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A critical review utilization of anti-histamine drugs under Prescription drug monitoring

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Abstract : **Prescription (Drug) Monitoring Programs (PMPs/PDMPs) proactively gather and examine data on the prescribing and dispensing of certain monitored pharmaceuticals. The main goals of PMPs of anti histamine drugs include "improving patient care and assisting in the safe use of controlled prescription drugs by monitoring outpatient prescription dispensing information, helping to reduce the harms resulting from the use of controlled prescription drugs, and helping to reduce the diversion of controlled prescription drugs." This report's objective is to provide a concise summary of the clinical research on PMP safety as well as research-based recommendations for using PMPs for harm minimization and medication adherence.**

Keywords: Antihistamines, cetirizine, chlorpheniramine maleate, diphenhydramine HCL, PDMP Prescription Drug Monitoring Program, promethazine

INTRODUCTION

Drug usage study was described by the World Health Organization (WHO) as "the marketing, distribution, prescription, and use of medications in a society, with particular focus on the consequent medical, social, and economic repercussions" in 1977. Drug use research's main goal is to encourage the people to take medications responsibly. For the specific patient, rational drug usage entails the prescription of a well-researched medication at the ideal dosage for the appropriate indication, with the relevant information, and at a reasonable cost. [1] International organizations like the World Health Organization and the International Network for the Rational Use of Drugs (INRUD) have worked hard to create common drug use indicators in order to reduce general drug use, especially in poor nations. We occasionally increase our performance thanks to these indications. Drug usage indicators are prescribed by the WHO for use in drug utilization investigations. In order to do this, the Anatomic Therapeutic Chemical (ATC) classification/Defined Daily Dosage (DDD) system must be used to identify the drug use patterns and monitor the drug use profiles. [2]

As it defines the volume, type, and drivers of drug exposure, drug consumption research is therefore a crucial component of pharmaco-epidemiology. The following features of drug usage and prescription are illuminated by drug utilization research and pharmaco-epidemiology together: Quality of usage: This is assessed by audits that contrast actual use with regional or local drug formularies or national prescription standards. Drug dosage (knowledge of inter-individual variations in dose requirements and age-dependence), drug choice (compliance with recommended assortment), drug cost (compliance with budgetary recommendations), knowledge of drug interactions and adverse drug reactions, and the percentage of patients who are aware of or unaware of the costs and benefits of the treatment are all examples of indicators of the quality of drug use.[3]

A research intended to objectively and qualitatively describe the population of users of a certain drug (or class of drugs) and/or the conditions of usage are therefore called a drug use study (for example, indications, duration of treatment, dosage, previous or associated treatments and compliance). Studies on drug usage might be quantitative or qualitative. To be able to infer medical and societal implications, it is necessary to collect quantitative data on the scope, variability, and costs of medication therapy. Studies on drug use may serve as the foundation for more qualitative research.[4]

In the US, remedy checking programs (PMPs) or doctor prescribed drug observing projects (PDMPs) are state-run programs which gather and convey information about the medicine and regulation of governmentally controlled substances and, as the singular states consider proper, other possibly habit-forming or abusable physician endorsed drugs. PMPs help to forestall antagonistic medication related occasions through narcotic excesses, drug redirection, and substance maltreatment by diminishing the sum as well as recurrence of narcotic recommending. [5-6]

Most US medical care laborers support PMPs, which mean to help doctors, doctor aides, nurture specialists, dental specialists and other prescribers, the drug specialists, scientific experts and care staff of apportioning foundations, as well as policing. The coordinated effort upholds the genuine clinical utilization of controlled substances while restricting their maltreatment and redirection. [7] Drug stores administering controlled substances and prescribers are commonly expected to enlist with their particular state PMPs and (for drug stores and suppliers who apportion controlled substances from their workplaces) to report the

allotment of such solutions to an electronic internet based data set. Albeit 49 states have executed PDMPs, little is had some significant awareness of these projects and their general adequacy.[8]

1.1 Histamine

Receptor is a monoamine with the compound equation C5H9N3. It is water dissolvable with two fundamental habitats, so goes about as an independently charged cation. Other comparable organic mono-and diamines incorporate adrenalin (C9H13NO3), noradrenalin (C8H11NO3) and serotonin (C10H12N2O). Receptor is orchestrated from histidine by means of the reactant protein l-histidine decarboxylase. Receptor is either put away in granules or on the other hand quickly utilized in three ways: by means of diamine oxidase, (DAO); by means of receptor - N-methyltransferase or through monoamine oxidase (MAO). The stomach and placenta have elevated degrees of DAO. Most receptor is produced and put away in pole cells and basophils, which gather and dwell at destinations of expected injury or disease -, for example, the nose, mouth, feet and the covering surfaces of the stomach, lungs and veins. Pole cells have huge ranges of receptors on their surfaces and can be enacted by a huge number of particles, including supplement. Non-pole cell receptor happens in enterochromaffin-like cells (ECL cells) tracked down in the stomach and stomach. In the cerebrum, receptor goes about as a synapse

1.1.1Mechanism of action of histamine 2, 3

There are two types of histamine receptors.

1. G-protein coupled receptors: - The second messenger systems adenylate cyclase (H2 receptors) and inositol phosphate are activated by histamine when it binds to the four subtypes of G-protein coupled histamine receptors, designated H1R through H4R. (H1 receptors). These cause phospholipase levels to rise and intracellular calcium (Ca2+) to build up).

2. Ligand gated chloride channel:- In the stomach and brain, histamine binds to ligand-gated chloride channels and inhibits post-synaptic potentials, which are the source of secretions like secretory diarrhea. **Table I** lists the histamine receptors and their functions.

Histamine receptor	Actions
H_1R • ubiquitously expressed in many organs, including lungs, blood vessels and mast cells, hepatic cells, epithelium	Regulates the maturation and activation of leucocytes and directs their migration to target sites, where they cause inflammation. Mediates many other types of immune functions – modulates the effect of monocytes, T cells, B cells, macrophages, dendritic cells and eosinophils. Causes Type 1 hypersensitivity reactions with • bronchoconstriction. • vasodilation with decreased blood pressure. • increased blood vessel permeability and local oedema – causes the initial, rapid onset of hypersensitivity symptoms. Mediates the cutaneous "triple response" and allergic skin reactions. Is involved in hyper-nociception of visceral and cutaneous pain; is especially associated with itch perception (sneezing-sensory stimulation mediated by histamine). Hypersecretion from glandular tissue.
H_2R • on ECL cells, lymphocytes also found on blood vessels, lungs and urinary bladder • widely present in the central nervous system – function uncertain	H_2Rs are the final common pathway for gastric acid secretion. Stimulates the production of cytokines from lymphocytes. Provokes the later and sustained drop in blood pressure associated with hypersensitivity reactions. Mediates chronotropic response of heart.
H_3R • exclusively in central nervous system	Important in maintaining the normal blood–brain barrier. Involved in regulation of • sleep-wakefulness cycle, • appetite and feeding, and • memory. Implicated in migraine and headaches. Acts as a neurotransmitter, modulating release of dopamine, acetylcholine, noradrenaline, GABA. Involved in modulation of nociception, itch sensation. Protects against convulsions, stress, dementia.
H_4R • preferentially expressed on various cells of the immune system and on mast cells, also present in epithelia, central nervous system	Involved in the activation of chemotaxis of eosinophils, mast cells, basophils and lymphocyte T cells; controls the release of IL-16 from lymphocytes. Implicated with H_1R in the progression and modulation of histamine mediated allergic diseases.

1.1.2 Pharmacology of drugs related to histamine [9]

Drugs that block histamine's actions at H1R and H2R are often utilized. H3R and H4R antagonists are not yet accessible in therapeutic settings.

First-generation H1 antihistamines

Instead of being called antagonists, H1R antagonists are really inverse agonists at the receptor and are referred to be antihistamines. Since the 1950s, they have been used to treat nausea and vomiting as well as psychosis, sleeplessness, and allergy problems. [10]

H1 antihistamine effects can be seen in a wide range of chemical compounds. Due to their low receptor selectivity, they interact with both acetylcholine (C7H16NO2) and -adrenergic receptors to generate anti-muscarinic and anti—adrenergic actions. The "first" generation of antihistamines were lipophilic and easily penetrated the blood-brain barrier, resulting in central nervous system adverse effects. These included tardive dyskinesia, akathisia, extrapyramidal symptoms, sleepiness, drowsiness, sedation, seizures, and neuroleptic malignant syndrome. Phenothiazine promethazine, sometimes known as "Phenergan," was first prescribed to treat psychosis. However, its antipsychotic efficacy is only around one-tenth that of chlorpromazine. There are now indications for usage for treating allergies, sedation, and motion sickness. Promethazine is not advised for usage in elderly people or children under the age of two due to the potential for respiratory depression. [11]

A typical topical and oral first-generation antihistamine used for allergies and sleeplessness is diphenhydramine (brand name: "Benadryl").

Anti cholinergic effects can be strong, much like with promethazine (dry mouth, increased heart rate, urinary retention, pupillary dilation). Diphenhydramine has the ability to block sodium channels, which gives it the ability to serve as a local anesthetic (and has been used as such in individuals who are allergic to the common local anesthetic). [12]

Second-generation H1 antihistamines12

To lessen the anti-cholinergic and sedative adverse effects of previous medications, second-generation antihistamines were created. They are employed in the management of allergic rhinitis, allergic conjunctivitis, urticaria, atopic eczema-related pruritis, insect bites, and angioedema. [13] Before they were withdrawn, older H1R antihistamines were linked to QT prolongation. In situations when anaphylaxis is predicted, H1R antihistamines can be given as a pretreatment together with H2R antagonists. The advantages of being more lipophobic and less likely to pass the blood-brain barrier include ketotifen (Zaditor), loratadine (Claritin), and cetirizine (Zyrtec). [14]

I. Methodology

In order to enhance the rational prescribing of antihistamines, the current review's goal is to identify antihistamines medication prescribing patterns. Both public and private websites, PubMed, the Web of Science, and newspapers are all searched for the review.

Selection and criteria method

Studies were chosen and citations were reviewed by one reviewer. In the initial round of screening, articles that could be pertinent were retrieved and their inclusion was judged based on their titles and abstracts. Based on the inclusion criteria shown in **Table 2**, the final full-text article selection was made.

Population	Patients receiving monitored drugs
Intervention	Electronic submission prescription monitoring programs (e.g., immediate, end-of-day, or weekly submission of prescription data to the database, or access to the database by clinicians for purposes of verifying patient prescription data)
Comparator	Q1: No prescription monitoring program; Standard of care; Other monitoring programs (such as: multiple copy paper prescriptions, hotlines, telefacsimile alerts, etc.)
Outcomes	Q1: Safety (such as: unintended patient consequences, unintended redirection of patient to illicit sources, inadequate therapeutic management [e.g., therapy discontinued without taper, delayed or missed doses, etc], street diversion, dispensing errors, etc.) Q2: Guidelines on appropriate use.
Study Designs	Q1: Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, nonrandomized studies Q2: Evidence-based guidelines

A pilot research was carried out at PUHC with the Chief Medical Officer's prior approval to gather data from patients using a chance random approach. Between November 2005 and April 2006, 500 patients were observed in the OPD between the hours of 9.00 am and 12.30 pm (morning session) and 5.00 pm and 6:00 pm (evening session). In the study, only prescriptions for antihistamines were included. The research did not include patients with incomplete prescriptions or non-responding individuals. [15]

According to the study, the majority of prescriptions included the patient's name (500, 100%), age (394, 78.8%), and sex (500, 100%). The majority of the patients (174, 34.8%) were between the ages of 21 and 40. fig. 1. Furthermore, according to demographic information, out of the 500 patients, 293 (58.6%) were men and 207 (41.4%) were women. Most prescriptions (415, 65.14%) provided a provisional illness diagnosis. [15]

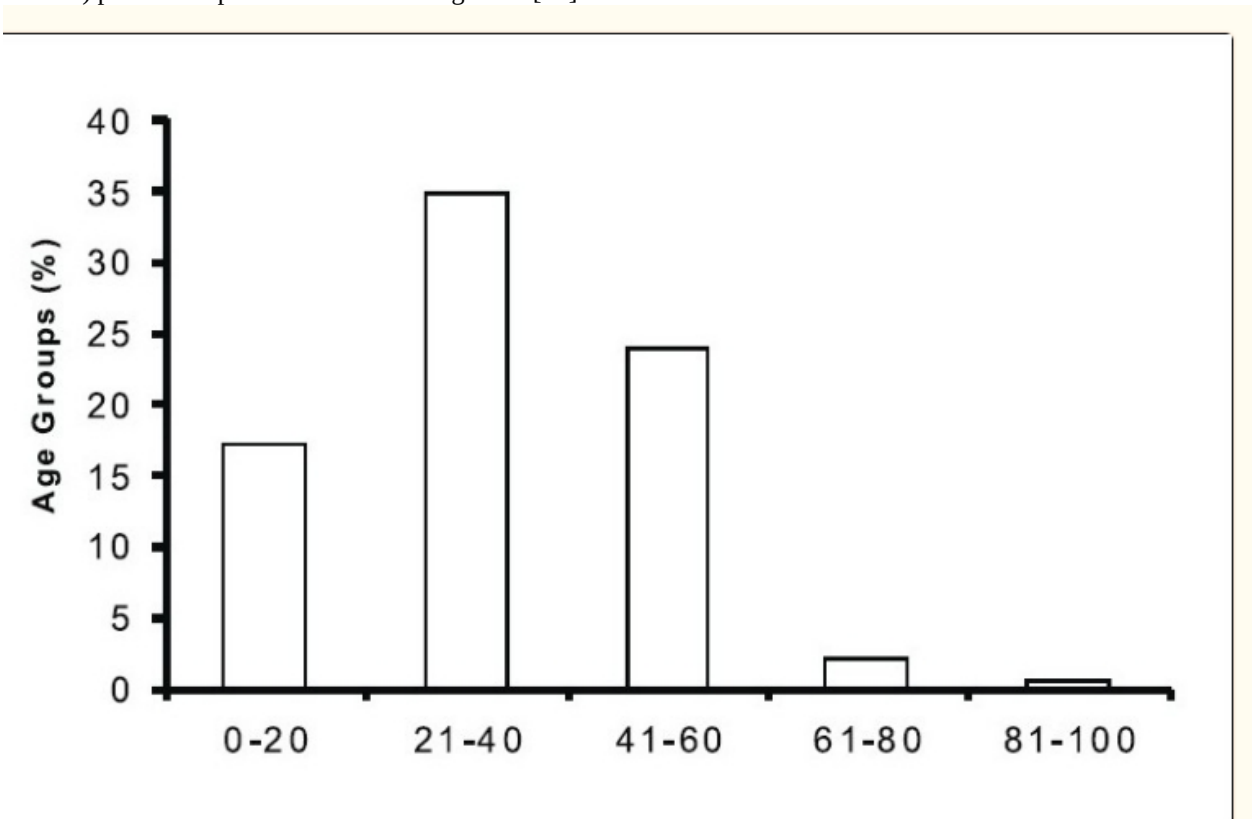

Fig 1 Antihistamines prescribed to different age group at PUHC. The figure shows the plot between percentages of antihistamines prescribed to different age group of the patients at PUHC.

Statistical analysis

The number of occasions saw during the treatment time frame in every individual patient is recorded and the rate thickness for every occasion is determined utilizing the condition:

Formula

The rate thickness is the proportion of the quantity of reports of every occasion per thousand patient-long stretches of openness to the medication. We determined frequency densities for different time stretches: the primary month of openness (ID1), during months 2-6 (ID2), and during the entire long periods of treatment (IDA). The contrast between the occurrence thickness in the primary month and that in the second to 6th months (ID1−ID2) and the almost 100% certainty stretch for this distinction were additionally determined. Occurrence densities were determined for every one of the occasions answered, to give a sign of which occasions were accounted for essentially more habitually in the primary month of openness. We determined non-changed and age and sex changed chances proportions for sleepiness or sedation for fexofenadine, cetirizine, and acrivastine utilizing loratadine as gauge. [16]

III. Conclusion

After collecting data from various sources I am concluded that there is rationale use of antihistamines in the hospitals mostly in rural areas. The Prescription Drug Monitoring Program (PDMP) was established to keep track of and analyze data on controlled substance prescriptions and dispensing, as well as to lessen prescription abuse and diversion. The PDMP system keeps track of prescriptions for restricted medications within a given state using separate statewide computer databases. Health authorities can use this data to get up-to-date information on patient behaviors and prescribing habits. The purpose of this study is to provide a concise summary of the clinical research demonstrating the safety of PMPs and the evidence-based recommendations guiding their usage for enhancing medication adherence and reducing risks.

IV. Discussion

Drug safety is dependent not just on preclinical research but also on post-marketing surveillance, as has been acknowledged for more than 30 years. [17] The goal of post-marketing prescription-event monitoring studies is to collect information on around 10,000 patients for each medicine by keeping track of big cohorts. Different prescription-event monitoring advantages and disadvantages exist. The approach is non-interventional and does not influence general practitioners' choices on a patient's best course of therapy. Consequently, it does not have the selection bias that clinical studies have. It is conducted on a nationwide level and is representative of the entire drug-using community. The method can identify trends in incidents that may not be connected to the medicine by doctors treating specific patients since all events are being tracked. Data on the use of particular medicines during the first trimester of pregnancy have been published, and other information, such as use during pregnancy, can be tracked. The method's reliance on general practitioners returning completed green forms is a drawback. As a result, the absence of information from non-responders may introduce bias. There is no evidence, nevertheless, to suggest that any such bias would be different for the medications studied in this study. We are not aware of any publicity that may have had an impact on the reporting of sedation, despite the fact that the data collecting period for fexofenadine was later than for the other medications. Additionally, since all of the medicines are taken for clear, comparable reasons, there is unlikely to be any hidden confounding of these data. The odds ratios were little changed when age and gender were taken into account.

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