



Research Paper

PRESCRIBING PATTERN OF ANTI-ALLERGIC DRUGS IN PEDIATRIC CLINICS

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Growing industrialization and fast changing biodiversity coupled with sedentary lifestyles are causing a surge in allergic diseases like allergic rhinitis, asthma, conjunctivitis, atopic dermatitis, especially among pediatric population in the country, the World Allergy Organization (WAO) has warned. Variety of drugs like H₁ Antihistamines, corticosteroids, leukotriene antagonists and several other drugs are being prescribed as anti-allergic drugs to treat those allergic symptoms of children in India. A prospective observational study including only outpatients was carried out in different units of AMRI Hospitals, Kolkata and data of 514 patients were collected and analyzed. 53.1% were male patients 46.9% were female patients. The mean age of the patients was 3.63±3.19 years with range 0.02 - 14 years and the median age was 2.7 years. Total 662 numbers of drugs were prescribed among the study population out of which 42.4% was mostly prescribed H₁ Antihistamines and it was prescribed mostly for the age group 1-5 years. Fexofenadine (43.1%) was commonly prescribed H₁ Antihistamines. It was observed that different combinations of anti-allergic drugs were prescribed in which H₁ Antihistamines based regimen were prescribed in most cases and H₁ Antihistamines+Decongestant was commonest drug therapy. Prescriptions with H₁ Antihistamines were made mostly for upper respiratory allergic symptoms. Leukotriene antagonists were used for longer duration in most patients. Mostly H₁ Antihistamines had been widely prescribed as anti-allergic drug either as single or in combination for pediatric study population attending pediatric outpatient clinics and in certain cases H₁ antihistaminic drugs had often overused in combinations.

Keywords: Kolkata, Pediatric population, Anti-allergic, H₁ Antihistamines

INTRODUCTION

Allergies are among the most common chronic conditions worldwide. Allergy refers to an exaggerated reaction by our immune system in response to exposure to certain foreign

substances like dust, pollen grains, different foods and drugs. It is a hypersensitivity disorder of the immune system. In the early stages of allergy, a type I hypersensitivity reaction against an allergen encounters for the first time. Exposure to an

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allergen activates B cells to form IgE secreting plasma cells. These plasma cells are stimulated by TH2 cells, which are a type of T helper lymphocytes. This interaction stimulates the B cell to begin production of a large amount of a particular type of antibody known as IgE. Secreted IgE circulates in the blood and binds on the surface of other kinds of immune cells called mast cells and basophils, which are both involved in the acute inflammatory response (Janeway *et al.*, 2001). This process makes the mast cells ready to react the next time the allergen is encountered. If later exposure to the same allergen occurs, the allergen can bind to the IgE molecules held on the surface of the mast cells or basophils. Activated mast cells and basophils undergo a process called degranulation, during which they release histamine and other inflammatory chemical mediators from their granules into the surrounding tissue causing systemic effects. The mediators that are immediately released include histamine, tryptase, chymase, kinins, and heparin (Walls *et al.*, 2001; Haberal and Corel, 2003). The mast cells quickly synthesize other mediators, including leukotriene and prostaglandin D₂ (Iwasaki *et al.*, 2003; Cates *et al.*, 2003; Salib *et al.*, 2004). This is acute response. Histamine can cause airways to tighten (broncho constriction) such as in asthma or can cause blood vessels to become more permeable, leading to (edema) which causes hives/urticaria. Leukotriene can cause prolonged airway constriction and can also cause other immune cells to arrive and act. They can also cause too much mucus to be created which can be seen in allergic rhinitis. After the chemical mediators of the acute response subside, late-phase responses can often occur. In this phase, other cells become involved. Many of the

chemicals that mast cell release can be used to draw other cells of the immune system especially lymphocytes, neutrophils, eosinophils. This usually happens 4-6 h after initial contact with allergen. Cytokines from mast cells play a role in the persistence of long term effects. Late phase responses seen in asthma are slightly different from those seen in other allergic reactions, although they are still caused by the release of mediators from eosinophils and are still dependent on activity of T_H2 cells (Holt, 2007).

Different allergic conditions that affect children are respiratory allergies like allergic rhinitis and asthma. Tree, grass, dust mites, cat, dog and rodent tender cause respiratory allergies. Urticaria and atopic dermatitis are common skin allergies and triggered by skin contact with certain insects like cockroach, dust mites, certain foods. Allergic conjunctivitis mainly affects eye caused by pollen grains, dust mites. Treatments of allergies include avoiding known allergen and use of anti-allergic drugs. New technology approaches to decreasing IgE overproduction and regulating histamine release in allergic individuals have demonstrated statistically significant reduction on total nasal symptom scores. Antiallergic drugs used for children either alone or in combination with each other are:

H₁ Antihistamines like Chlorpheniramine and Cyproheptadine (1st Generation), cetirizine and loratadine (2nd generation), desloratadine (3rd generation), H₂ Antihistamines like ranitidine, famotidine only as adjuvant to H₁ Antihistamines, Topical nasal corticosteroids and Inhaled corticosteroids like beclomethasone, budesonide, mometasone, Fluticasone, etc., Leukotriene antagonists like montelukast, Zileuton, Adrenergic decongestants like xylometazoline, oxymetazoline,

phenylephrine, mast cell stabilizer like cromolyn sodium.

Irrational prescription of drugs for pediatric population is of common occurrence in clinical practice. The study of prescribing pattern is an important component of medical audit which helps in monitoring, evaluating and making necessary modifications in the prescribing practices to achieve a rational and cost effective medical care. The benefits obtained from H₁ Antihistamines and other antiallergic drugs often vary depending upon their usage pattern. Given the number of choices and wide availability of anti-allergics, choosing the right agent that will provide optimum effects with a least risk for adverse events is essential. Hence the present study was undertaken to evaluate the pattern of H₁-antihistamine and Other antiallergics usage for children in allergic reactions.

MATERIALS AND METHODS

This prospective observational study was carried out in the out-patient department of a tertiary care hospital. Data were collected from prescriptions of outdoor pediatric patients of Advanced Medical Research Institute, a tertiary care hospital located at Dhakuria and Mukundapur, Advanced Medical Research Institute Medical Centre located at Southern Avenue. 514 patients were studied during the study period commencing from July 2014 to March 2015. All pediatric patients under the age of 18 receiving anti-allergic drugs were included in the study and pediatric in patients of the same hospital and patients unwilling to participate in the study were excluded. Due to the observational nature of the study, formal consent form was waived by the Ethics Committee.

METHODOLOGY

1. Data were collected from the patients (by personal interviews and prescriptions) and then documented.
2. Patients' demographics— name, age and gender were recorded.
3. Patients receiving anti-allergic drugs were assessed for the types of drugs used for different allergic conditions.
4. Presenting Symptoms and prescribed dose, frequency and duration of anti-allergic drugs were assessed throughout the study.
5. A structured questionnaire was prepared to document all the information.

RESULTS AND DISCUSSION

The burden of allergic diseases in India has been on an uprising trend in terms of prevalence as well as severity. Growing industrialization and fast changing biodiversity coupled with sedentary lifestyles are causing this surge in allergic diseases, especially among children in the country, the World Allergy Organization (WAO) has warned. These allergic diseases comprise of asthma, rhinitis, anaphylaxis, allergic conjunctivitis, drug, food and insect allergy, eczema and urticaria and angioedema. Approximately 20% to 30% of total pediatric population suffers from at least one of these allergic diseases in India. Hence as the incident of allergic disorders is increasing day by day, the numbers of drugs and variability of drugs prescribed against those allergies are also increasing in India. The study was based in the eastern region of India and showed the prescribing pattern of antiallergic drugs and hope this study will be important for clinical, educational and economic purpose.

The study was based on data collection through structured questionnaire. It was mainly an observational study. Data collection process for this research project started in July 2014 and continued till March 2015. Data were analysed statistically with help of Epi Info (TM) 3.5.3. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC). During the study period 514 patients were included who were prescribed with anti-allergic drugs. The study population was children with 273 male patients and female patients. Test of proportion showed that proportion of males 273 (53.1%) was significantly higher than that of females 241 (46.9%) ($p=0.04$).

Table 1 shows age wise distribution of total study population. Mean age (mean $\pm$ S.D.) of the

Table 1: Age Wise Distribution of the Study Population		
AGE GROUP	NUMBER	%
< < 6 months	73	14.2%
6 months -1 Year	52	10.1%
1-5 Year	266	51.8%
5-10 Year	93	18.1%
10-15 Year	30	5.8%

patients was 3.63 ± 3.19 years with range 0.02 - 14 years and the median age was 2.7 years. Test of proportion showed that proportion of patients in the age group between 1-5 years (51.8%) was significantly higher than other groups ($p=0.0001$). The maximum number of patients who were prescribed with anti-allergic drugs belongs to the age group 1-5 years (51.8%).

Table 2: Age and Gender Distribution

Age group(in years)	Gender		Total
	Male	Female	
<6 month	34	39	73
Row %	46.6	53.4	100
Col %	15.2	14.9	15.1
6 months -1 Year	27	21	48
Row %	56.3	43.8	100
Col %	12.1	8	9.9
1 - 5 Year	109	141	250
Row %	43.6	56.4	100
Col %	48.9	53.8	51.5
5 - 10 Year	40	47	87
Row %	46	54	100
Col %	17.9	17.9	17.9
10 - 15 Year	13	14	27
Row %	48.1	51.9	100
Col %	5.8	5.3	5.6
TOTAL	223	262	485
Row %	46	54	100
Col %	100	100	100

From Table 2 it can be seen that there was no significant association between age and gender of the patients ($p=0.61$). Males and females are evenly distributed over age. It was obtained from Corrected Chi-square (χ^2) test statistically.

Table 3 shows that the total number of anti-allergic drugs prescribed (662) was more than the number of prescriptions (514) meaning that some prescriptions had more than a single anti-allergic prescribed. Out of 662 drugs, H_1 Antihistamines (42.4%) was used significantly higher than the other types of anti-allergic drugs followed by H_1 Antihistaminic+ Decongestant

combination (24.2%) ($p=0.0001$) which is in accordance with a study conducted by Morais-Almeida *et al.* (2014) which also stated that H_1 antihistaminic drugs are most commonly prescribed drugs for different allergic conditions in children.

From Table 4 it was found that fexofenadine (43.1%) was the most commonly prescribed H_1 antihistaminic drug followed by Cetirizine (41.3%). But no significant difference was found between them statistically ($p=0.66$). It can be compared to a study conducted Yogesh A Garje *et al.* where fexofenadine was most commonly prescribed H_1 antihistaminic drug.

Table 3: Distribution of Different Types of Anti-allergic Drugs Prescribed

ANTIALLERGIC DRUGS	NUMBER	%
H_1 Antihistamines	281	42.4
H_2 Antihistamines	1	0.2
H_1 Antihistaminic + Decongestant	160	24.2
Leukotriene Antagonists	93	14.0
Corticosteroids	83	12.5
Adrenergic Decongestants	37	5.6
H_1 Antihistaminic + Leukotriene Antagonist	6	0.9
Mast Cell Stabilizers	1	0.2

Table 4: Distribution of Different Types of H_1 Antihistamines

Type	Number	%
Cetirizine	116	41.3%
Fexofenadine	121	43.1%
Hydroxazine	12	4.3%
Ketotifen	9	3.2%
Loratadine	13	4.6%
Olopatadine	10	3.6%

Table 5: Routes of Administration of Different Types of H_1 Antihistamines Prescribed

Route	Number	%
Oral	271	96.4%
Topical	10	3.6%

Table 5 represents that the usage of oral H_1 antihistamines (96.4%) was more than other H_1 antihistamines prescribed for administration by different routes. Few H_1 antihistamines were prescribed by topical route (3.6%). This type of

trend in usage of H₁ antihistamines shows that in case of pediatric population oral formulations are more prescribed than other formulations though further studies are required to confirm if this type of trend in prescriptions are followed all over the world or not.

Table 6 shows the types of corticosteroids prescribed for different allergic symptoms and among them budesonide (45.8%) was the highest prescribed corticosteroids for the pediatric study population but statistically no significant difference was found between the usage of budesonide and fluticasone for the pediatric study population (p=0.31).

Table 6: Distribution of Different Types of Corticosteroids		
Types of Steroids	Number	%
Budesonide	38	45.80%
Fluticasone	31	37.30%
Mometasone	11	13.30%
Deflazacort	3	3.60%

From Table 7 it can be seen that the usage of inhaled corticosteroids (50.6%) was more than other corticosteroids prescribed for administration by different routes. Usage of topical corticosteroids was 45.8%. It also showed that the usage of oral corticosteroids was very less for the study population. This is the trend seen all over the world for pediatric population.

Table 7: Route of Administration of Different Types of Corticosteroids Prescribed		
Route	Number	%
Oral	3	3.6%
Topical	38	45.8%
Inhalation	42	50.6%

Table 8 shows that Xylometazoline (73%) was the most commonly prescribed adrenergic decongestant followed by Phenylephrine though few types of adrenergic decongestants were prescribed for the study population.

Table 8: Distribution of Different Types of Adrenergic Decongestants		
Adrenergic Decongestants	Number	%
Xylometazoline	27	73.0%
Phenylephrine	10	27.0%

From Table 9 the usage of different combinations of antiallergic drugs prescribed are seen in which H₁ antihistaminic based regimen was found predominant than other types of combinations. H₁D (H₁ antihistaminic+ Decongestant) combination was the commonest drug therapy used as 53.6% for the study population. Apart from that H₁antihistaminic+ corticosteroid combination had also been used as 13.6% followed by H₁ antihistaminic + leukotriene combination as 11.7%. It also showed that in certain cases two types H₁ antihistamines

Table 9: Combination of Different Anti-allergic Drugs Prescribed		
Types of Combinations	Number	%
H ₁ D	142	53.6%
H ₁ +CS	36	13.6%
H ₁ +L	31	11.7%
CS+L	12	4.6%
H ₁ +AD	9	3.4%
H ₁ +CS+L	9	3.4%
AD+H ₁ D	7	2.7%
H ₁ +H ₁ D	4	1.5%
H ₁ L	3	1.2%

Table 9 (Cont.)

Types of Combinations	Number	%
AD+L	2	.7%
H ₁ +AD+H ₁ D	2	.7%
L+H ₁ D	2	.7%
CS+H ₁ D	2	.7%
CS+H ₁ L	2	.7%
H ₁ +H ₁ L	1	.4%
H ₁ +H ₂	1	.4%

were prescribed simultaneously. This type of trend shows that H₁ antihistamines may have been overused in combinations though further studies are required to support the findings.

Table 10 shows the distribution of different antiallergic drugs according to age. It shows that for all the age groups mostly H₁ was used as compared to other drugs except the age group of below 6 months where use of combined H₁+Decongestant drugs is significantly higher than other drugs. Also H₁ was used for patients of the age group between 1-5 years which was significantly higher than other age groups. Corrected Chi-square (X^2) test showed that there was significant association between age and drug used [(p=0.014) S-Significant].

Table 11 shows the distribution of prescriptions made according to systems affected/symptoms. It shows that most of the antiallergic containing prescriptions were made for allergic symptoms

Table 10: Distribution of Different Antiallergic Drugs Prescribed According to Age

Age Group	H1 Anti histaminic	H2 Anti histaminic	Cortico steroids	Leukotriene Antagonists	Adrenergic Decongestant	Mast cell Stabilizers	H1 +Decogestant	H1 + Leukotriene
<6 month	5	0	4	0	8	0	31	0
6month-1 year	53	0	13	17	3	0	38	0
1-5 year	142	1	43	46	10	0	29	4
5-10 year	49	0	20	23	6	0	60	2
10-15 year	32	0	3	7	10	1	2	0
Total	281	1	83	93	37	1	160	6

Table 11: Distribution of Prescriptions Made According to Systems Affected / Symptoms

Systems Affected	Number	%
Dermatological	76	14.3%
Eye	13	2.4%
Lower respiratory	75	14.1%
Upper respiratory	368	69.2%
Total	532*	100.0%

Note: * 18 patients had more than one affected system.

related to upper respiratory tract 368 (69.2%) which means upper respiratory allergic symptoms are most common symptoms found in the study populations. it is significantly higher than others (p<0.0001). It may be due to increasing prevalence of allergic rhinitis and asthma in children in India (Kumar *et al.*, 2008; Pal, 2009).

Table 12 depicts that H₁ antihistaminic drugs were most commonly used drugs for all systems affected with allergic manifestations except in

Table 12: Usage of Antiallergic Drugs According to Systems Affected

Systems Affected	H1 Anti histaminic		H2 Anti histaminic		Cortico steroids		Leukotriene Antagonists		Adrenergic Decongestant		Mast cell Stabilizers		H1 +Decogestant		H1 + Leukotriene	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
D	51	18.1	1	100.0	22	26.5	3	3.2	0	0.0	0	0.0	7	4.4	0	0.0
E	13	4.6	0	0.0	0	0.0	0	0.0	0	0.0	1	100.0	0	0.0	0	0.0
UR	183	65.1	0	0.0	30	36.1	60	64.5	36	97.3	0	0.0	141	88.1	3	50.0
LR	34	12.1	0	0.0	31	37.3	30	32.2	1	2.7	0	0.0	12	7.5	3	50.0
Total	281	100.0	1	100.0	83	100.0	93	100.0	37	100.0	1	100.0	160	100.0	6	100.0

Note: Where D-Dermatological, E-eye, UR-Upper Respiratory, LR-Lower Respiratory.

Table 13: Distribution of Prescribed Duration of Different Antiallergic Drugs

Type of Antiallergic Drugs	Duration (In Days)		
	Mean $\pm$ S.D.	Median	Range
H ₁ Antihistaminic (n=281)	18.34 $\pm$ 29.34	7	2 – 180
H ₂ Antihistaminic (n=1)	7.00 $\pm$ 0.0	7	7
Corticosteroids (n=83)	63.24 $\pm$ 7.56	30	3 – 365
Adrenergic decongestant (n=37)	4.97 $\pm$ 2.19	5	3 – 10
leukotriene antagonist (n=93)	123.47 $\pm$ 77.63	90	7 – 365
Mast cell stabilizers (n=1)	7.00 $\pm$ 0.0	7	7
H ₁ Antihistaminic + Decongestant (n=160)	4.85 $\pm$ 1.79	5	2 – 14
H ₁ Antihistaminic + leukotriene antagonist (n=6)	45.00 $\pm$ 6.68	20	10 – 180

case of lower respiratory symptoms where corticosteroids (37.3%) were more than H₁antihistaminic (36.1%) in numbers. It also shows that no corticosteroid was used for allergic symptoms related to eye. S-Significant, Corrected Chi-square (X^2) test showed that there was significant association between usage of drugs and system affected of the patients ($p=0.000001$).

Table 13 shows that the duration of antiallergic drugs therapy was more with leukotriene antagonist (median-90) meaning that in case of

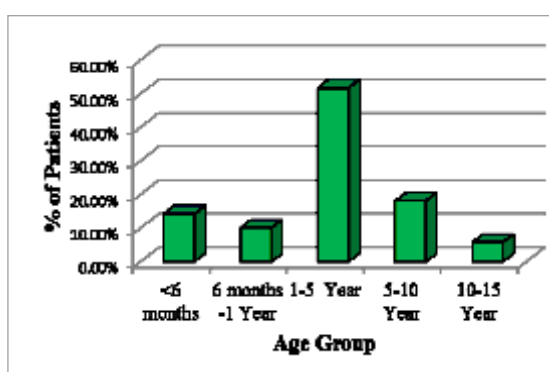
Figure 1: Graphical Representation Age Wise Distribution Of The Study Population

Figure 2: Graphical Representation of Age and Gender

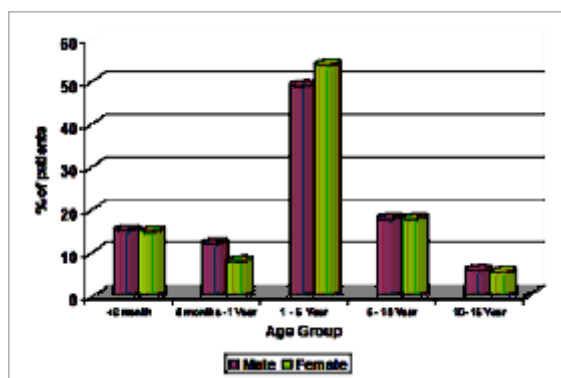


Figure 5: Graphical Representation Of Route Of Administration Of Different Types Of H1 Antihistamines Prescribed

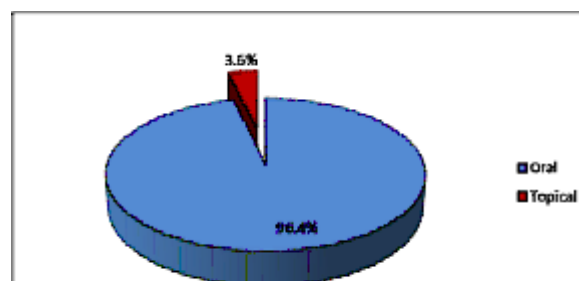


Figure 3: Graphical Representation Of Distribution Of Different Types Of Anti-allergic Drugs Prescribed

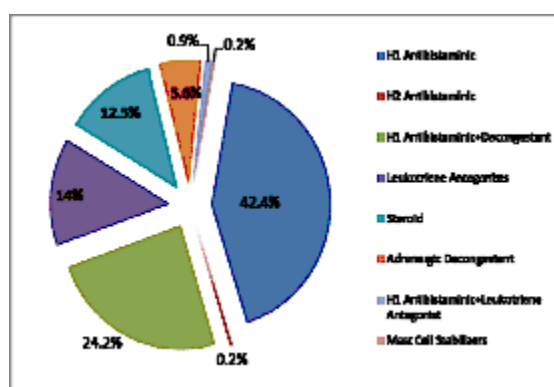


Figure 6: Graphical Representation Of Distribution Of Different Types Of Corticosteroids

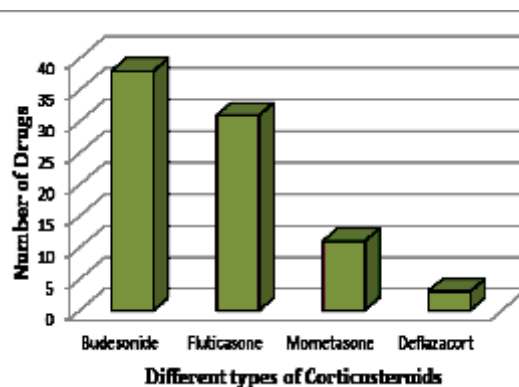


Figure 4: Graphical Representation of Distribution of Different Types of h1 Antihistaminic

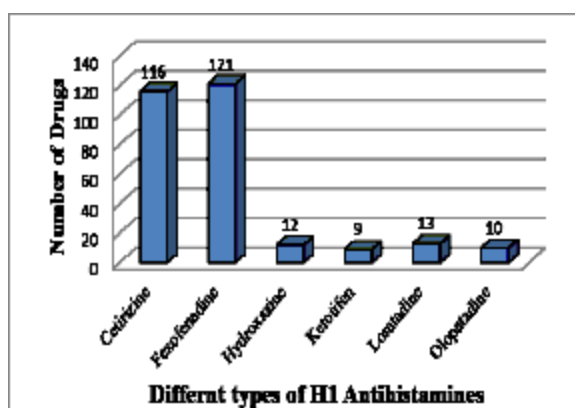


Figure 7: Graphical Representation Of Routes Of Administration Of Different Types Of Corticosteroids Prescribed

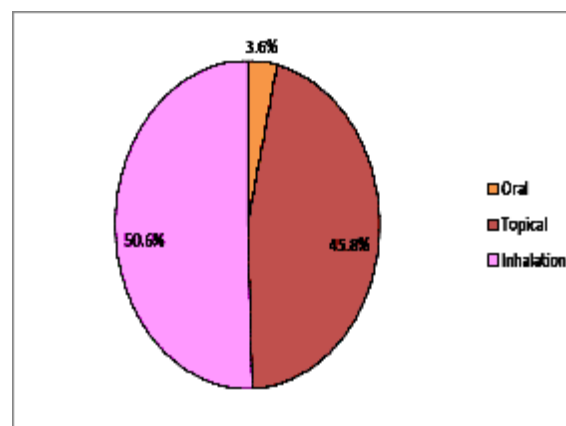


Figure 8: Graphical Representation Of Distribution Of Different Types Of Adrenergic Decongestants

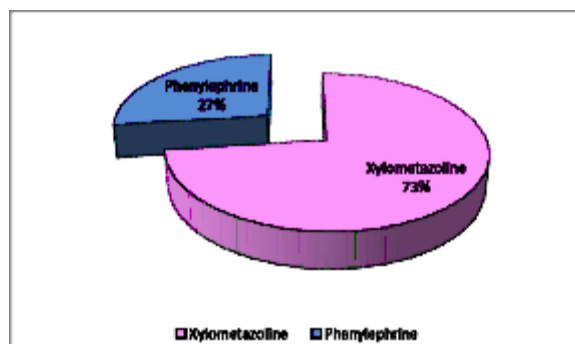


Figure 11: Graphical Representation Of Distribution Of Prescriptions Made According To Systems Affected / Symptoms

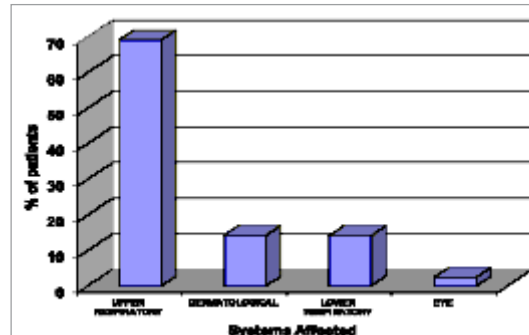


Figure 9: Graphical representation of combination of different antiallergic drugs prescribed

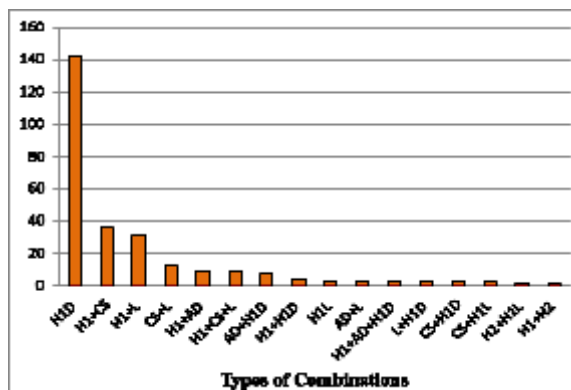


Figure 12: Graphical Representation Of Usage Of Antiallergic Drugs According To Systems Affected

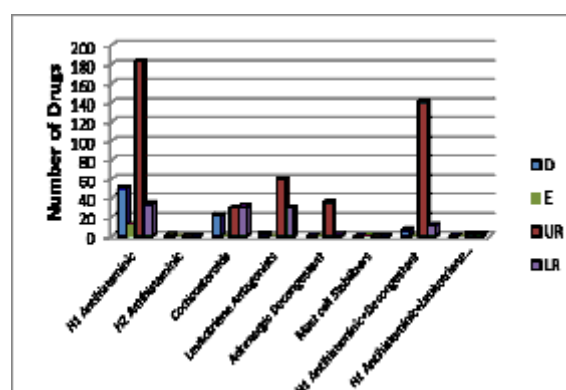


Figure 10: Graphical Representation Of Distribution Of Different Antiallergic Drugs Prescribed According To Age

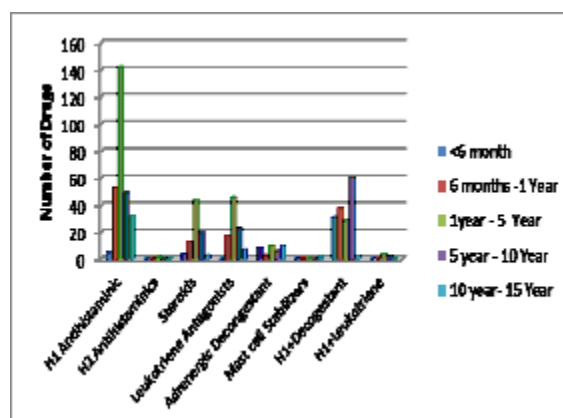
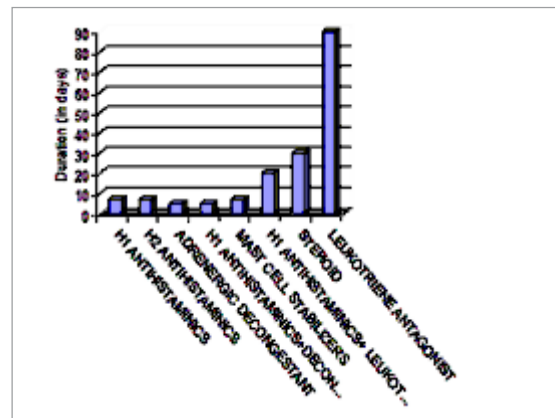


Figure 13: Graphical Representation Of Distribution Of Prescribed Duration Of Different Antiallergic Drugs Using Median



long term therapy with anti-allergic drugs, leukotriene antagonist was prescribed more. Statistically T-Test supported this result.

CONCLUSION

A prospective observational study was carried out in pediatric outpatient clinics of different units of a tertiary care hospital from July 2014 to March 2015. Salient observations were that male pediatric patients of the age group 1-5 years were exposed to anti-allergic drugs mostly for upper respiratory allergic symptoms. H₁ antihistamines were most commonly prescribed as anti-allergic drugs though several combinations of anti-allergic drugs were also prescribed and in few prescriptions two types of H₁ Antihistamines were prescribed simultaneously. Leukotriene receptor antagonists were used for longer duration of time. H₁ antihistamines were mostly prescribed by oral route. So, we can conclude that H₁ Antihistaminic drugs have been widely prescribed as anti-allergic drug either as single or in combination for pediatric study population attending pediatric outpatient clinics and in certain cases H₁ antihistaminic drugs have often overused in combinations. This study might help pediatrician to choose between different anti-allergic drugs for their pediatric patients presenting with allergic symptoms. This study will also help pharmaceutical companies to come up with newer antihistaminic agents with minimal side effects for common allergic symptoms for pediatric population.

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