Pharmacovigilance Study of Antihistamines Containing Formulation in Patient

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Abstract: Antihistamines are medications used to treat allergies, allergic rhinitis, the common cold, influenza, and other conditions. Upper respiratory tract infections, followed by lower respiratory tract infections, rhinitis, asthma, allergic cough, non-specific dry cough, and others, were the most frequent illnesses for which cough and cold medications were recommended. Most viral causes of upper respiratory tract infections, the most common reason for coughing Coughing is a helpful physiological function that helps to remove excess fluids and foreign objects from the respiratory tract. Mast cells and basophils, which serve as histamine storage cells, produce it in cycloplamic granules. Antihistamines block histamine intestinal tract (GIT) uterus by combating histamine's stimulating effects on the smooth muscles of the GIT uterus and blood vessels. A total of 150 (77 Male and 73 Female). Headache was the most frequent ADR reported by patients using antihistamines in the current study. Understanding the relationship between a drug's adverse effects and the severity and preventability of the reported reactions is aided by ADR assessment.

Keywords: **Pharmacovigilance, Antihistamine, Mast cells, Histidine, Spo2, Piperoxam, Receptor, Etc.**

Introduction: Drugs called antihistamines are used to treat allergies, the common cold, influenza, and other allergic conditions. Antihistamines are a broad class of medications with the capacity to obstruct a range of histamine actions. Antihistamines are typically taken by humans as a cheap, generic (not patented), over-the-counter medication that relieves nasal congestion, sneezing, or hives brought on by pollen, dust mites, or animal allergies with little adverse effects [1]. Antihistamines are typically used as a short-term remedy. Chronic allergies raise the risk of illnesses that antihistamines may not be able to address, such as infection, sinusitis, and asthma. If you plan to use antihistamines for a longer period of time, you should speak with a doctor first [1]. Nasal congestion, rhinorrhea, sneezing, nasal itching, and other ocular symptoms (such as pruritus, lacrimation, and redness) are all signs of allergic rhinitis (AR), a chronic inflammatory condition of the nasal mucosa [2-3]. Upper respiratory tract infections, followed by lower respiratory tract infections, rhinitis, asthma, allergic cough, non-specific dry cough, and others, were the most frequent illnesses for which cough and cold medications were recommended. Most viral causes of upper respiratory tract infections, the most common reason for coughing Coughing is a helpful physiological function that helps to remove excess fluids and foreign objects from the respiratory tract. It is also one of the most typical symptoms for which individuals seek medical attention when it is extreme or unpleasant [1] Over 75% of ADRs occurred in children under 2 months of age, and 70% of ADRs were linked to pharmaceuticals operating on the central nervous system,

according to a review of 53 case reports of ADRs in breastfed newborns exposed to all types of medications18. Antihistamines were not mentioned in any of the case reports. One antihistamine (loratadine) and 16 systematic studies on ADRs in breastfed infants were assessed in a review, which found no ADRs. [4] Mothers reported ADRs in 85 cases in another investigation including breastfed infants. Eight of these worried infants received an antihistamine injection. All of these side effects, such as irritation and sleepiness, were deemed to be minimal and didn't necessitate medical treatment. [5]

The first antihistamines

The 1930s saw the beginning of the quest for chemicals that could counteract the harmful effects of histamine at the Pasteur Institute in Paris, where Bovet was working, as a result of the findings that histamine had a direct part in allergy and anaphylaxis. Given the similarities between histamine, acetylcholine, and epinephrine, he had access to Fourneau's compound library and, as he said in his Nobel lecture, "we looked for antagonism comparable to that exhibited by sympatholytic compounds towards epinephrine and by parasympatholytic compounds towards acetylcholine." Piperoxam (933F), an adrenolytic benzodioxan, was the first substance Ungar, Parrot, and Bovet identified as an antihistamine in 1937. It prevented histamine from having an effect on the guinea-pig ileum. Soon after, Bovet & Staub (1937) reported on structurally related aryl ethers such the thymol ether 929F, which shielded the guinea pig from the fatal effects of histamine-induced anaphylaxis. The latter molecule turned out to be too poisonous for therapeutic application, but the amino group's replacement of the ether oxygen resulted in the discovery of derivatives of aniline ethylene diamine. Bovet won the 1957 Nobel Prize for Physiology or Medicine for his research on antihistamines and curare. [6

Review of literature:

1.Mike E. Parsons, et. al. (2006) This article reviews the development in our knowledge of histamine's effects during the course of the 20th century. Histamine has been shown to serve a crucial physiological role in controlling the release of stomach acid as well as a pathologic role in a number of allergic diseases. As a result of the production of and pharmacological research on selective agonists and antagonists, histamine receptor antagonists have discovered a number of significant medicinal uses. There are four different types of histamine receptors. As a result, H1-receptor antagonists (commonly known as "the antihistamines") were created in the 1940s and are still useful for treating allergy illnesses like hay fever and rhinitis. [34].

2.Heber Anandan, et. al. (2009) Cough and cold treatments, in particular anti-histamine-containing syrups, are readily accessible on the Indian market even though the majority of them lack scientific evidence of their effectiveness in treating this common condition. The strictest safety guidelines must be followed when administering any medication to youngsters, and unnecessary challenges should not arise. Effects of providing children antihistamine-containing syrup for a cold or a cough have been examined. Resources and methods The researcher can quickly ascertain how an exposure has affected the outcome in a retrospective cohort study. 100 children in each group, ranging in age from 0 to 5, were gathered for this study. Results: Grunting, rapid breathing, and difficulties accepting things were more prevalent in children in the antihistamine group [35].

3.Joris C.VersterPhD, et. al. (2003) In a literature search (using MEDLINE and cross-references), the terms driving and antihistamine were entered. Sixteen studies that took the driving test on the road in regular traffic are included in the review. Studies included a positive control, used a placebo, and were double-blinded [36].

4.S. GOMEZ PEREZ, et. al. (2020) When first-generation antihistamines with sedative effects are used by patients 65 years of age and older, there is an increased risk of falls. There is currently no solid evidence to either confirm or deny this worry. This retrospective, non-interventional safety study's primary objective was to investigate any possible associations between first-generation antihistamine use and falls in patients younger than 65 [37].

5.Mike E Parsons, et. al. (2006) The development of our knowledge of the effects of histamine during the course of the 20th century is examined in this article. Histamine has been shown to have a pathophysiological impact on a number of allergic disorders and to have a critical physiological role in controlling the secretion of stomach acid. The creation of selective agonists and antagonists as well as pharmacological studies on these substances have allowed for the identification of four distinct types of histamine receptors, and histamine receptor antagonists have found wide-ranging applications in medicine. Due to this, H (1)-receptor antagonists (often referred to as "the antihistamines") were created and still play a crucial role in the treatment of allergic diseases like hay fever and rhinitis. In the late 1970s and early 1980s, the two authors were directly involved in the development of H(2)-receptor antagonists, which transformed the treatment of peptic ulcer and other illnesses brought on by gastric acid. H (3)-receptor antagonists have taken more time to discover a therapeutic use even though they have been accessible since 1987 [38].

6.Mauro Cataldi, et. al. (2014) It was possible to synthesise histamine, and this finding revolutionised pharmacological and immunological research. Since Sir Henry Dale and Patrick Laidlaw initially described some of histamine's physiological activities in vivo in 1910, it has been established that histamine plays a crucial role in the regulation of gastric acid output and in allergic diseases. Utilising selective agonists and antagonists as well as molecular biology techniques, four histamine receptors (H1R, H2R, H3R, and H4R) have been identified. Antihistamines (anti-H1R) were discovered by Daniel Bovet in 1957, and anti-H2R antagonists were discovered by Sir James Black in 1988, both of whom shared the Nobel Prize in Physiology or Medicine. Anti-H1R and anti-H2R histamine receptor antagonists, respectively, have changed the course of some allergy illnesses and ailments associated with gastric acid [39].

7.Yusuke Ohsawa, et. al. (2014) Histamine is a key player in the irritation and inflammation of the nervous system (AD) in allergic diseases such atopic dermatitis. It has been shown to regulate the expression of irritating factors in skin keratinocytes, such as semaphorin 3A and nerve growth factor (H1R), through the histamine H1 receptor. The amount of IL-31, a cytokine linked to the skin barrier and pruritus, was also lowered by H1R antagonist in chronic dermatitis lesions in NC/Nga mice and AD patients. Histamine plays a role in the emergence of allergic inflammation by activating eosinophils, mast cells, basophils, and Th2 cells through the histamine H4 receptor (H4R). Animals lacking H4R or given an H4R antagonist demonstrated a decrease in scratching behaviours. In addition to H1R, H4R is expressed on sensory neurons [40].

8.Hanna Köchling, et. al. (2017) Atopic dermatitis (AD) has responded well to initial clinical trials using histamine 4 receptor (H4R) antagonists. Histamine 1 receptor (H1R) antagonists are frequently employed in the treatment of Alzheimer's disease, despite the lack of evidence supporting their efficacy. Combining H1R and H4R blockade could have anti-inflammatory effects that work in concert [41].

9.Robin L Thurmond, et. al. (2017) The discovery of the histamine H4 receptor (H4R) provided a new avenue for investigation into the physiological effects of histamine as well as a new target for the development of antihistamines. The first step in this method was the finding of selective antagonists to gain a better understanding of the pharmacology of the H4R in comparison to other histamine receptors. The H4R's role in inflammation and pruritus was demonstrated thanks to the specific H4R antagonist JNJ 7777120, which was discovered. The substance was stopped from moving further in clinical studies due to a short in vivo half-life and hypoadrenocorticism toxicity in rats and dogs [42].

10. Anne B Chang, et. al. (2008) If a cough is not productive and there is no recognised aetiology or identified respiratory disease, it is classified as non-specific. In the practise of paediatrics, it happens regularly. One of the various medications used to treat these children is antihistamine. Additionally, antihistamines are suggested as a trial treatment for those with chronic cough [43].

11. Janice Garcia-Quiroz, et. al. (2011) One of the main causes of death worldwide, cancer patients have one of the highest mortality-to-incidence ratios. Even though there are now hundreds of anti-cancer drug trials being conducted, the majority of clinical trials for innovative medicinal treatments do not make it past Phase I. However, previously developed drugs with fresh anti-tumor characteristics present a practical and cost-effective cancer treatment option. Both healthy and malignant cells can proliferate more quickly when histamine is present. One anti-histamine drug that can slow the proliferation of cancer cells is astemizole. Astemizole has garnered a lot of interest since it also inhibits the potassium channel proteins ether à-go-go 1 (Eag1) and Eag-related gene (Erg), which are two important proteins involved in the growth of cancer. As a therapeutic target for a number of malignancies, Eag1 is also regarded as an important marker. [44].

12. Domenico Motola, et. al. (2017) Young children and newborns are routinely given H1-antihistamines to alleviate histamine-mediated symptoms brought on by a number of illnesses. Little is known about their safety profile in these patients. We conducted a comparison study of the safety profiles of H1-antihistamines (VigiBase) using data from the WHO database [45].

13. M A González, et. al. (1998) Particular H1 antihistamines are now the go-to therapy for the symptomatic alleviation of seasonal allergic rhinitis. First-generation antihistamines are tiny, lipophilic molecules associated with a variety of adverse effects due to their tendency to cross the blood-brain barrier and their cholinergic activity. Second-generation antihistamines have an advantage over first-generation antihistamines in that they are less lipophobic, which results in the absence of CNS and cholinergic side effects such drowsiness and dry mouth. In addition, its prolonged duration of action makes it possible for a more accommodating dosing schedule, which enhances patient compliance [46].

BIOSYNTHESIS OF HISTAMINE: [14- 31]

Mast cells and basophils, which are histamine's storage cells, produce it in cytoplasmic granules. It is created from the amino acid S-histidine, which occurs naturally, by the enzyme histidine decarboxylase, which is pyridoxal phosphate dependent.Imidazolylethylamine is what histamine is. Locally produced from the amino acid histidine, it degrades quickly by oxidation and methylation (Fig. 1). Histamine, which is positively charged, is maintained within intracellular granules of mast cells by an acidic protein and heparin, which is negatively charged. Histamine is liberated from the granules by an exchange between Na+ ions in etc. and histamine (Fig. 2) during exocytosis. Histamine release is inhibited by an increase in intracellular cAMP. Due to liver degradation of all histamine absorbed from the intestines, histamine is inert when consumed orally.

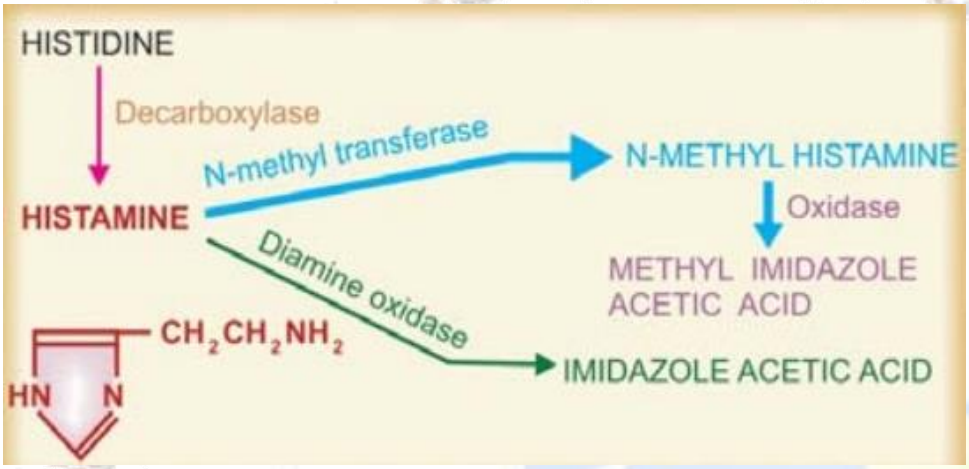


Fig.1 Synthesis and degradation of histamine

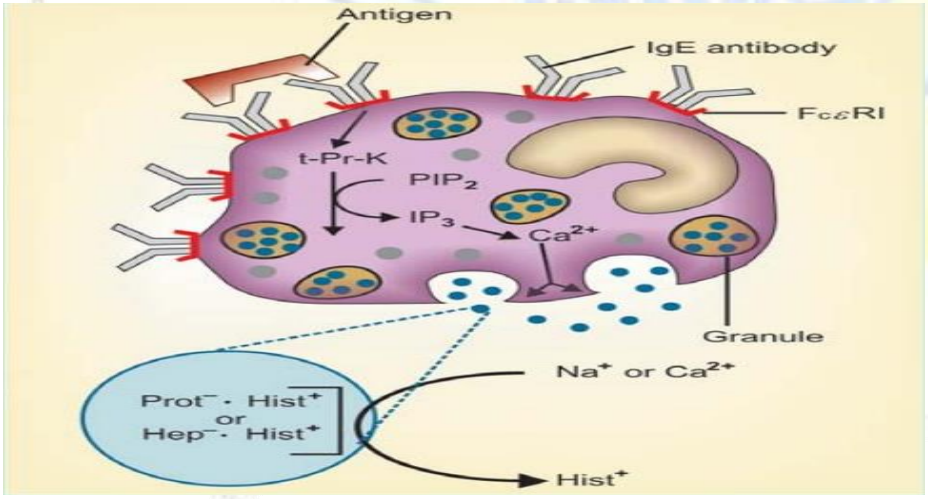


Fig.2 Mechanism of antigen-antibody reaction induced release induced increase of histamine from mast cell.

STEPS INVOLVED IN RELEASE OF HISTAMINE: [17]

Antigen + IgE antibody in mast cells.

↓

Activates tyrosine-protein kinase.

↓ Phosphotidyl inositol triphosphate

Inositol triphosphate

Phosphorylation and activation of phospholipase C

Triggers Ca^{2+}

↓

Granule contents were released as a result of the fusing of the granule membrane caused by Ca2+.

↓

Histamine is complexed with negatively charged protein and positively charged protein in granules. Extracellular Na+ causes cationic exchange, which releases histamine and causes it to act on target cells. [14]

Histamine Receptors: [18-19]

Histamine receptor belonging the family G-Protein coupled receptor

Receptor	**H1**	**H2**	**H3**	**H4**
Location	Brain GIT CVS Lymphocytes	Myocardial cells, parietal cells	cvs myentric plexus , gastric mucosa	spleen thymus, T-cells, eosinophil's

The Histamine H_1-receptor

The G-protein-coupled receptors (GPCRs) superfamily includes the histamine H1-receptor. GPCRs can be thought of as "cellular switches" that reside in an equilibrium between the active and inactive (or "off" and "on") states [7]. The equilibrium shifts to the "on" state in the case of the histamine H1-receptor because histamine cross-links sites on Trans membrane domains III and V to stabilise the receptor in its active conformation [8].

H1-antihistamines, which are physically unrelated to histamine, do not interfere with histamine's ability to bind to receptors; rather, they bind to various places on the receptor to have the opposite effect. To stabilise the receptor in the inactive state and shift the equilibrium to the "off" position, for instance, cetirizine cross connects sites on Trans membrane domains IV and VI [9].

It is typically stored in inactive bound state, from which it is released as a result of an antigen-antibody response started by various stimuli such venoms, poisons, protolytic enzyme, detergents, food ingredients, and a variety of chemicals. Histamine causes vasodilation, low blood pressure, and an increase in heart rate throughout the body. It also contracts smooth muscle in the lungs and digestive system. It also results in symptoms including sneezing, watery eyes, running nose, and itching. Histamine interacts with the very specialised H1 H2 and H3 receptors to carry out its biological function.

Historically: A medication that works on H1 and H2 receptors has been referred to as an antihistamine. Additionally, antihistaminic medications should ideally stop the formation or release of these acataconoids by obstructing basophils' and mast cells' sensitivity to particular antigens.

Histamine H2 receptors

The pharmacological effects of histamine were still being researched. Code and colleagues focused on histamine's stimulant effect on gastric acid secretion in particular, and they came to the conclusion that this action was not just a pharmacological phenomenon but also that histamine played a physiological role in regulating acid secretion. This conclusion was later confirmed some 16 years later with the discovery of histamine H2-receptor antagonists.

Despite being a powerful vasodilator, histamine's involvement in a number of peripheral circulation-related vasodilator events, such as immersion in cold water, has not been established. This was partly due to the unfavourable effects of the antihistamines in use at the time, before H2 receptors on the vasculature were discovered. It was also suggested that histaminergic nerves exist, but their activities would have to wait until the identification of histamine H3 receptors and the agonists and antagonists of these receptors[24].

Histamine H3 receptors

The central nervous system's (CNS) histaminergic neurones produce and release histamine, and histamine H3 receptors function as presynaptic autoreceptors that prevent this from happening. Additionally, they exist as hetero-receptors on nonhistaminergic neurones, controlling the release of several neurotransmitters in the CNS and peripheral areas, including 5-hydroxytryptamine, dopamine, acetylcholine, noradrenaline, and GABA [22].

Histamine H4 receptors

The mast cells and other immune system cells express the H4 receptor preferentially. Histamine causes the chemotaxis of, for instance, eosinophils and mast cells and is governed by the applicable Creative Commons Licence. See S132 M.E. Parsons & C.R. Ganellin Histamine and its receptors on Wiley Online Library for usage guidelines. It has also been found on basophils, dendritic cells, and lymphocyte T cells. It has been hypothesised that an H4-selective antagonist may be helpful in the treatment of asthma since it is believed that the H4 receptor, along with the H2 receptor, is involved in the regulation of IL-16 production from human cells. In certain forms of inflammation, antagonists, such as have also been reported to be beneficial. Many of the known H3 agonists and antagonists also bind to the H4 receptor, which shares significant homology

with the H3 receptor (58% for the Trans membrane sections but 34–35% overall). However, it appears that the receptor affinities vary significantly between species. The H4 receptors have just 65-70% homology with human, mouse, rat, and guinea-pig receptors, while the H3 receptor has more than 92% sequence identity [23].

Adverse reactions of histamine release: [31]

- Itching, Urticarial
- Flushing
- Hypotension
- Tachycardia
- Bronchospasm
- Angioedema
- Wakefulness
- Increased acidity

Anti-histamine drugs: [32]

1.Antihistamine are drugs that competitively blocks the H1creceptors.
2.Antihistamines antagonize the stimulant action of histamine on the smooth muscles of GIT uterus and blood vessel and inhibit histamine intestinal tract (GIT) uterus.
3.H1 receptors antagonist have been used clinically to treat various allergic rhinitis and chronic urticarial.

Histamine antagonist

drugs that prevent histamine from acting on the H1, H2, H3, and H4 receptors. The discovery of piperoxam sparked the creation of antihistamines.

1.The drug that inhibit the histamine release.
2.Drugs that inhibits the action of release histamine.
a) H1 antagonist (fist, second, third generation)
b) H2 antagonist
c) H3 antagonist
3.Drug having dual action.

First-generation H1-antihistamines

First-generation H1-antihistamines have poor receptor selectivity and frequently interact with the receptors of other biologically active amines, resulting in anti-muscarinic, anti-adrenergic, and antiserotonin effects. This is because they come from the same chemical source from which cholinergic muscarinic antagonists, tranquillizers, antipsychotics, and antihypertensive agents were also developed. However, their capacity to traverse the blood-brain barrier and obstruct histaminergic transmission may be their biggest shortcoming. The human brain's 64,000 histamine-producing neurons, which are found in the

tuberomamillary nucleus, are a key neuromediator. These neurones activate H1-receptors in the spinal cord, posterior pituitary, cerebellum, and all of the major brain regions [10]

Drugs: Tripelennamina, Diphenhydramine, Doxylamine, Cyclizine

Second-generation H1-antihistamines

Second-generation H1-antihistamines, which are little or completely nonsedating due to their restricted blood brain barrier penetration, were introduced in the 1980s, marking a significant advancement in the development of antihistamines. These medications don't have any anticholinergic effects and are also very selective for the histamine H1-receptor. Patients look for qualities in an H1-antihistamine such as good efficacy, a quick beginning of action, a long duration of action, and absence of side effects. Although pharmacokinetic and preclinical studies may be able to anticipate some of these characteristics, it is only in the clinical setting that they can be proven beyond a doubt [11].

Antihistamines of the second generation penetrate the blood-brain barrier substantially less than those of the first generation. Due to their concentrated impact on peripheral histamine receptors, they reduce sedative effects. Second-generation antihistamines can cause drowsiness when taken in larger quantities since they start to affect the central nervous system at high doses. Furthermore, some CNS-active medications including bupropion and benzodiazepines may interact with various second-generation antihistamines, most notably cetirizine.[31]

Drugs: Loratadine, Cetirizine, fexofenadine, Commonly Sodium. [25]

Third-generation H1-antihistamines

H1 antihistamines are particularly good at controlling rhinitis and urticaria, two common allergic diseases. First-generation H1 antihistamine side effects prompted researchers to look for substances that would be more efficient and better tolerated, leading to the development of second-generation H1 antihistamines. Even though they have a higher therapeutic index, some second generation H1 antihistamines have been linked to various side effects, most notably cardiotoxicity (terfenadine and astemizole). Other substances were created through further improvements, many of which were active metabolites. At this point, certain H1 antihistamines started to be referred to as "thirdgeneration" in the literature, which was discovered throughout the course of this review.

According to reports, the phrase "third-generation" arose on its own, without a clear definition or explanation of what it meant. This surely led to a great deal of uncertainty among general practitioners and specialists alike. In response to this reality, scientists and medical professionals who were not connected to the pharmaceutical industry formed the Consensus Group on New Generation Antihistamines (CONGA), which examined a number of crucial issues and made recommendations on the minimal requirements that would need to be met before H1 antihistamines could be reclassified and be referred to as a "new class or generation of H1 antihistamine".6 Below is a summary of some of the CONGA's primary suggestions.

Drugs: cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine. [26]

Mode of Action of Antihistamines:-

Histamine is released by mast cells and then binds to histaminergic receptors (H1, H2, and H3) to cause a cascade of events that are then used by second messenger systems to mediate the typical responses. G protein coupled histaminergic receptors are the kind. When phospholipase-C, which is connected to H1 receptors, is activated, inositol phosphate (Ip3) and diacylglycerol (DAG), respectively, are produced from phospholipids in the cell membrane.Ip3 induces the endoplasmic reticulum to release Ca2+ quickly. The protein kinase C is turned on by DAG. Together, the release of Ca2+ and protein kinase-C activates Ca2+/calmodulin-dependent protein kinase, phospholipase A2 antihistaminergic (H1- antagonist) binds to the H1 receptors and reduces the production of phospholipase-C; this, in turn, causes the activation of Ip3 and DAG, which subsequently blocks the characteristic signal. Histamine causes cAMP-dependent protein kinase, also known as cyclic AMP or 3'- 5'-cyclic adenosine monophosphate, to be produced on H2 receptors to cause a reaction in the gastrointestinal tract.The proton pump is activated by the H2 antagonist's reversible binding of the H2 recptors, which lowers the production of cAMP, which thus lowers gastric acid production in the GIT. In contrast to H1 and H2, H3 receptors decrease Ca2+ influx and are G-protein couple receptors. By reducing calcium influx into the cells in the central nervous system (CNS), H3 receptors serve as feedback inhibitors for histamine and other neurotransmitters. In the gastrointestinal tract (GIT), they limit gastrin release and down-regulate histamine through auto-regulatory effects. H3 receptor blockade counteracts these H3. [30-32-33]

H2-antihistamines

The body contains a large number of H2 receptors. H2-antihistamines reduce basal gastric secretions by acting as an antagonist at H2 receptors on parietal cells, which secrete acid in the gastric mucosa. They reduce vascular permeability, hypotension, flushing, headaches, and tachycardia by acting as an antagonist at H2 receptors on vascular smooth muscle cells, cardiac cells, and other cells. Additionally, they lessen the development of mucus, particularly in the airways. Adults in good health can experience the symptoms of anaphylaxis after receiving an intravenous infusion of histamine [12]. Vasodilation, a potential reduction in the amount of blood flowing through the body, hypotension, and distributive shock are the next steps after enhanced vascular permeability and vascular smooth muscle relaxation. It contributes to laryngeal edoema in the upper airway and smooth muscle contraction in the lower airways. Histamine-induced smooth muscle spasm, plasma extravasation, and glandular secretion in the gastrointestinal system can cause crampy abdominal pain, vomiting, and diarrhoea. [13]

Drugs: Ranitidine, famotidine, Cimetidine, and Etc. [27]

MODE OF ACTION OF H2 ANTIHISTAMINE:

- These medications prevent the generation of acid by reversibly competing with histamine and binding to the basolateral membrane of parietal cells' H2 receptor.
- Basal acid secretion is the H2 receptor antagonist's most important action. cAMP-dependent protein kinase is produced by histamine on the H2 receptor to cause the response in the digestive system.

• The H2 antagonist binds to the H2 receptors reversibly and inhibits the production of cAMP, which activates the proton pump and causes subsequent creation in the GIT. [28-29]

MECHANISM OF ACTION H2 ANTIHISTAMINE: [27]

• Histamine increases proton pump through the camp route by acting on H2 receptors, which causes the release of acid. These medications prevent histamine-mediated acid production by antagonisting the H2 receptor.

Ranitidine

⇩

Competitively block H2 receptors

⇩

Histamine cannot ACT

⇩

Decrease cAMP formation.

⇩

cAMP reduce acid secretion

⇩

Healing Of Ulcer

Adverse reaction of Antihistaminic drugs:

Due to their lack of H1 receptor specificity and anti-cholinergic effect, they are connected to the first generation H1 antihistamines. When the BBB is crossed, side effects from CNS depression result: [16]

- Sedation
- Dizziness
- Tinnitus (ringing in the ear)
- Blurred vision
- Insomnia
- Tremor
- Nausea/vomiting
- Dry mouth/dry cough.

• Since they don't cross the blood-brain barrier (BBB), more recent second generation H1 antihistamines are more selective for peripheral histamine receptors and have significantly less side effects.

- Drowsiness
- Fatigue

- Headache
- Nausea

Side effects of antihistamines that make you drowsy can include: [15]

- After taking these antihistamines, you may have sleepiness (drowsiness), decreased coordination, response time, and judgement. Do not drive or operate machinery.
- Dry mouth
- Blurred vision
- Difficulty peeing

Side effects of non-drowsy antihistamines can include:

- Headache
- Dry mouth
- Feeling sick
- Drowsiness-although this is less common than with older types of antihistamines.

SpO2: [21]

You may need to check SpO2 if you have study on ADR of antihistaminic drugs.

➢ **What is SpO2?**

SpO2, also referred to as oxygen saturation, is a measurement of the proportion of oxygen-carrying haemoglobin to non-oxygen-carrying haemoglobin in the blood. The blood must have a specific amount of oxygen for the body to function properly. In actuality, extremely low SpO2 values can cause quite severe symptoms. The medical term for this state is hypoxemia. The blue (cyan) colour the skin acquires causes a noticeable condition known as cyanosis. Low oxygen levels in the blood can develop into hypoxia, which is low oxygen levels in the tissue. It's crucial to comprehend this evolution and the differences between the two states.

➢ **How the Body Maintains Normal SpO2 levels**

To avoid hypoxia, normal oxygen saturation levels must be maintained. Fortunately, the body normally takes care of this on its own. Breathing is the body's primary means of preserving a healthy SpO2 level. When oxygen is inhaled, the lungs attach it to haemoglobin, which subsequently carries the oxygen throughout the body as the payload. The body requires more oxygen at higher elevations and during periods of intense physiological stress (such as while lifting heavy objects or sprinting). If the increases are not too drastic, the body can usually adjust to them.

➢ **Measuring SpO2**

The blood can be examined in a variety of ways to make sure its oxygen levels are normal. The most typical method is to measure the blood's SpO2 levels using a pulse oximeter. The usage of pulse oximeters is generally simple, and they are widely available in homes and healthcare settings. Despite being inexpensive, they are highly accurate.

Fig.3 Spo2 Pulse Oximeter

Aim:

Pharmacovigilance study of anti-Histamine containing formulation in patient.

Objectives:

1.To access the anti-histaminic drug related problem.

2.To identify factors influencing antihistaminic drug related problem.

3.To summarize the effects of antihistamine drugs.

4.To discuss some of drug interactions & common side effect of anti-histaminic drugs.

5.To discuss drug basic pharmacology.

Plan of work:

In our study regarding ADRs assessment due to anti-histaminic medications.

1.We perform retrospective study on 150 patients

2.We measure ADR frequency of the drug taken by patients.

3.We also monitor the SPO2 level of patient who will take the antihistaminic medications.

4.We collect patient history.

5. Following points will be carried out during research

- Literature survey
- Individual Case report form
- Hospital visit
- Collection of data.
- Compilation of all data.
- Analysis/Statistics of result of data.

Materials and methods:

Data have been collected from 150 patients in Maharashtra region; Medicure Hospital (Nashik), Apex hospital and Bhagwati hospital (Satana), Surana Hospital (Deola).Data have been collected by the help of questionnaire based survey on the basis of research we found adverse effect of Anti-histamine drugs in Patients.

ANTIHISTAMINE REPORT FORM

DIVINE COLLEGE OF PHARMACY, SATANA

Form No.	Date:

SITE DETAIL

Hospital Name:

Physician name:

PATIENT INFORMATION:

Patient name:		Age:
Sex:	Height:	Weight:

Allergic conditions : Mild / Moderate / Severe

SUSPECTED ADVERSE REATION:

Date of reaction started (dd/mm/yyyy):

Date of recovery (dd/mm/yyyy):

Adverse effect:

Stomach upset		Headache		Sore throat	
Drowsiness		Blurred vision		Post tussive vomiting	
Fast breathing		Difficulties in ingestion of food		Grunting	
Others:				SPO_2	

ADDICTIONS:

Alcohol		Tobacco		Smoking	
Relevant medical/ medication history:					

SUSPECTED MEDICATION:

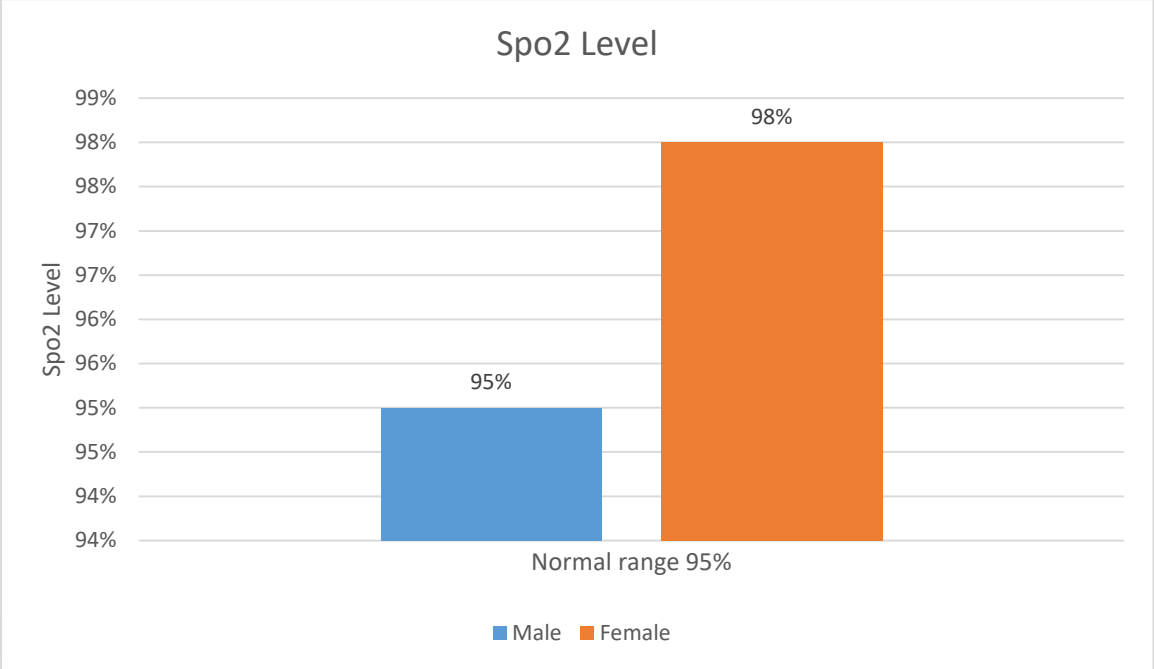
Sr.no.	Name (Brand/Generic)	Dose Used	Route used
1.			
2.			

Antihistaminic Medication:

Sr.No.	Drug/Brand Name	Picture
1.	Tab.Allegra 120 mg	
2.	Grilinctus Syrup 100 ml	
3.	Inj. Avil	
4.	Tab. Cetirizine	
5.	Cap. Benadryl	
6.	Tab.Ceknac Plus	

RESULT:

1) Age Paediatric Patient Spo2 Male or Female-:



2) ADR reported in Paediatric Patient 0-16-:

Sr.No.	Name of medications	ADR
1.	Tab.clarinex 10 mg	Tiredness, Stomach upset
2.	Tab.adliz-m	Headache
3.	Tab.Betnesol 0.5mg	Nausea
4.	Syp.Kufril Ls	Stomach upset
5.	Tab.Levocetrizine	Dark urine
6.	Tab.azithromycin	Headache
7.	Syp.Brozeet LS	Diarrhea
8.	Tab.Montair LC	Sleepiness

Number of ADR was found to be- 8.

3) Geriatric patient:

a) Male-:

Sr.No.	Medication	ADR
1.	Tab.Azithromycin	Sore throat
2.	Tab.Ofoxam O2	Skin rashes
3.	Tab.Tramadol	Stomach upset
4.	Tab.Zerodol SP	Diarrhoea
5.	Tab.Aceclofenac	Headache
6.	Tab.Tramadol	Drowsinss
7.	Tab.Doxylamine	Skin rashes
8.	Tab.Diclopam	Fast breathing
9.	Tab.Amoxyclo 625	Naussea
10.	Tab.Legen-C	Skin rashes
11.	Tab.Atrax 25	Constipation
12.	Tab.Leveta M	Dry mouth
13.	Tab.Defcort 6	Weight Gain
14.	Tab.Axid 250	Difficult in Breath
15.	Tab.Loratadine	Grunting
16.	Inj.Deladaryl	Redness

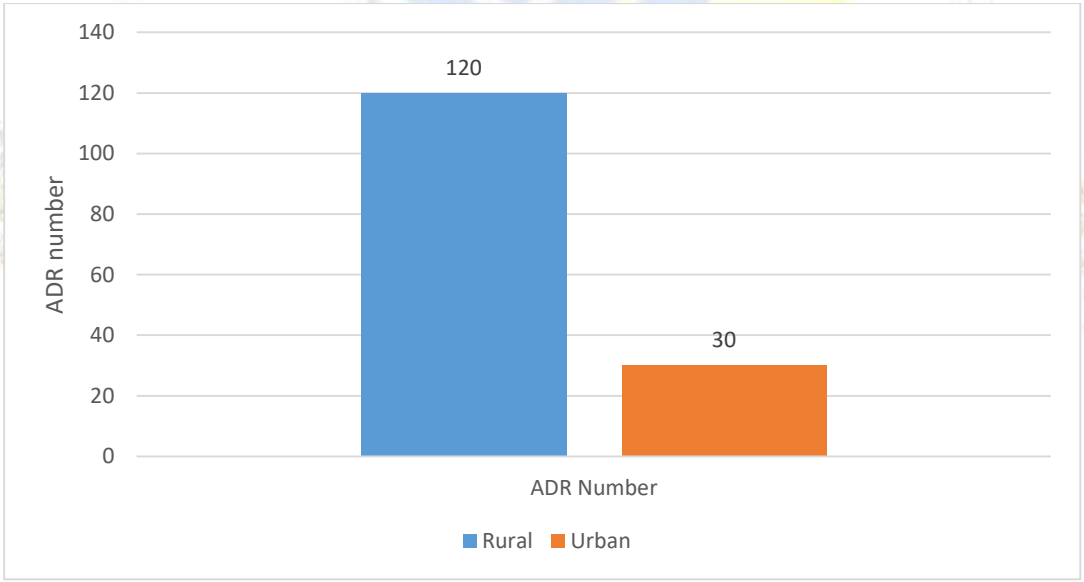
Number of ADR was found to be male is- 16

b) Female-:

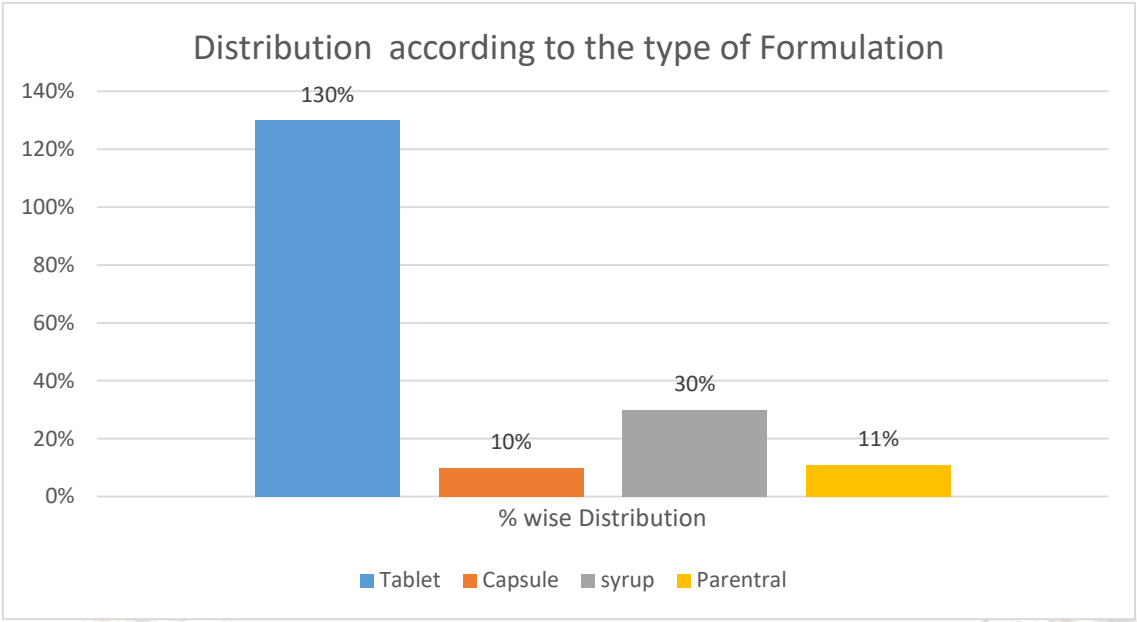
Sr.No	Medication	ADR
1.	Tab.Levocetrizine	Dark urine
2.	Syp.Grillinctus LS	Sleepiness
3.	Tab.Azithromycin	Sore throat
4.	Tab.Senofoputtin	Grunting
5.	Tab.Neuotel	Dry mouth
6.	Tab.Cetirizine	Headache
7.	Syp.Benadryl	Constipation
8	Tab.Allegra	Vomiting
9.	Tab.Claritin	Loss of appetite
10.	Tab.Telicast F	Dizziness
11.	Tab.Deflocort 6	Diarrhoea
12.	Tab.PRU-25	Stomach upset
13.	Syp.OZO Kuff-D	Blurred vision
14.	Inj.Avil	Drowsiness
15.	Tab.Nice	Acidity

Number of ADR was found to be in Female- 15.

4) Survey on Rural/Urban area-:



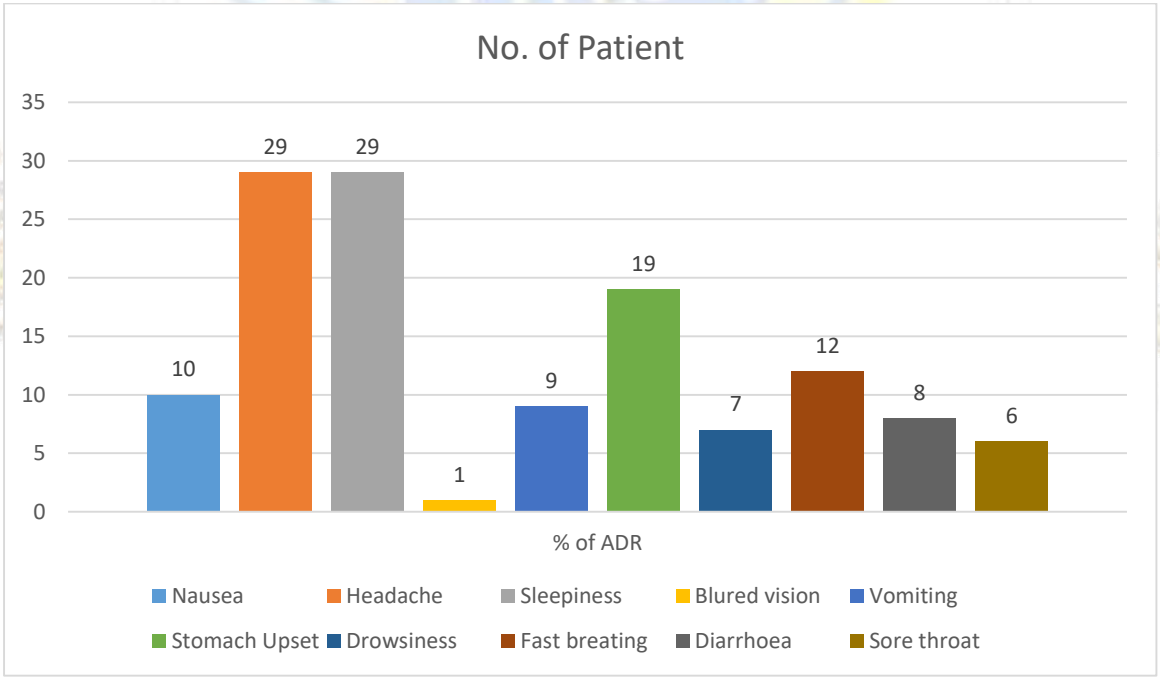
5) On the Basis survey report of ADR distribution according type of formulation-:



6) According to the route of IV/Oral:-

Sr.No.	Route Of Administration	No. of ADR
1.	IV	11
2.	ORAL	139

7) The ADR reported due to antihistamine Drug:-



Future prospect:

- This survey will be used when new antihistaminic drugs are studied in future.
- This survey is about the safety of drugs active surveillance is necessary.
- This pharmacovigilance survey must be able to describe which patients are at risk of developing an ADR.

• This survey is important for avoid the adverse drug reaction in future and implements effective in risk management plans ensure the safety of their marketed antihistaminic medicine.

Discussion:-

The present cross-sectional study established the adverse drug reaction profile and causality assessment of antihistamine drugs in the outpatient department of Medicine, Bhagwati Hospital, Samarth hospital & Apex Hospital Behind Bus Stand Satana Medicure hospital Dist. Nashik. A total of 150 (77 Male and 73 Female). In the current study Headache was the most commonly experienced ADR by the Antihistamine taking patients. Assessment of ADRs helps in understanding the relationship of drug and the adverse effect, severity and preventability of the reactions reported. This can gain confidence and improve adherence to the treatment given. Hence appropriate dose according to the patient's requirement and appropriate instructions by the treating physician can prevent the ADRs. During the study no serious adverse drug reactions was reported. Most of the ADRs were mild to moderate. Period of study for a longer period could have made the significance of study more powerful. Appropriate medication and effective monitoring of ADR is the best way to safeguard the public. In a country like India with varied socioeconomic status, it is important to have a vigilant pharmacovigilance programme. This can improve adherence to therapy and prolong the time for development of micro vascular and macro vascular complication thereby effectively reducing the morbidity.

A. Total no. of paediatric patient of Spo2 (Male & Female)

The total no. of paediatric patient was found 12. In which 7 male & 5 female.

B. ADR reporting in paediatric Patient

The total 9 of ADRs found in paediatric patient.

C. According to the Rural and Urban Area.

In 150 patients there was 120 patient found in rural area & 30 patient found in urban area.

Conclusion:-

The current work about pharmacolovigillance study that was carried out in several regions has provided baseline data about the prevalence of adverse drug reactions (ADRs) and their distribution across various age groups, administration routes, and therapeutic classes of medications.

• The results of the above study would be useful for the physicians in rational selection of drug therapy for treatment.

• various antihistamine medicines have higher number of ADRs

• When referencing antihistamine medications, two extremely typical ailments of many peoples are cough and cold medications. Many of which are widely available as OTC medicines, has no function to play and May become the cause of adverse effects.

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