

RESEARCH ARTICLE

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Prescribing and Utilization Trends of Anti-Asthmatic Drugs amongst Children in a Tertiary Care Hospital in Lahore, Pakistan

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Received: 27 December 2016

Accepted: 20 February 2017

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Abstract

Objective: To describe and analyze the prevalent prescribing trends of anti-asthmatics drugs among 1-12 year old children in Lahore, a major city of Pakistan, is the objective of this study. In addition, the study attempts to determine the most prevalent type of asthma amongst the stated age group of subjects. **Method:** Drug utilization data was recorded from 100 prescriptions collected from Children Hospital, Model Town, Lahore, during the study period of December 2014 to December 2015. The study subjects were randomly selected with 18% falling in the age group of 0-4, 48% from the age group 4-8 and 34% falling in the age range of 8-12. There were 44% of female subjects and 56% of males. Combination therapy utilization was found in 99 patients while mono-therapy was employed in 1 subject. **Results:** The Study results reveal that the most common form of asthma prevalent in the study sample is intermittent asthma. The majority of the patients receiving therapeutic regimens have at least 3 drugs per prescription. An interesting aspect highlighted by the study is the practice of using trade names in prescribing drugs and its implications. Albuterol was prescribed in 34.90% of the subjects, followed Montelukast at 29.41%, flixitide occupied the third rank at 12.16% followed by Salmeterol + fluticasone combination at 7.84%, Clenil and loratidine occupied 5.49%, prednisolone 3.14%, and lastly Cetirizine at 1.18%.

Conclusion: Polypharmacy was practiced in all patients with the exception of one. We also found that therapeutic regimens were irrationally prescribed to children which could cause damage to their vital organs. Thus, intensifying the need of proper strategy development to ensure appropriate and efficient use of resources. Furthermore, continuing educational programs for the physicians and patients on rational drug prescribing and utilization are needed to pave way for positive patient outcomes.

Key words: Asthma, Children, drug utilization review, prescribing pattern, Pakistan.

INTRODUCTION

The respiratory disease, asthma, is best defined as a chronic disorder characterized by pulmonary airways inflammation coupled with hyper-reactivity of bronchial tract culminating in reversible airway obstruction.^[1] In child population, asthma constitutes a clinically complex syndrome. The delineation of the underlying mechanisms involved in the precipitation of asthmatic disorder has not been achieved so far.^[2] In accordance with a report published in 2013, WHO estimated that worldwide



253 million individuals had asthma which invariably accounts for at least 3.5% of the world wide population. The same report revealed that amongst children, asthma constitutes the most common non-communicable disease.^[3] Environmental coupled with genetic factors mediate a crucial role in development of the intricate risk structure demonstrated consistently by the disease. Meta-analysis studies conducted on individuals of multiple ethnicities has revealed five different susceptibility loci namely 17q21, IL1RL1, IL33, TSLP, and more recently a new loci has been identified which is referred to as PYHIN1. The former four susceptibility loci are associated with risk structure in American Europeans, Caribbean Africans, and in individuals of having a Latino ancestry. The latter susceptibility locus is responsible for mediating incidence risk in individuals possessing an African descent. Such results reveal that asthma, indeed, has susceptibility loci which demonstrate a practical robustness to ancestry differences when sample sizes investigated are sufficiently large and also that the intricate genetic framework of asthma is influenced by associations which show a specificity to ancestry.^[4] Factors that trigger an asthmatic episode are many such as strenuous exercise, certain viral infections, allergens, exposures that are associated with occupation and most importantly, airborne factors or irritants.^[5] The airway morphological changes that occur inevitably include changes like smooth muscle mass increase, fibrosis of the sub epithelial tissue, edema as well as damage is also observed in epithelial cells. An essential factor which not only initiates the inflammatory response but also serves to maintain is the recruitment as well as activation of eosinophils and subsequent release of cytokines.^[6] All morphological and pathophysiological changes initiated by the inflammatory response ultimately results in profound hyper-responsiveness of the airways.⁷ Asthma affects both small and large conducting airways. The airway morphological changes that occur inevitably include changes like smooth muscle mass increase, fibrosis of the sub epithelial tissue, edema as well as damage is also observed in epithelial cells. An essential factor which not only initiates the inflammatory response but also serves to maintain is the recruitment as well as activation of eosinophils and subsequent release of cytokines.^[7] *In vitro*, the smooth airway muscle cell proliferation and expression of metalloproteinase-9 matrix, involves the biological activity of Nerve growth factor. Thus, the factor mediates an integral role in the pathogenesis of asthma induced by an allergen.^[8] Across all age groups of patients, one of the most common problems encountered, regardless of disease type, is non-compliance or lack of adherence to the prescribed therapeutic regimen. The problem is particularly more pronounced in elderly patients.^[9]

According to British National formulary for children,^[10] mild to moderate asthma is treated by short term beta 2 agonist with a dose of 1 puff every 15-30 seconds and repeating the dose after every 10-20 minutes. Or oral prednisolone 1mg/kg OD for 3 days or longer if necessary. If the acute asthma is severe or life-threatening, administer high flow oxygen through face mask or nasal prongs and treat the patient with short acting beta 2 agonist ,i.e. salbutamol 2.5mg or terbutaline 5 mg or oral prednisolone is administered 1-2mg/kg OD for 3 days or longer if necessary. Chronic asthma in patients of 2-18 years of age is treated on the basis of a step-wise process^[10] according to which, therapy is initiated in step-I by administering occasional relief bronchodilators ,i.e. inhaled short-acting beta 2 agonist, Step II involves regular inhaled prophylactic therapy which is initiated in combination with a short acting beta 2 agonist, inhaled corticosteroids are also administered. If the patient is still not relieved, then there comes a step III involving administration OD inhaled corticosteroids with long acting beta 2 agonist. If this treatment is not effective then in the Step IV high dose inhaled corticosteroid is administered in addition to a regular bronchodilator. If the child is under 5 years, then therapy is initiated by using short acting beta2 agonist, if not relieved then regular dose of inhaled corticosteroid is also given with it. If still not managed then leukotriene receptor antagonist is administered along with it (add on therapy).

METHOD

The cross-sectional study was retrospective and concurrent conducted by collecting prescriptions from tertiary care children hospital Lahore. Necessary approval from hospital ethical committee was obtained for conducting the research. Study was also approved from university pharmacy department for necessary approval. The time span of the study is one year from December 2014 to December 2015. The data was collected from the general medicine ward. The patients added in the study were having problems related respiratory system and later prescribed anti-asthmatic drugs. Mostly data related to the paper is collected from the clinical notes, patients' data. The study evaluates the pattern of drug prescribing in tertiary care hospitals. Statistical analysis was performed using Microsoft Excel 2010. The data was entered into the software and analyzed and was presented with frequencies, percentages along with graphs and charts. *Inclusion Criteria:* Subjects with asthmatic symptoms falling in the age group of 1-12 years were included in the study. Premature babies with asthmatic symptoms were excluded. Healthy weight children were selected. *Exclusion Criteria:* Subjects with co-morbidities were excluded from the study.

Under weight or malnourished children were also excluded. The study was approved by Department of Pharmacy, Quaid-i- Azam University, Islamabad, Pakistan.

RESULTS

A total of 100 prescriptions for asthmatic patients were collected during the study according to a well characterized and defined inclusion exclusion criteria developed for data analysis. The study was conducted from December 2014 to December 2015 at children Hospital, model town, Lahore. The patients were divided into three groups on the basis of their age. Most of the pediatric patients suffering from asthma were found in the age group 4-8 years (Table 1). Analysis showed that, 56% of the patients were male while 44% were females. Out of 100 prescriptions, 68% of the patients were suffering from mild intermittent asthma, 29 % and 3% were suffering from mild persistent and moderate persistent asthma respectively.

| Age-wise distribution | | |
|-----------------------|-----------------|-------|
| Age in year | No. of patients | % age |
| 0 to 4 | 18 | 18% |
| 4 to 8 | 48 | 48% |
| 8 to 12 | 34 | 34% |
| Total | 100 | 100% |

The mean number of drugs per prescription is 3.19. The minimum and maximum number of drugs per prescription is 1 and 6 respectively. From the total subjects, 1% of the patients were treated with mono therapy while 99% of the patients were treated with anti-asthmatic drug combinations. The results showed that majority of the patients received multiple drug therapy. Among multiple drug therapy, three drug combination were mostly prescribed (44%) followed by two drug combinations (23%), four drug combination (22%) or five drug combination (8%) were prescribed. (Table 2). All drugs were prescribed by their Trade names. (Table 2a).

The overall utilization of anti-asthmatic drugs in asthmatic children were found to be beta 2 agonist (35.29%), leukotriene inhibitors (29.41%), corticosteroids (20.79%), corticosteroid plus beta 2 agonist (7.84%) and anti-histamines (6.67%). Among beta 2 agonists, Albuterol is most widely used in 34.9% of the patients which is a short acting beta 2 agonist. Among corticosteroids, Fluticasone is most widely used.

| Monotherapy | Combined | DETAILS |
|--|------------------|---------|
| PARAMETERS | | |
| Total number of prescription | | 100 |
| Total number of drugs prescribed | | 319 |
| Average drugs per prescription | | 3.19 |
| No. of anti-asthmatic drugs prescribed | Mono therapy | 1% |
| | Multiple therapy | 99% |
| No. of drugs (Anti-asthmatic+ others) | 2 Drugs | 23% |
| | 3 Drugs | 44% |
| | 4 Drugs | 22% |
| | 5 Drugs | 8% |
| | 6 Drugs | 2% |
| Encounter with Trade Names | | 100% |
| Encounter with Antibiotics | | 5.96% |

| | | |
|---|----------------|----------------|
| Concomitant Medication other than anti-asthmatics | Erythromycin | Cefixime |
| | Clarithromycin | Panadol |
| | Co-Amoxiclave | Ibuprofen |
| | Ciprofloxacin | Maltofer |
| | | Ca supplements |
| | | Multi-Vitamins |

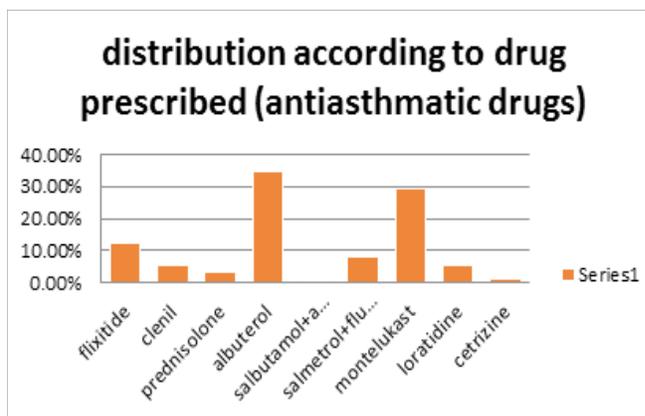


Figure 1: anti-asthmatic drugs distribution.

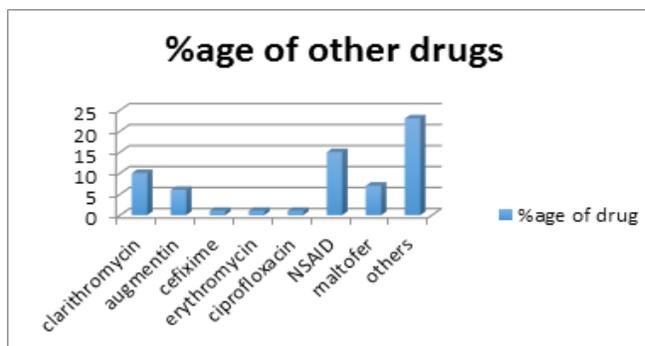


Figure 2: other than anti-asthmatic drugs distribution.

Among pediatrics, 57.64% were found to be prescribed with inhalers while 42.35% with oral medication. (Figure 3).

Distribution according to route (anti asthmatic drugs)

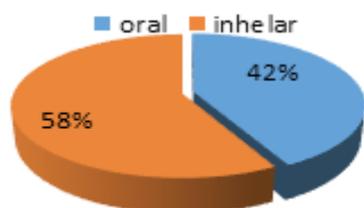


Figure 3: Distribution of Route of Administration (anti-asthmatic drugs).

While in other medication 95.31% were prescribed with oral medication, 3.13% with injectable and 1.56% with topical preparations.

DISCUSSION

Asthma is a disease of the inflammation of the airways and obstruction of the airways, including the intermittent symptoms of this disease are wheezing, chest tightness, cough and difficulty in breathing. It is a major health problem in recent times both in adults and children. In Pakistan 2 million of the population is patients of the asthma and 20 to 30 percent are children. It is a worldwide problem, 235 peoples were worldwide affected by this chronic disease with high rate of mortality and morbidity. Mortality rate can be increased up to 10 % within 10 years if urgent actions were not taken; the mortality rate is more in developing countries. There is no cure for this disease but the effective drug treatment is available which required a long time use of medicines. This study is aimed to check the prescribing trends among the children.

The present study was conducted on the 100 prescriptions of the pediatric patients. During analysis it was found that the asthma was reported in males (56%) in comparison to females (44%). Majority of the patients were suffering from mild intermittent (68%), mild persistent (29%) and (3%) with moderate persistent asthma. There was no patient with severe persistent symptoms. Prime prevention of this disease includes the detection of the environmental factors and potential allergens. Reduction of the exposure of the allergen and elimination of the patient from such environment leading to the reduction in the inflammation of the airways belongs to secondary prevention. To minimize the increasing prevalence of asthma we need to pay attention towards the indoor environment in which

they spent most of their time. The Average number of drugs per prescription in pediatric patients was found to be 3.19. Out of the total number of the patients in the study only 1% patient were treated by monotherapy and 99% of the patients were treated with the combined therapy. In another study of Yogesh *et al* 20% of the patients were receiving monotherapy and 80% treated with combined therapy. In yet another study of Shimpi *et al* were found patients receiving 24% monotherapy and 76% patient with combined therapy.^[11] A study was conducted in India, reported that 16% were on monotherapy and 84% on multidrug therapy.^[12]

Among asthmatic patients receiving multi drug therapy, three drug combination was mostly used (44%) than two drugs (23%) or four drugs (22%). All the drugs were prescribed by their trade names. Antibiotics (5.96%) were also used along with anti-asthmatic drugs. The overall use of the anti-asthmatic drugs in pediatric patients were found to be beta 2 agonist (35.29%),inhaled and oral corticosteroids (20.79%) and leukotrienes inhibitors (29.41%). Albuterol was the most commonly used inhaled beta 2 agonist and fluticasone was the most commonly used inhaled corticosteroid. Combination of the beta 2 agonist and corticosteroids was also used including salmeterol+ fluticasone. Our finding is also in agreement with study conducted by Kumar *et al.*^[13]

Our study found that in anti-asthmatic drugs 57.64% of the patients were prescribed with the inhaled medicaments and 42.35% were prescribed with the oral medicaments. In medications other than anti-asthmatic drugs 95.31% were prescribed with oral medications and 3.13% with injectable and 1.56% with topical preparations. Inhalational route is used commonly in asthmatic patients because this route ensures the local concentration of the drug in lungs with the low systemic effects. Most of the care givers of patients were aware of the drug schedule and inadequate knowledge about spacers and meter dose inhalers was found. Our study concern is to take some solid steps towards patient education for better prognosis. Patient education is also important for awareness about the use of medicine and management of asthma. In future, informative leaflets will be distributed among patients for better awareness. The first ever guideline about asthma was in mid-1980's when asthma became public health problem in most of the country. GINA guidelines were published in 1995 with the collaboration of the NHLBI and WHO. The recent addition of 2009 is an evidence based addition. Asthma guidelines were used to minimize the global burden of the asthma. According to GINA LABA bronchodilator with ICS is useful in the treatment of persistent asthma. GINA guidelines support

the use of LABA/ICS combination because inhaled LABA potentiate the effect of corticosteroid so dose of this is reduced and minimize the possible risks. LABA/ICS in a single inhaler improves the compliance of the patient and is used as maintenance medication. According to the GINA guidelines LABA is given always in combination with ICS but in different inhaler. In our study 7.84% were prescribed with LABA and ICS in fixed dose. Fixed dose combination of LABA and ICS is cost effective for the patients as compared to SABA and ICS combination in adjustable form.

Many studies reveal that combination of ICS and LABA is more beneficial for improving the lung function and symptoms. There were fewer withdrawals with combination therapy than the high dose corticosteroids. ICS and LABA therapy reduces the risk of hospitalization of asthmatic patients. The study about drug utilization can play an important role in helping the health care organization to interpret, understand and improve the use of anti-asthmatic drugs. Information from such study may help other hospitals to design different educational programs for the improvement of prescribing, use of drug and patient education.^[14, 15]

CONCLUSION

Prescribing trend of the prescription observed in this study showed high use of beta 2 agonist (35.29%) followed by leukotrienes inhibitors (29.41%), corticosteroids (20.79%), combination of corticosteroid+LABA (7.84%) and antihistamines (6.67%). In pediatric asthmatic patients, playing in dust was the most common environmental trigger for asthma coupled with respiratory illnesses possessing as an additional factor. Asthma symptoms among children worsen during night time. Among drugs short term beta 2 agonist is the class of drug to be prescribed more in pediatrics. Combination therapy is commonly prescribed to the entire study patients. We need to improve awareness level of the patients and prescribing with the trade names is the major concern in hospitals. Furthermore, awareness level needs to improve in every healthcare sector at provider levels in an effort to make mono-therapy as main stream practice. Evidence based practice and medicine incorporation in our health care system is vital for providing optimal care to the patients in an effort to not only yield positive patient outcomes but also to ensure that scarce therapeutic resources are efficiently and effectively utilized.

ACKNOWLEDGEMENT

We are grateful to Dr. Dawood Ahmad Hamdani, for sincere and valuable guidance and encouragement extended to us.

CONFLICT OF INTEREST

None

ABBREVIATIONS USED

WHO: World health organization; **NHLBI:** National Heart, Lung, and Blood Institute; **GINA:** Global initiative for asthma; **LABA:** Long acting beta agonist; **ICS:** Inhaled Corticosteroids; **SABA:** Short acting beta agonist.

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Cite this article as: Ahmed A, Tanveer M, Khan GM, Hanif K. Prescribing and Utilization Trends of Anti-Asthmatic Drugs amongst Children in a Tertiary Care Hospital in Lahore, Pakistan. 2017;3(2):70-5