

**ANTI-HISTAMINIC DRUGS UTILIZATION AMONG PAEDIATRIC POPULATION OF A SECONDARY CARE HOSPITAL IN ERNAKULAM DISTRICT OF KERALA, INDIA**Jeena Jacob<sup>a</sup>, Amratha K. Thomas<sup>a</sup>, Josteena J.<sup>a</sup> and Shaji George<sup>b\*</sup><sup>a</sup>Pharm d Intern, Nirmala College of Pharmacy Muvattupuzha, India.<sup>b</sup>Professor and Head, Department of Pharmacy Practice, Nirmala College of Pharmacy Muvattupuzha, India.**\*Corresponding Author: Shaji George**

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**ABSTRACT**

**Background and Objectives:** In paediatrics, first generation antihistaminic drug prescribing is a common practice for treating allergic conditions for many years. The aim of the study is to comprises the indications for use as well as safety and efficacy of newer antihistamines used in paediatric population. **Patients and Methods:** The study conducted was a prospective observational study on antihistamine utilization and carried out for a period of 6months in the department of paediatrics in a private hospital. The study involved, 100 paediatric patients with inclusion criteria of patients admitted in the department of pediatrics (under 12 years). **Results:** From the total sample of 100, about 60% receiving at least one antihistamine, out of which 81.6 % received first generation antihistamines and 38.3 % received multiple antihistamines. The total 6.6% showcased adverse drug reaction indicating need for pharmacist intervention. **Conclusion:** The study concluded by stating that the first-generation antihistamines were most commonly prescribed for paediatric population and the reason was its safe utilization for decades as well as their sedating property in patients with allergic rhinitis and urticaria.

**KEYWORDS:** Antihistamines, Paediatrics, Drug Utilization, Interventions, Indications, ADR.**1. INTRODUCTION**

Drug Utilization Evaluation is a systematic, ongoing and authorized quality improvement process, that is designed to review the drug usage, providing feedback of results to physician, developing appropriate standards and criteria for optimal use of drug and hence promote proper drug use by education and intervention.<sup>[1]</sup> H<sub>1</sub>-antihistamines are inverse agonists that combine with and stabilize the inactive conformation of H<sub>1</sub>-receptors and thus interfere with the actions of histamine at H<sub>1</sub>-receptor. Histamines resembles neurotransmitter and hence antagonism of histamine effects the state of awareness or arousal resulting in drowsiness.<sup>[2]</sup>

These drugs are widely used for the treatment of urticarial, allergic rhinitis, coughs, allergic conjunctivitis, insomnia and cold.<sup>[3]</sup> They can also be used as a second line treatment for anaphylaxis.<sup>[4]</sup> These drugs are classified in to two categories; Older referred as first-generation antihistamines and newer the 2<sup>nd</sup> generation antihistamine. First generation antihistamines, has been widely used clinically since 1940s and 50s. Their weak receptor selectivity and interaction with other biologically active aminereceptors, causes antiadrenergic, antimuscarinic and antiserotonin effects. They can readily penetrate the Blood-Brain-Barrier (BBB) and interfere with histamine neurotransmission of CNS-H<sub>1</sub> receptors and poten can lead to sedation,

somnolence, fatigue, drowsiness, thus, leading to impaired psychomotor performance, cognitive function and memory. Examples are; Diphenhydramine, Brompheniramine, hydroxyzine, chlorpheniramine, Phenergan.<sup>[3]</sup>

The introduction of second-generation antihistamines occurred in 1980s which brought a major advance in the development of antihistamine with minimal or non-sedating action and lesser penetration through the BBB. In addition, second generation antihistamines have greater selectivity for H<sub>1</sub>- receptor without any anticholinergic effects. Examples are; levocetirizine, loratadine, Fexofenadine.<sup>[3]</sup> Some of the second-generation antihistamines mostly used in European countries can result in signals of torsadogenic risk.<sup>[4]</sup> Both first- and second-generation antihistamines can cause Immediate-type hypersensitivity reactions such as angioedema and urticarial.<sup>[5]</sup> Antihistamines are available in different formulations for adults and children: tablets, liquids, creams, nasal sprays and eye drops. Generally, antihistamines are absorbed well following the administration of both liquid and solid formulations, reaching the maximum plasma concentrations below 1-4 hours after administration.<sup>[6]</sup>

Despite the WHO Guideline ARIA (Allergic Rhinitis and its impact on Asthma) guideline recommendations for

the utilization of second-generation antihistamines, first generation antihistamines are most widely used in both children and adults for the self-medication of various allergic symptoms.<sup>[7]</sup> The difficulties increase considerably to the drug development Research when paediatric age range is involved. The pharmacokinetic and pharmacodynamic properties of antihistamines can differ depending on the age. Multiple medication errors are seen in children since they vary in weight, body surface area and organ system maturity that can affect their metabolism and excretion.<sup>[10]</sup> These properties determine the safety and efficacy, particularly making it possible to predict the drug behavior in the body. Hence the utilization of any drugs in paediatric age groups should offer maximum guarantees of efficacy and must adhere the strict safety criteria without any side effects / Adverse drug reaction.

According to international medical statistics, almost two million antihistamine units were sold for paediatric use in Spain at 6 million euros during 2006 which implies the importance of this study in India, where there is no control over sale of any drugs.

The 1<sup>st</sup> generation antihistamines which does not have adequately safety studies in paediatrics, but are still widely used. While 2<sup>nd</sup> generation antihistamines are investigated for their efficacy and safety in paediatrics. Thus, it requires to understand the pharmacology, safety and efficacy for an ideal use in patients.<sup>[6]</sup>

Thus, the current study focuses on the antihistamine utilization trends in pediatric inpatients based on the scientific evidence available.

## 2. METHODS

A prospective observational study was performed to estimate the safety and efficacy of antihistamines among paediatric population. This study was conducted for a period of 6 months in a secondary care private hospital in Ernakulam district of Kerala after obtaining the prior approval of Hospital and a clearance from institutional Human ethics Committee.

All case records of paediatric patients admitted to the hospital were scrutinized for antihistamine utilization and all relevant demographic information along with treatment plan (class of drug, type of drug, dose, route, frequency, duration etc.), patient condition and day by day development, were recorded into a predesigned standard patient profile form.

### a. Inclusion criteria

- All patients admitted to the paediatric department irrespective of gender and disease.
- All patients having age below 12 years.

### b. Exclusion criteria

- All out patients.

## 3. RESULTS AND DISCUSSION

The study involved randomly selected 100 paediatric inpatients with 60% male dominance and 40% female (table 1). Age distribution indicated 10 % of total population were in between the age of 1 month to 1 year, 36 % between 1 year to 3 years, 29 % between 3 years to 5 years, 25% between 6 and 12 years (table 1).

Among the enrolled inpatients, 66% of the patients had respiratory problems, followed by 14% having gastrointestinal problems. The rest of the population were represented by 3% or less than 3% with diseases like CNS complaints, hematology disease, urinary system related problems, and 3% have dermal disease (table 1).

**Table 1: Demographic Details.**

Gender distribution		n = 100
Males		60%
Females		40%
Age Distribution		
Infants (1mon-1yr)		10 %
Toddlers (1yr-3yr)		36%
Pre-schoolers (3 yr-5 yr)		29%
School age (6-12 yrs)		25%
Classification based on diagnosis		
CNS system		3%
Respiratory System		66%
Hematology		3%
Urinary System		3%
G I System		14%
Dermal System		3%
Others		8%

The study also indicated, that a huge percentage (60%) of population is receiving antihistamine and the most commonly prescribed antihistamines are promethazine, phenylephrine hydrochloride, cetirizine, levocetirizine and fexofenadine. The antihistamine combinations commonly used are phenylephrine hydrochloride and chlorpheniramine maleate, levocetirizine, montelukast and pholcodine.

Among the 60% of the cases, on analyzing for antihistamine prescribing, it was found that, 61.7% of the paediatric inpatients were prescribed with single antihistamines, 33.3% with two antihistamines, 3.3% with three antihistamines and finally one patient corresponding to 1.7% was given four antihistamine (table 2).

In paediatrics, antihistamines were commonly prescribed for the patients with allergic rhinitis, chronic cough and urticaria. Though First-generation antihistamines are non-specific and lipophilic, they can induce central nervous system effects. The sedating effect of first-generation antihistamines are useful or desirable for nocturnal relief in atopic eczema and pruritis. The medicines and healthcare products Regulatory Agency in

the UK have advised that, first-generation antihistamines, should not be used in children under 6 years of age.<sup>[7]</sup> From the study it is found that for the treatment of allergic rhinitis, Promethazine is commonly prescribed. However Primary care as well as allergy textbooks recommends antihistamines as a first line therapy for allergic rhinitis. Cecil Text book of medicine states that avoiding allergens is to be considered as the primary therapy and if symptoms does not improve then only the antihistamines to be preferred.<sup>[8]</sup> Treatment with second-generation antihistamines or/ and intranasal steroids has been reduce the risk of emergency care.<sup>[7]</sup>

The study shows that 81.6% of paediatric inpatients are prescribed with first-generation antihistamines, whereas only 6.7% are prescribed with second generation antihistamines and 11.7% are prescribed with both first and second generation antihistamines(table5).

Although the common side effects of antihistamines are drowsiness, poor coordination, dry mouth, nausea, vomiting, and blurred vision, this study indicated an overall 6.6 % of the patients experienced some sort of side effects. The highest case experiencing side effect were drowsiness with 5% representation followed by constipation represented by 1.6% of the population under study (table 6).

**Table 2: No. of antihistamines prescribed (N = 60).**

S. No.	Cases With number of Antihistamines	Number	Percentage
1	One	37	61.7%
2	Two	20	33.3 %
3	Three	2	3.3%
4	Four	1	1.7%

**Table 3: Type of antihistamines (N = 60).**

S. No	Types	No. of Cases	Percentage
1	1 <sup>st</sup> generation antihistamines	49	81.6%
2	2 <sup>nd</sup> generation antihistamines	4	6.7%
3	Both 1 <sup>st</sup> and 2 <sup>nd</sup> generation antihistamines	7	11.7%

**Table 4: Side effects (N = 60).**

S. No	Side effects	No. of Cases	Percentage
1	drowsiness	3	5%
2	Constipation	1	1.6 %
3	Total	4	6.6 %

In a study published with a title “Risk of first-generation H1-antihistamines: a GA<sup>2</sup>LEN position paper” indicates the risk of first-generation antihistamines such as impaired learning ability and reducing working efficiency of pediatric population was stated as consequence. In this study, reports of serious or life-threatening ADR of promethazine in children is also stated which happened in US, and led to a boxed warning implemented in the year 2004 to the labeling of promethazine. The warning includes contraindication of using the drug in children below 2 years of age. The above study evaluated the antihistaminic use in both children and adults, while this study concentrates only on pediatric inpatients. Despite other studies, the current study evaluates the prescribing pattern and side effects of first-generation antihistamines as well as second generation antihistamines.<sup>[3]</sup>

One of the limitations of the study is that, the study was conducted in a small sample size, larger sample size can give a better outcome. In future, same study can be conducted with larger sample size, hence the researchers can utilize the study as a tool to carry out the same in large scale.<sup>[9]</sup>

#### 4. CONCLUSION

The study indicates a high usage of antihistamines among the paediatric inpatient (60%) with superior usage of first generation (82%) antihistamines, but the drawback was the use of multiple antihistamines in a single patient. The extensive use of primary antihistamines might be due to the availability of drugs for decades in market and well-established drug safety pattern and its effectiveness.

Hence prior to the treatment with any antihistamines, the child and family should be counseled on the appropriate use, dosing and frequency, possible side effects and expected clinical effects, especially when first generation antihistamines are commenced are used. Also, a regular drug audit can keep a check on physicians and thus can reduce the excess prescribing of antihistamines in paediatric population.

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#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

#### REFERENCES

1. G. Parthasarathy, Karin Nyfort-Hansen and Milap C Nahat. A Textbook of Clinical Pharmacy Practice: 2<sup>nd</sup> edition. Chennai: Orient longman private limited, 2004; 486-505.

2. Merk HF. Standard Treatment: The Role of Antihistamines. *Journal of Investigative Dermatology Symposium Proceedings*. Elsevier BV, 2001 Nov; 6(2): 153–6.
3. Church MK, Maurer M, Simons FE, Bindslev-Jensen C, Van Cauwenberge P, Bousquet J, Holgate ST, Zuberbier T. Risk of first-generation H1-antihistamines: a GA2LEN position paper. *Allergy*, 2010 Apr; 65(4): 459-66.
4. Poluzzi E, Raschi E, Godman B, Koci A, Moretti U, Kalaba M, et al. Pro-Arrhythmic Potential of Oral Antihistamines (H1): Combining Adverse Event Reports with Drug Utilization Data across Europe. Talkachova A, editor. *PLOS ONE* [Internet]. Public Library of Science (PLoS), 2015 Mar 18; 10(3): e0119551.
5. Rutkowski K, Li PH, Wagner A. The Paradox of Antihistamine Hypersensitivity. *The Journal of Allergy and Clinical Immunology: In Practice*. Elsevier BV, 2018 Jan; 6(1): 258–9.
6. Fitzsimons R, van der Poel L-A, Thornhill W, du Toit G, Shah N, Brough HA. Antihistamine use in children. *Archives of disease in childhood - Education & practice edition* [Internet]. *BMJ*, 2014 Aug 21; 100(3): 122–31.
7. Del Cuvillo A, Sastre J, Montoro J, Jáuregui I, Ferrer M, Dávila I, Bartra J, Mullol J, Valero A. Use of antihistamines in pediatrics. *J Investig Allergol ClinImmunol*, 2007 Jan 1; 17(Suppl 2): 28-40.
8. Stempel DA, Thomas M. Treatment of allergic rhinitis: an evidence-based evaluation of nasal corticosteroids versus nonsedating antihistamines. *The American journal of managed care*, 1998 Jan; 4(1): 89-96.
9. Patil N, Salimath P, Karimungi A, Gandage M, Clayton I, Krishnakiran K K. A Study on Drug Use Pattern Among Paediatric In-Patients at a Tertiary Care Hospital at Gulbarga. *Indian Journal of Pharmacy Practice* [Internet]. EManuscript Services, 2019 Feb 12; 12(1): 34–40.
10. Fernandez E, Perez R, Hernandez A, Tejada P, Arteta M, Ramos J. Factors and Mechanisms for Pharmacokinetic Differences between Pediatric Population and Adults. *Pharmaceutics* [Internet]. MDPI AG, 2011 Feb 7; 3(1): 53–72.