PRESCRIBING TRENDS IN ASTHMA IN PEDIATRICS: A LONGITUDINAL, OBSERVATIONAL STUDY

AMANPREET KAUR[1], ARSHIYA SEHGAL[1], VIJAY K SEHGAL[1], HARJINDER SINGH[2]*

[1]Department of Pharmacology, Government Medical College and Rajindra Hospital, Patiala, Punjab, India. [2]Department of Pediatrics, Government Medical College and Rajindra Hospital, Patiala, Punjab. India. Email: harjinder427@yahoo.com

ABSTRACT

Objectives: In recent years, the prevalence of asthma has globally increased. Despite intensive treatment, many children with asthma are not achieving good symptom control. The present study aims to analyze the prescribing trends in pediatric asthma according to the World Health Organization (WHO) prescribing indicators.

Methods: This was an observational, longitudinal study conducted for the duration of 6 months with a sample size of 62. Children with age 1–14 years with asthma, who fulfilled the inclusion criteria, were enrolled after obtaining the written informed consent. Data were collected from outpatient department prescription slips for 2 times, one at 1st enrollment and the next after 1 month and changes in the prescription were noted. Peak expiratory flow rate (PEFR) was measured on both visits and the change in PEFR was noted.

Results: Male predominance was seen (67.74%) with age of 5–9 years (40.32%). Average number of drugs per prescription was 1.96. The most commonly prescribed anti-asthmatic drug was inhaled corticosteroids (ICS) (78.22%). Only 1.5% drugs were prescribed by generic names and 22.22% drugs from the essential drug list. Inhalational route (38.71%) was preferred over the oral route (20.97%). After 1 month of treatment, change in PEFR was found to be statistically significant.

Conclusion: The study concluded that average number of drugs per prescription and use of antibiotics was conforming to the WHO prescribing standards but prescribing from essential medicines list and by generic name need to be encouraged.

Keywords: Pediatrics, Asthma, Prescription.

INTRODUCTION

Asthma is a common chronic disease in children, striking a constant burden on the health system. In current years, the prevalence of asthma has increased globally in children and adolescents, particularly in low-middle income countries [1]. It is characterized by recurrent reversible airway obstruction in response to irritant stimuli that are too weak to affect non-asthmatic subjects [2]. According to the Global Asthma report 2018, the prevalence of asthma is <5% in the Indian subcontinent [3], yet it imposes a significant clinical burden in a state like Punjab due to increased environmental pollution, especially in months of April–May and October–November due to stubble (paddy remains) burning in the fields.

Inflammation of airways, reversible airway obstruction, and bronchial hyper-reactivity are the characteristic features of asthma. In asthma, prolonged, pathogenic inflammation, and abnormal repair of injured airway tissues can be stimulated as a result of immune response to common airway exposures (e.g., allergens, respiratory viruses, and air pollutants) in the susceptible host [4]. Lung dysfunction and airway remodeling may develop. These pathogenic processes unfavorably affect the growth and differentiation of airways in the growing lung during early life leading to altered airways at mature ages. Even though the cause of childhood asthma has not been determined clearly, a combination of environmental factors and inherent biological and genetic susceptibilities has been drawn in [5].

Diagnosis of asthma is mainly clinical which includes at least three reversible episodes of wheezing. Pulmonary function test with spirometer is the gold standard for diagnosis. There is a decrease peak expiratory flow rate (PEFR), decreased forced vital capacity, deceased forced expiratory volume (FEV1), and decreased forced expiratory flow (FEF) at 25–75% (FEF25→FEF75).

Asthma management is aimed at reducing airway inflammation and controlling comorbid conditions that can worsen asthma. The long-term goal of asthma management is the achievement of optimal asthma control.

Significant morbidity and mortality are caused by asthma worldwide and there is minimal improvement in vital outcomes over the last decade in spite of increasing treatment cost [6]. Studies have shown that management of asthma in children is short of goals because many physicians fail to adhere to asthma guidelines in diagnostic approach and treatment [7].

There is a scarcity of Indian data in the evaluation of prescription patterns in bronchial asthma. Hence, this study was designed to assess the prescription trends of bronchial asthma patients by the World Health Organization (WHO) Prescribing Indicators at a tertiary care hospital in Punjab and to determine the areas which require further research.

METHODS

Study design

This was an observational and longitudinal study with a follow-up of 1 month.

Study site

This study was outdoor patient department (OPD) of the Department of Paediatrics, Government Medical College and Rajindra Hospital, Patiala.

Study duration

This study was carried over a period of 6 months after the approval from the Institutional Ethics Committee and the Clinical trials registry-India.

Sample size

A total of 62 patients were enrolled.

Inclusion criteria

The following criteria were included in the study:
1. Children with age 1–14 years.
2. Presence of wheeze, with a history of more than 4 episodes of documented wheeze, or use of bronchodilators in preceding 12 months.

Exclusion criteria

The following criteria were excluded from the study:
1. Children having any other respiratory disease or with the alternative cause of recurrent wheezing.

Ethical approval

Prior approval from Institutional Ethics Committee and Clinical Trials registry-India with CTRI Number – CTRI/2019/10/021739 was obtained.

Study procedure and data collection

Patients attending the pediatrics outdoor department were screened according to inclusion/exclusion criteria. Patients eligible for the study were enrolled after explaining the aim of the study to the patients and parents of the patients. Written informed consent and assent were obtained from each patient/parent of the patient.

Data were collected in the form of OPD prescription slips 2 times, one at 1st enrollment of the patient and then after 1 month from the first enrollment, and by direct conversation with the patient and parents of the patient. Change in PEFR was checked with a peak flow meter.

PEFR

PEFR was recorded with peak flow meter, during 1st visit and after 1 month of treatment and difference was noted. During each visit, 3 readings of PEFR were taken and the maximum value was picked up. The same peak flow meter was used every time to minimize the error.

Statistical analysis

Descriptive analysis was done. IBM SPSS version 22 was used. Qualitative data were measured as frequency and percentage. Quantitative data were measured as mean, median, and standard deviation. Change in PEFR was evaluated with the Pearson Chi-square test. $p < 0.05$ was considered significant.

RESULTS

Out of a total of 62 children enrolled in the study, male patients (67.74%) were more than female patients (32.26%). Maximum patients (40.32%) were in age between 5 and 9 years, followed by 30.65% with age between 10 and 14 years. Mean age was 8.60 (3.37), as shown in Table1.

Prescriptions were analyzed according to WHO Prescribing indicators, as shown in Table 2. Average number of drugs prescribed per prescription was 1.96. Antibiotics were prescribed in 07 (11.79%) patients. Cefpodoxime was the most commonly prescribed antibiotic (8.06%) followed by cefixime and azithromycin (1.61% each). Injectables were not prescribed in any patient. Only 1.5% drugs were prescribed by generic name and 22.22% drugs were prescribed from the essential drug list.

The most commonly prescribed anti-asthmatic drugs were ICS such as fluticasone propionate (58.05%) and budesonide (20.17%). Long-acting beta-2 agonists (LABA) such as salmeterol (54.83%)

and formoterol (3.22%) were used in combination with fluticasone propionate. Leukotriene receptor antagonist (LTRA) like montelukast was prescribed in 47.58% children and short-acting beta-2 agonists (SABA) such as salbutamol (20.40%) and levosalbutamol (15.08%) were prescribed in 35.48% children. Oral steroids (OS) were prescribed in 4.48% children. The prescriptions of ICS, OS, LABA, and LTRA were increased on visit 2 (follow up after 1 month) but there was a decrease in the prescription of SABA on follow up as shown in Fig. 1.

Combinations therapy was used in 79.03% children. The most commonly prescribed fixed-dose combination (FDC) was that of ICS+LABA (Fluticasone propionate+Salmeterol) (54.83%) and Fluticasone+Formoterol (3.22%). Montelukast+Levocetirizine combination was used in 20.96% children, as shown in Table 3.

As shown in Fig. 2, 24.19% patients were treated with monotherapy and 75.80% patients with polytherapy (>one anti-asthmatic drug). Three drug therapy was most commonly used (35.48%) followed by two drug therapy (32.25%).

Most patients were prescribed with both oral and inhalational route (40.32%) followed by inhalational alone (38.71%) and oral alone (20.97%).

It was observed that mean PEFR in children of 0–5 years age group was 140 L/min, in 6–11 years, age group was 202.20 L/min and in 12–14 years was 277.37 L/min, and this difference was found to be statistically significant.

Table 1: Baseline characteristics of the study population

Characteristics	Patients (n)	Percentage
Gender		
Female	20	32.26
Male	42	67.74
Age (years)		
0–4	18	29.03
5–9	25	40.32
10–14	19	30.65
Total	62	100
Mean±SD	8.60±3.37	
Median	8.00	
Range	3–14	

Table 2: WHO prescribing indicators

S. No.	Name of the indicator	Result (%)	Optimal value (%)
1.	Average number of drugs per prescription	1.96	1.6–1.8
2.	Percentage of drugs prescribed by generic name	1.5	100
3.	Percentage of prescriptions with an antibiotic prescribed	11.79	20.0–26.8
4.	Percentage of prescriptions with an injection prescribed	0	13.4–24.1
5	Percentage of drugs prescribed from essential drug list	22.22	100

Table 3: Drugs used in combination therapy

Combination	Drugs	Patients	Percentage
ICS+LABA	Fluticasone+Salmeterol	34	54.83
	Fluticasone+Formoterol	02	3.22
LTRA+H$_1$ Receptor Antagonist	Montelukast+ Levocetirizine	13	20.96
Total		49	79.03

ICS: Inhaled corticosteroids, LABA: Long acting beta-2 agonists,
LTRA: Leukotriene receptor antagonist

This shows that in the age group of 0–5 years, girls have higher PEFR than boys, but in other age groups, boys have higher PEFR than girls, but the difference is statistically insignificant.

PEFR was measured on both visits and change in the value of PEFR was noted. Rise in PEFR was seen in 61.29% patients, fall in PEFR was seen in 25.81% patients, and there was no change in PEFR in 12.90% patients. Maximum rise in PEFR was seen in Age group of 12–14 years (68.42%) and maximum fall of PEFR was seen in 6–11 years age group (32%). Change in PEFR was found to be statistically significant in all age groups.

The PEFR was analyzed according to the treatment given in children. It was seen that ICS and SABA were associated with a rise in PEFR and OS, LABA and LTRA were associated with a decrease in PEFR. The observed change in PEFR with respect to drugs used was found to be statistically significant.

DISCUSSION

In this study, the population of male patients was more than females which were in accordance with a study done by Fuseini and Newcomb [8] which showed that boys have an increased prevalence of asthma compared to girls (11.9% vs. 7.5%, respectively). Another study conducted by Schatz and Camargo [9] also showed the male predominance over females in pediatric asthma.

Maximum patients were in the age group of 5–9 years. This was in accordance with a study conducted by Kamfar and Koshak [10], which showed that asthma prevalence and severity increase in children in school-going age.

ICS were most commonly used (fluticasone propionate more than budesonide). OS were used in 9.6% of patients which is in accordance with a study done by Gupta *et al.* [11], in which the use of systemic steroids was 8.5%. Long-acting beta-agonists were used in 58.06% patients (salmeterol>formoterol). Short-acting beta-agonists were used in 40.3% of patients (salbutamol>levosalbutamol) and LTRAs (montelukast) were used in 45.1% of patients.

Since patients with asthma require more than one drug for the control of symptoms, so combination therapy is required for treatment [12]. Fixed-dose combinations were used in 79.03% of patients. The most commonly prescribed combination therapy was seroflo inhaler which contains salmeterol and fluticasone propionate. The use of this FDC was in accordance with a study done by Friedman *et al.* [13], in which the ICS-LABA combination was used in 55% of patients. Another study done by Thomas *et al.* [14] reported that combination therapy with ICS-LABA therapy was prescribed for 7% of patients which was quite low as compared to this study. Monotherapy was given in 24.19% of patients which is slightly higher than the study done in Gorakhpur by Pandey *et al.* [15] (19%) but is lower than in a study done by Prasad *et al.* [16], in which all patients were prescribed with multiple drug therapy.

The most commonly prescribed route was the inhalational route which is contrary to a study done by Pandey *et al.* [15], which demonstrated that oral dosage form (56.3%) was preferred over inhalation (33.8%). Srivastava *et al.* [17] also reported that oral dosage forms like tablets (54.93%) were preferred over inhalation (31.69%).
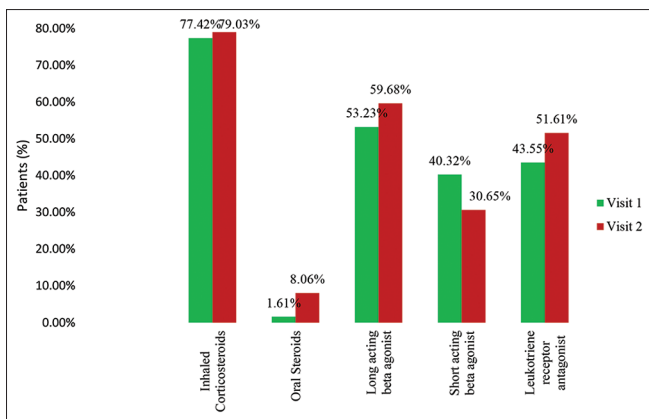

Fig. 1: Percentage of various groups of drugs prescribed in the study population during visit 1 and visit 2
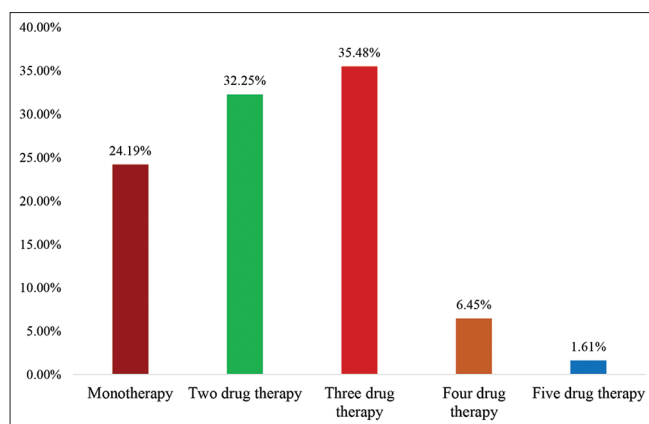

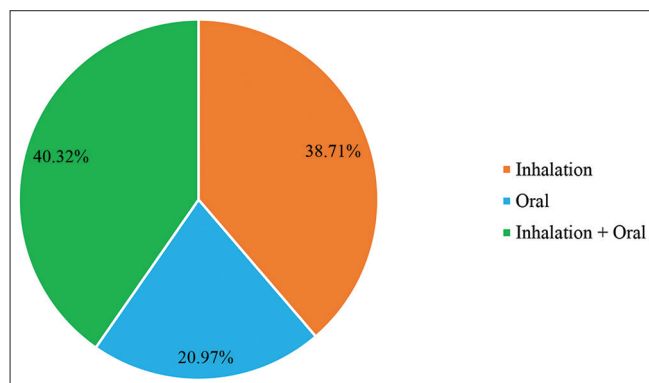**Fig. 2: Distribution of the study population prescribed with monotherapy and polytherapy**

Fig. 3: Routes of drug administration

Table 4: Mean and SD of PEFR according to age

Age group	Number of patients	Mean PEFR (L/min)	SD	F value	p value
0–5 years	18	140.00	23.70	57.948	0.001
6–11 years	25	202.20	34.64		
12–14 years	19	277.37	53.21		
Total	62	207.18	65.88		

PEFR: Peak expiratory flow rate, SD: Standard deviation

Table 5: Mean and SD of PEFR according to age and sex

Age group	Boys			Girls			t-test	p value
	Total	Mean PEFR	SD	Total	Mean PEFR	SD		
0–5 years	11	135.91	22.23	07	146.43	26.25	0.913	0.375
6–11 years	18	207.22	29.57	07	189.29	45.32	1.171	0.253
12–14 years	13	285.77	55.67	06	259.17	46.63	1.014	0.325
Total	42	212.86	68.40	20	195.25	60.16	0.983	0.329

PEFR: Peak expiratory flow rate, SD: Standard deviation

Table 6: Change in PEFR in different age groups of the study population

Age group (years)	Patients(Total) n (%)	PEFRIncreased (%)	PEFRDecreased (%)	PEFRNo change (%)	χ^2	p value
0–5	18 (29.03)	10 (55.56)	04 (22.22)	04 (22.22)	7.68	0.006
6–11	25 (40.32)	15 (60)	08 (32)	02 (8)	17.93	0.001
12–14	19 (30.65)	13 (68.42)	04 (21.05)	02 (10.53)	12.19	0.001
Total	62 (100)	38 (61.29)	16 (25.81)	08 (12.90)		

PEFR: Peak expiratory flow rate

Table 7: Change in PEFR according to various drugs used in the study population

Change in PEFR	Total (n)	Drugs used					χ^2	p value
		ICS (n %)	OS (%)	LABA (%)	SABA (%)	LTRA (%)		
Increased	38	29 (76.32)	01 (2.63)	20 (52.63)	12 (31.58)	21 (55.26)	4.39	0.036
Decreased	16	11 (68.75)	04 (25)	11 (68.75)	04 (25)	10 (62.50)	9.01	0.003
No Change	08	06 (75)	00 (0)	03 (37.50)	02 (25)	01 (12.50)	10.08	0.002

PEFR: Peak expiratory flow rate, ICS: Inhaled corticosteroids, OS: Oral steroids, LABA: Long-acting beta-2 agonists, SABA: Short-acting beta-2 agonists, LTRA: Leukotriene receptor antagonist

The WHO's prescribing indicators are a fast and effective means of assessing potential problems in drug use in healthcare settings [18]. The average number of drugs per prescription was 1.96, which was in accordance with the standard value (1.6–1.8) [19]. A higher value was reported by a study done by Michael *et al.* (5.95) and Aleemuddin *et al.* (13.25) [20,21].

The percentage of drugs prescribed by generic name in the present study was very less (1.5%) as compared to the standard value of 100%. A study done by Olurishe and Mohammed [22] observed that 45.5% of drugs were prescribed by generic name in asthma which was quite higher as compared to our study. However, it also indicates the availability of generic drugs in the hospital supply, which is often very erratic. The percentage of prescriptions with an antibiotic was 11.79% which is comparatively less than the study done by Lovinsky and Rastogi [23]. Injectable was not prescribed in any patient. The percentage of drugs prescribed from the essential drug list was 22.22% which is less as compared to the standard value of 100%. This also reflects the fact that free drug supply in the hospital pharmacy is short, as per EDL.

In the age group of 0–5 years, girls had higher PEFR than boys, but in other age groups (5–9 years, 10–14 years), boys had higher PEFR than girls, but the difference was statistically insignificant. A study conducted by Shiyas and Gopi [24] found that boys had significantly higher PEFR than girls in age 11 and 12 years, while in age 9 and 10 years, it was statistically insignificant.

CONCLUSION

Our study concluded that prescribing pattern of anti-asthmatic drugs in our setting does not completely conform to WHO prescribing indicators. The most commonly prescribed drug in children with asthma was ICS (fluticasone propionate). Combination therapy was preferred over monotherapy. The most commonly prescribed route was the inhalational route. Most drugs were prescribed by brand name, so we have not been able to achieve the prescribed standards in prescription with generic names and prescriptions from the essential drug list. The study underlines that there is scope for improvement in this field as a prescription by brand name increases the cost of the treatment and economic burden to the patient.

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