PHARMACOVIGILANCE STUDY IN CASES OF BRONCHIAL ASTHMA IN TERTIARY CARE HOSPITALS OF EASTERN INDIA

Shambo Samrat Samajdar[1], Parbaty Panda[2], Saumyajit Maiti[3,*], Anju Prasad[4], Chaitali Pattanayak[5], Kamal Lochan Das[6]

[1]Postgraduate Resident, [2]Professor & HOS, [4,5]Associate Professor, Dept. of Pharmacology,
[3]Postgraduate resident, [6]Associate Professor, Dept. of Biochemistry,
Hi-Tech Medical College & Hospital, Bhubaneswar, Odisha.

ABSTRACT

Background & Objective: *Bronchial asthma, a common chronic disease affecting 300 millions of people across the world. The number of patients suffering is increasing day by day. This study was conducted to evaluate adverse drug reactions in asthma patients attending outpatient department of Hi-Tech Medical College & Hospital, Bhubaneswar & Allergy & Asthma clinic Moulali, Kolkata.*

Methodology: *200asthmatic patients irrespective of age and sex on anti-asthmatic drugs were surveyed during the time period of September 2013 to August 2014.CDSCO ADR reporting forms were filled. Naranjo's adverse drug reaction probability scale was used to know the causality of the adverse drug reactions.*

Result: *Among the 200 patients on anti-asthmatic drugs, 20 patients presented with 38 types of adverse drug reactions. Oral thrush was the most common adverse drug reaction (31.58%) among all ADRs followed by palpitation(13.6%),running nose & sore throat(both 10.53%), tremor (7.9%) , dizziness & dry cough(both 5.26%),skin rashes, hepatitis, headache, loose motion, constipation, drowsiness(each 2.63%) in patients treating with inhalational corticosteroids, montelukast, long acting beta2 sympathomimetics like indicaterol, salmeterol sublingual allergen immunotherapy & theophylline.*

Conclusion: *This study reveals the importance of ADR monitoring in patients receiving drug therapy for asthma. Larger sample size with long duration of study is needed to get better result.*

INTRODUCTION

Bronchial Asthma is defined as reversible obstruction of airways of lungs due to its hyper responsiveness to external or internal allergen or nonspecific stimulus like exercise, cold and characterized pathologically by chronic airway inflammation and clinically by cough, wheeze, chest tightness and dyspnoea. The rising worldwide prevalence of bronchial asthma and the high health care costs on it have led to extensive study into its pathogenesis and treatment. Bronchial asthma, a common chronic disease affecting 300 millions of people across the world and the number is increasing day by day. As per the epidemiologic studies, a maximum number of asthmatic individuals in the community have genetic predisposition. Most of the asthmatic patients in developed countries are a topic, with allergic sensitization to the house dust mite *Dermatophagoidespteronyssinus*, environmental allergens like pollen, cockroach antigen etc and food allergens. [1] Asthma is characterized by activation of mast cells, infiltration of eosinophils, and T helper 2 (T_H2) lymphocytes. Mediators, secreted by allergens and physical stimuli activated mast cell, such as histamine, leukotriene D_4, and prostaglandin D_2 cause broncho constriction, micro vascular leakage, and plasma exudation. Increased numbers of mast cells in airway smooth muscle are a characteristic of asthma. Airway hyper responsiveness is the physiological hallmark of asthma. The mechanism of chronic inflammation in asthma is still not well understood. It may initially be driven by allergen exposure, but it appears to become autonomous so that asthma is essentially incurable. Dendritic cells regulate T_H2 cells that drive eosinophilic inflammation and also IgE formation by B lymphocytes. Airway epithelium plays an important role through the release of >100 inflammatory mediators and through the release of growth factors in an attempt to repair the damage caused by inflammation. Complex cytokine networks, including chemokines and growth factors play important roles in the inflammation process. [2] Bronchial asthma, a heterogeneous disease, is exacerbated due to endogenous factors including genetic predisposition, atopy etc and side by side some environmental factors. These both factors have a great importance in the patho-physiology of asthma. Risk Factors and Triggers Involved in Asthma are as follows:

Table 1: Shows Endogenous & Environmental Risk Factors and Triggers of Bronchial Asthma[1].

Endogenous Factors	Environmental Factors
Genetic predisposition	Indoor allergens
Atopy	Outdoor allergens
Airway hyper responsiveness	Occupational sensitizers
Gender	Passive smoking
Ethnicity?	Respiratory infections
Obesity?	Early viral infections?
Triggers	
Allergens	
Upper respiratory tract viral infections	
Exercise and hyperventilation	
Cold air	
Sulphur dioxide and irritant gases	
Drugs (beta-blockers, aspirin)	
Stress	
Irritants (household sprays, paint fumes)	

The goal of asthma treatment is to achieve and maintain clinical control. Clinical studies have shown that asthma can be effectively controlled by intervening to suppress and reverse the inflammation as well as treating the broncho constriction and related symptoms.

Medications to treat asthma are

a) Bronchodilators,
b) Leukotriene antagonists,
c) Mast cell stabilizers,
d) Corticosteroids &
e) Anti IgE antibody.

Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions or any other drug-related problems. As many drugs have been used for bronchial asthma there are many adverse drug reactions occurring in patients. Some new drugs also come into the market as sub lingual allergen immunotherapy against environmental allergens, long acting beta 2 agonist like indicaterol inhalation. Post marketing surveillance is also important regarding this drugs.WHO (1975) defines an Adverse Drug Reaction (ADR) as "any response to a drug which is noxious, and unintended, and which occurs at doses normally used in a man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function". [3]ADRs are unfortunate burden of society both financially and in terms of human suffering. Systemized ADR monitoring and reporting helps physicians to rational prescribing of drugs. Several studies explored the vital role of pharmacologists making specific workout in reporting ADRs. ADRs reporting by pharmacologists to national pharmacovigilance centres show concerns for patients about ADRs they experience in relation to the drugs they are prescribed by the physicians. [4] [5] [6] [7] For assessment of causality Naranjo scale is used. According to Naranjo scale, the probability of the adverse event to drug therapy is expressed as definite, probable, possible, or doubtful. [8] [9]

Previous literatures on monitoring of ADRs in India are very less. A pharmacovigilance study in Mumbai, Indiaon asthmatic patients, depicted that common adverse effect seen was oral thrush (35%) followed by tremor and palpitation (20%), throat irritation (20%), and cough (10%).[10]

Simple advice on rinsing mouth with water after taking inhalational steroids can prevent oral thrush. Dilution of SLIT vaccines can prevent its toxicity to a maximum.

OBJECTIVE

The present study was conducted to monitor adverse drug reactions in asthma patients attending outpatient department of Hi-Tech Medical College & Hospital, Bhubaneswar & Allergy & Asthma clinic Moulali, Kolkata.

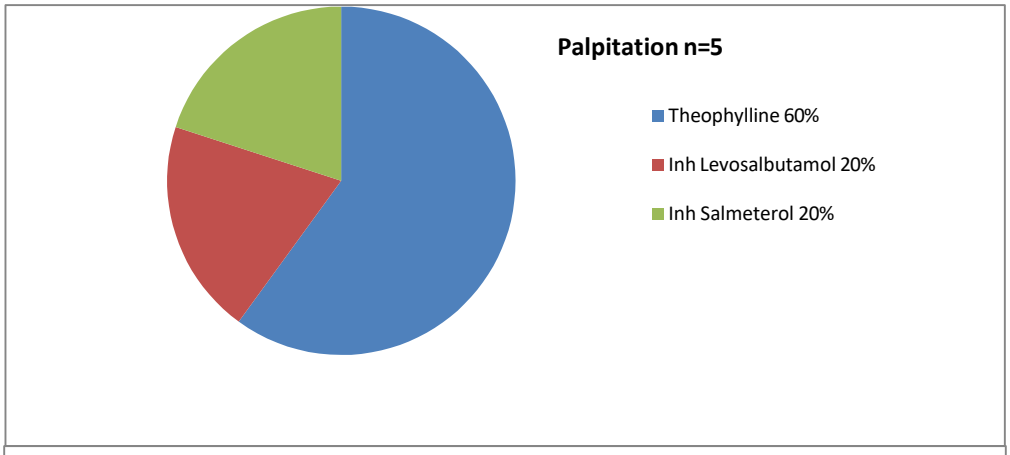
METHODOLOGY

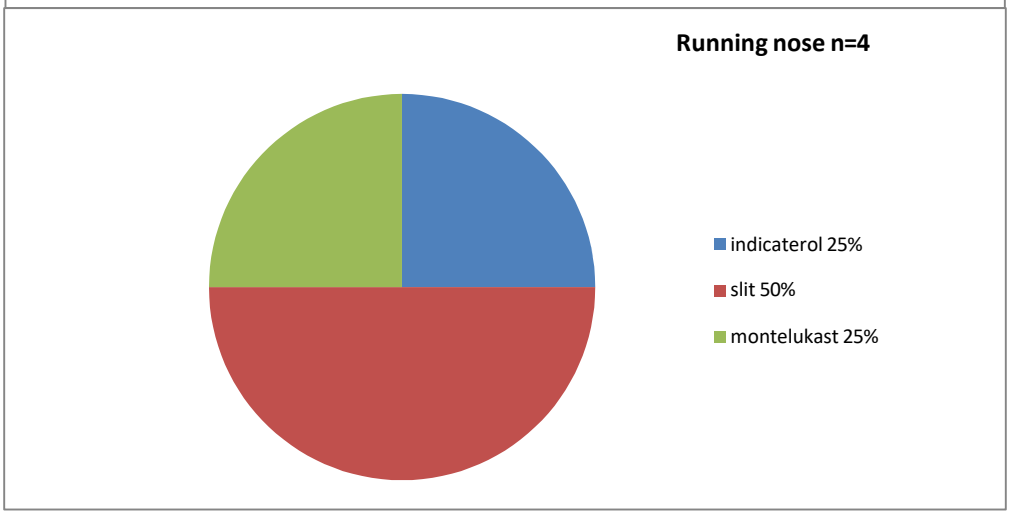
It was a non-comparative and open hospital based cross sectional type of observational study, based on an ADR monitoring form which is prepared according to CDSCO monitoring guidelines. The information collected included (age & sex), past medical history, present drug therapy, description, assessment, and treatment of ADR. The study was conducted in the outpatient department of Hi-Tech Medical College & Hospital Bhubaneswar & Allergy & Asthma clinic Moulali, Kolkata. ADR monitoring was done from September 2013 to August 2014. Irrespective of age and sex a total 200 asthmatic patients were included in the study. A verbal consent was granted from patients participating in the study. The Naranjo's probability scale was used for causality assessment of adverse events.

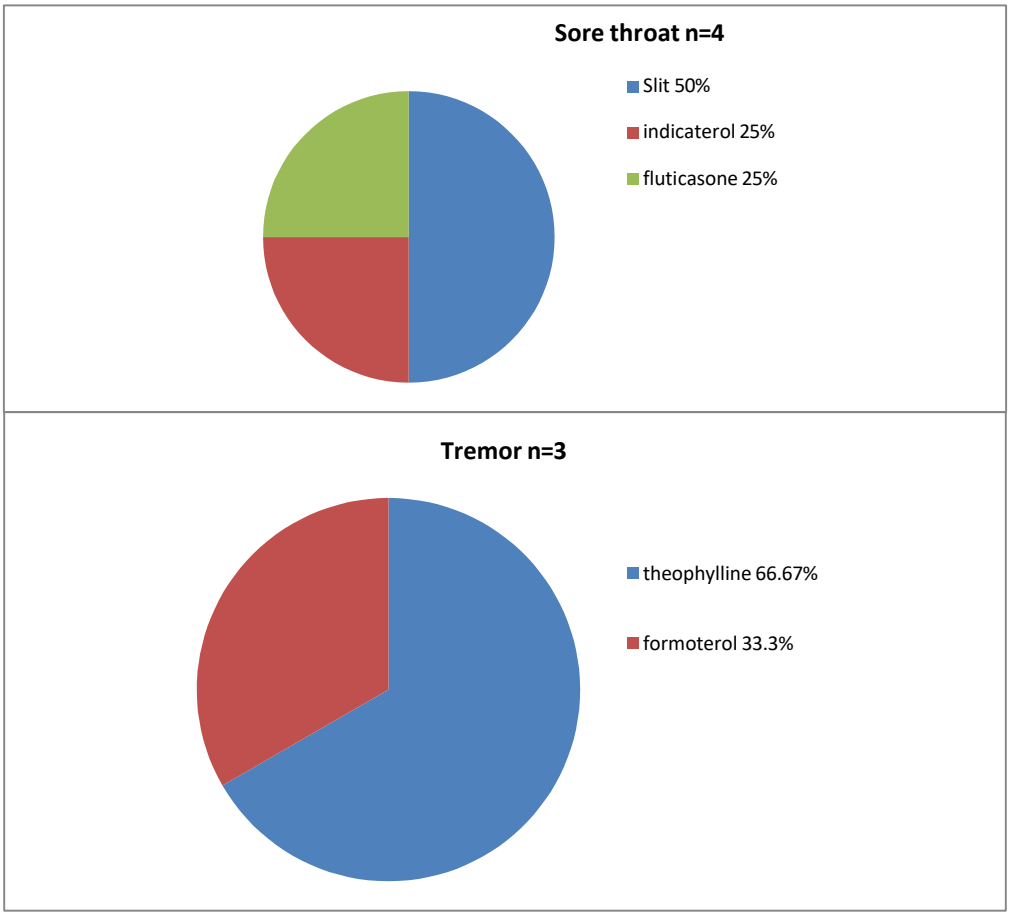
RESULTS

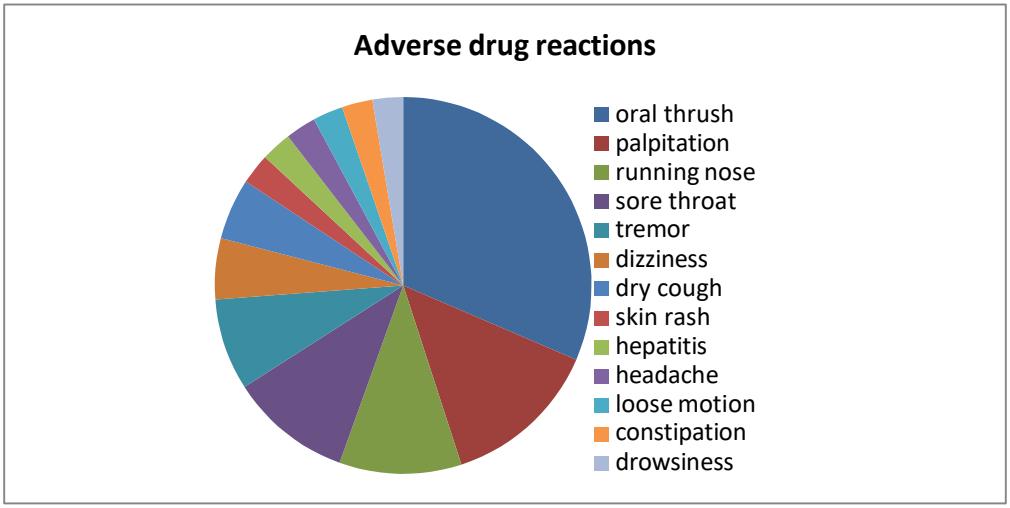
Table 2: Shows the Number & Type of Adverse Drug Reactions and its Suspected Drugs during this Study.

S No	Number of Patients of Adverse Drug Reaction (Total=200)	Adverse Drug Reaction (38 out of 200 patients)	Suspected drugs	% of total ADR
1	12	Oral thrush	Inhalational Budesonide & Inhalational Fluticasone	31.58%
2	5	Palpitation	Theophylline, Levosalbutamol, Inhalational Salbutamol	13.6%
3	4	Sore throat	SLIT, Indicaterol, Inhalational Fluticasone	10.53%
4	4	Running nose	Indicaterol, SLIT, Montelukast	10.53%
5	3	Tremor	Theophylline, Inhalational Formoterol	7.9%
6	2	Dry cough	Montelukast	5.26%
7	2	Dizziness	Levocetrizine	5.26%
8	1	Skin rash	Inhalational Indicaterol	2.63%
9	1	Hepatitis	Montelukast	2.63%
10	1	Drowsiness	Levocetrizine	2.63%
11	1	Loose motion	Azithromycin	2.63%
12	1	Headache	Montelukast	2.63%
13	1	Constipation	Fexofenadine	2.63%









DISCUSSION

176 patients were receiving inhalational steroids among 200 patients, among them 48 (24%) patients not washing their mouth after taking inhalational steroids. Among 176 patients only 69 patients (39.2%) were advised properly regarding mouth washing advice after taking inhalation steroids. With a novel long acting beta 2 sympathomimetic drug named indicaterol 2 Adverse Drug Reaction (ADR) s were seen as skin rash & running nose. Sublingual allergen immunotherapy (SLIT) caused ADRs in 2 patients, one suffered from sore throat and running nose and another patient suffered from sore throat only who required dilution of their vial 1 for SLIT (HD80 COCO20) & SLIT (HD1OO) which were1:10000 at beginning diluted to 1:100000 and given to patients.

CONCLUSION

The study results highlighted the need of ADR monitoring in patients receiving drug therapy for asthma. Simple advice like rinsing mouth with water after taking inhalational steroids can reduce adverse drug reactions like oral thrush. All the prescriptions advising inhalational steroids should contain mouth washing advice.SLIT vials to be diluted if any adverse reaction occurs in the first few doses. Skin rash followed by indicaterol inhalation, hepatitis followed by montelukast requires early discontinuation of those drugs. The above findings were constrained by a small sample size and need to be corroborated by conducting long-term studies using a larger sample size.

REFERENCE

1. Harrison's principles of internal medicine 18th edition: Harrison's Online > Chapter 254. Asthma.
2. Goodman & Gilman's The Pharmacological Basis of Therapeutics > Section IV. Inflammation, Immunomodulation, and Hematopoiesis > Chapter36. Pulmonary Pharmacology. Geneva: World Health organization; 1975. WHO. Requirements for adverse drug reaction reporting; pp. 1039–109.
3. Garg KC, Singhal KC, Kumar S. Monitoring the adverse profile of atenolol a collaborative study. Indian J Physiol Pharmacol. 1993;37:213–216.
4. Grootheest KV, Berg LJ, Puijanbrok EP. Do pharmacist reports of adverse drug reactions reflect patient concern? Pham World Sci. 2004;26:155–159.
5. Groothest KV, Olsson S, Couper M, Berg LJ. Pharmacist role in reporting adverse reaction in an international perspective. Pharmacoepidemiol Drug Saf. 2004;13:457–64.
6. Grootheest KV, Berg LJ, Puijanbrok EP. Contribution of pharmacist to the reporting of ADR. Pharmacoepidemiol Drug Saf. 2002;11:205–210.
7. Naranjo CA, Pontigo E, Valdenegro C, Gonzalez G, Ruiz I, Busto U. Furosemide-induced adverse reactions in cirrhosis of the liver. Clinical Pharmacology Ther. 1979;25:154–160.
8. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clinical Pharmacology Ther. 1981;30:239–245.
9. Bajaj A, Balakrishna S, Sawarkar S. Assessment of therapeutic performances of inhalation aerosols and clinical pharmacist's services in PFT lab. Indian J Hosp Pham. 1999;36:138–142.