 21. Category B drugs were prescribed in 7 (33.3%) and category C drugs were prescribed in 14 (66.7%) such patients. Among the 7 pregnant females, category C drugs prescribed were inhalational fluticasone (5), inhalational salmeterol (4),

inhalational formoterol (3), inhalational salbutamol (2). Category B drugs prescribed were oral cetirizine (3), inhalational budesonide (2) and oral cefpodoxime proxetil (2).

Non pharmacological advices are very important tools for management of asthma. Following advices were given

1. Steps to minimise allergen exposure (n=179)
2. Regular breathing exercise (n=154)
3. Technique to take inhalation drugs (n=233)
4. To stop smoking or alcohol intake (n=133)
5. To do physical exercise (n=140)
6. Occupational rehabilitation (n=147)

DISCUSSION:

Asthma is a chronic inflammatory disease of airway. Number of patients suffering from asthma is increasing day by day. Treatment of asthma comprises of multiple therapeutic options. Drug utilization evaluation is most important for the promotion of rational uses of drug. Recommendation of various international bodies on asthma will help to improve prescribing practices of physician and make availability of standard guidelines. Irrational use of drug & inappropriate prescribing are the two common phenomenon in the developing countries, which cause a big problem for providing the effective health care facilities.^[6] Rational use of drug requires that patient receiving medications appropriate to their clinical needs in their individual required dose, for adequate period of time at lowest cost. This upsurges the need for pharmacotherapeutic studies. The present study was thus conducted with a view to assess the drug usage pattern in patients with asthma attending the medicine and chest department in a tertiary care hospital in eastern India. The study included 370 asthma patients suffering from asthma with male preponderance. 42.4% of the study population was addicted to tobacco smoking & alcohol. Tobacco smoking has direct causal relationship with asthma. 42.1% of total patients were involved in tobacco smoking. It was concluded by Siroux et al that smoking is not risk factor for in adulthood, but the smoking increases asthma severity.^[7] Stopping of smoking is important non pharmacological tool for the management of asthma. In the present study 85.3% of smokers were advised to quit smoking. Proper health education is required to convince the patients.

7% of female population was pregnant. Control of asthma in pregnancy is very much required because each exacerbation leads to increase in maternal & foetal mortality & morbidity. Prescribing drugs to pregnant woman needs careful knowledge regarding teratogenicity. In our study population 66.7% of the drugs prescribed to pregnant women were belonging to Category C, whereas 33.3% were from category B. Before prescribing category C drug to a pregnant lady it should be kept in mind that these drugs are only recommended for use during pregnancy when there are no alternation and benefit outweighs risk. Inhalational corticosteroid budesonide, a category B drug can be promoted instead. As management of asthma consists of multiple drug therapy it is important to know the impact of concomitant disease, its management, interaction of drugs used & outcome possibilities. Patients were interviewed for associated comorbidities, where diabetes was highest, followed by hypertension, allergic rhinitis, hypothyroidism and COPD. Inhalational corticosteroids are one of the most important tools for managing asthma, but the effect of these drugs to hypertension & diabetic patient is important. Multiple drug therapy may produce negative impact to the patients due to economic or mental disturbances.

Pulmonary function test reports are very important regarding management and follow up of the patients. In the present study population only 26% of patient had pulmonary function test report. For classifying the asthmatic patients into stages, to see the compliance of therapy every prescription should contain the PFT reports. Drummond et al (1994)^[8] suggested that improving access to spirometry in primary care may improve diagnosis and compliance with guidelines. Armugam V et al^[9] concluded that many general practitioners especially those from rural areas, thought spirometers were too expensive, and some of them lacked confidence in their use. That study also suggested that there was a significant difference between recommendation regarding spirometry and general physicians' confidence to perform and interpret the tests. So lack of pulmonary function test reports also hints to increase awareness on spirometry among the physicians.

Number of drugs per prescription was 4.09. Poly pharmacy is very common for treating the patients with asthma. Only 12.6% of drugs

prescribed for asthma belonged to National List of Essential Medicine 2011. This is in contrast to other studies by Prasad et al,^[10] where 34% of the prescribed drugs were from the essential drug list. Essential drugs are selected with due regard to public health relevance, evidence on efficacy and safety and comparative cost effectiveness. More usage of Essential Medicines would provide safe and efficacious therapy at cheap rate. The figures also upsurges the need to include more anti-asthmatic drugs in the national essential drug list. Our study found very few generic prescriptions, which is alarming. Beside this, it is suggested that hospital managers should regulate and monitor drug advertising and promotional activities in their settings to improve compliance with rational prescription practice.

In the present study population 27% of patients were on anti-microbial agent. A study done by Patel Pinal D et. it was seen that antibiotics prescribed in urban area 32% and rural area 36%. It was also seen that all anti-microbial agent belonged to the group tetracycline and fluoroquinolone.^[11] In other studies by Pandey et al.^[12] and Prasad et al^[10] showed less number of antibiotics prescribed among their study population. These findings were corroborated with our study result. Asthma is an atopic disorder which triggers with exposure to allergen. Infective etiology of asthma is very uncommon and mostly viral. Viral infections are associated with asthma exacerbations. So use of antimicrobial agent should be restricted to prevent emergence of resistance. Antibiotics are mostly required in cases of associated community acquired pneumonia. In the present study azithromycin was most commonly prescribed antibiotic followed by moxifloxacin and ceftriaxone. Our study showed similarity of empirical antibiotics choices as per standard guidelines.^[13] Rational choice of antibiotic is most important tool for preventing emergence of resistance.

8% of study population were on systemic corticosteroids, majority being prescribed oral deflazacort and rest on injection hydrocortisone. However, there was no usage of prednisolone which is more potent than deflazacort and also very cheap with respect to deflazacort. Prednisolone also belongs to essential list of medicines. Short courses of oral steroids are indicated for exacerbations of asthma. 74% patients on systemic corticosteroids presented to OPD with moderate stages of asthma, while 16% were in severe stages of asthma. 10% patients were not categorised in stages. Clinical and investigational correlation is required to identify associated allergic broncho pulmonary aspergillosis, where systemic corticosteroids have much important role to play.

As per GINA 2019 guideline^[2] long term goals of asthma management are to achieve good control of symptoms and maintain normal activity levels, and also to minimize future risk of exacerbations, fixed airflow limitation and side effects. Inhalation corticosteroids help to reach the goal with success. Inhalation drugs should be the first line approach in treating asthma. In our study population 96.5% of patients were on inhalation drugs. This is in contrast to the study by Prasad et al^[10] who reported the usage as 60 % in their set-up and Srivastava et al^[14] who reported the figure as 31.69% in their study. Thus the rational choice of inhalational drugs for treating maximum patients was appreciable in this set-up.

Among the inhalational beta2 agonist prescribed among study population formoterol was prescribed more than salmeterol as long acting beta2 agonist, whereas salbutamol and levosalbutamol were prescribed almost equally. Short acting beta2 agonists were used less in number in comparison with long acting beta2 agonist. For long term control use of long acting beta2 agonist was much helpful; while short acting beta 2 agonists were mainly used as reliever drugs, important to treat exacerbations. A study by Noord J A et al showed that formoterol (24 mcg) and salmeterol (50mcg) had equal bronchodilator capacity, which was similar to salbutamol 200 mg and lasted for atleast 12hrs in asthma patients, however, formoterol had a more rapid onset of action as compared to salmeterol, equal to that of salbutamol.^[15] Formoterol combination drugs also beneficial to control acute attack. That may be a cause for prescribing formoterol more than salmeterol.

Our study however showed only 2% patients being on monotherapy, which is much lower than other studies by Vijayakumar S et al^[16] where it was 20% and Patel Pinal D et al^[11] where it was 16%. Since asthma patients often require more than one drug for control of symptoms hence combination are required to manage asthmatic patients and percentage of being in monotherapy is lower. Our study participants were given non pharmacological advices like steps to minimize

allergen exposure, regular breathing exercise, techniques of taking inhalation drugs. Advices to stop addiction and start regular physical exercises, along with occupational rehabilitations were advised. However larger sample size and multicentric conduct of this study would help in better generalizability of the study results.

CONCLUSION

Asthma, a common chronic disease has multiple therapeutic options. Guidelines like GINA have enlightened physicians about the rational prescribing in asthmatic patients. The usage pattern as assessed in our study was in conformation to GINA guidelines. Various asthma education programs would benefit to improve knowledge and increase awareness regarding current asthma management paradigms in the medical community. Effective patient education measures and awareness campaigns in the community can also help in achieving better outcomes.

Figures

Figure 1: Spectrum of usage of various anti-asthma drug classes

Tables

Age Group (years)	Number of Patients	Male	Female
0-12	13 (3.5%)	7 (1.9%)	6 (1.6%)
13-20	49 (13.2%)	27 (7.3%)	22 (5.9%)
21-30	89 (24%)	56 (15.1%)	33 (8.9%)
31-40	77 (20.8%)	52 (14%)	25 (6.8%)
41-50	90 (24.3%)	86 (23.2%)	4 (1.08%)
51-60	34 (9.2%)	31 (8.3%)	3 (1.12%)
>60	18 (5%)	11 (2.9%)	7 (1.9%)
Total	370	270	100

Name of the drugs	Number of drugs	% of patients taking the drugs	% of total prescribed drugs
Anti-Asthma Drugs			
Budesonide	202	54.6	13.3
Formoterol	176	47.5	11.6
Inhalational Fluticasone	163	44	10.8
Montelukast	147	39.7	9.7
Salmeterol	135	36.5	8.9
Ipratropium	60	16.2	3.96
Inhalational Salbutamol	56	15.1	3.7
Tiotropium	36	9.7	2.4
Deflazacort	26	7.02	1.7
Doxophylline	14	3.8	0.9
Acebrophylline	8	2.2	0.53
Injection hydrocortisone	5	1.4	0.3
Beclomethasone	3	0.8	0.2
Other Drugs			
Levocetirizine	111	30	7.3
Levosolbutamol	62	16.8	4.1
Azithromycin	47	12.7	3.1
Mometasone nasal spray	38	10.3	2.5
Multivitamin	35	8.9	2.3
Moxifloxacin	30	8.1	1.98
Injection Pantoprazole	27	7.4	1.78
Injectable Ondansetron	22	5.9	1.45
Ceftriaxone	22	5.9	1.45
Oral Pantoprazole	15	4	1

Fexofenadine	11	2.9	0.72
Cefixime	11	2.9	0.72
Bromhexine	11	2.9	0.72
Cefpodoxime proxetil	8	2.2	0.53
Fluticasone Nasal Spray	7	1.9	0.5
Levofloxacin	6	1.62	0.4
Amoxicillin+Clavulanic acid Injection	5	1.4	0.3
Moist O2	5	1.4	0.3
Diethyl Carbamazine citrate	3	0.8	0.2
Cetirizine	3	0.8	0.2
Amoxicillin+Clavulanic acid Oral	2	0.5	0.2
Clarithromycin	1	0.3	0.07
Rabeprazole	1	0.3	0.07

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REFERENCES

1. World Health Organization. Information on Asthma. Accessed from <https://www.who.int/news-room/q-a-detail/asthma>. Accessed on April 21, 2020
2. Global Initiative for Asthma. A Pocket Guide for Health Professionals Updated 2019. Accessed from <https://ginasthma.org/wp-content/uploads/2019/04/GINA-2019-main-Pocket-Guide-wms.pdf>. Accessed on April 21, 2020
3. Storms WW. Unmet needs in the treatment of allergic asthma: potential role of novel biologic therapies. *J Manag Care Pharm*. 2003;9:534-43
4. Pitts SR, Niska RW, Xu J, Burt CW. National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary. *Natl Health Stat Report*. 2008;(7):1-38.
5. National List of essential Medicines (NLEM 2015). Accessed from <http://cdsco.nic.in/WriteReadData/NLEM-2015/NLEM,%202015.pdf>. Accessed on April 21, 2020
6. Dartnell J. Activities to improve hospital prescribing. *Aust Prescr* 2001;24:29-31
7. Siroux V, Pin I, Oryszczyn MP, Le Moual N, Kauffmann F. Relationships of active smoking to asthma and asthma severity in the EGEA study. *Epidemiological study on the Genetics and Environment of Asthma. Eur Respir J*. 2000;15(3):470-477.
8. Drummond N, Abdalla M, Beattie J, Buckingham J, Lindsay T, Osman L et al. Effectiveness of routine self monitoring of peak flow in patients with asthma. *BMJ*. 1994; 308: 564-567
9. Arumugam V, Kothiyal P, Juyal V, Pandey A, Tripathi P. Drug Utilization Assessment in Asthma Therapy through Prescription Monitoring at Dehradun Hospitals. *Indian J Allergy Asthma Immunol* 2008; 22(1): 15-18
10. Prasad A, Pradhan SP, Datta PP, Samajdar SS, Panda P. Drug prescription pattern for bronchial asthma in a tertiary-care hospital in Eastern India. *Natl J Physiol Pharm Pharmacol* 2015;5:263-266
11. Patel PD, Patel RK, Patel NJ. Analysis of prescription pattern and drug utilization in asthma therapy. *Int Res J Pharm* 2012;3:257-60
12. Pandey A, Tripathi P, Pandey RD. Prescription pattern in asthma therapy at Gorakhpur hospitals. *Lung India* 2010;27:8-10
13. Mandell LA et al: Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia. *Clin Infect Dis* 44(Suppl 2): S27, 2007
14. Srivastava R, Sharma S, Keshri L, Wal P. Assessment of prescription pattern in asthma therapy at Shamli hospitals. *Rev Recent Clin Trials*. 2012;7(2):158-166. doi:10.2174/157488712800100224
15. van Noord JA, Smeets JJ, Raaijmakers JA, Bommer AM, Maesen FP. Salmeterol versus formoterol in patients with moderately severe asthma: onset and duration of action. *Eur Respir J*. 1996;9(8):1684-1688. doi:10.1183/09031936.96.09081684
16. Vijaya Kumar S, Sasi Kala M, Mohamed Saleem TS, Gauthaman K. Drug Utilization and Prescription Monitoring of Asthma Patients. *Journal of Young Pharmacists*, 2009; 1(2):180-183