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Research Article

AN OBSERVATIONAL STUDY TO ASSESS THE ADVERSE DRUG REACTION OF ANTI-ASTHMATIC DRUGS AMONG ADULTS IN WESTERN RAJASTHAN

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ABSTRACT

Objective: Asthma is one of the most common chronic illness worldwide. For prevention of exacerbations, patients of bronchial asthma are kept on long-term treatment that is why they are amenable for adverse drug reactions (ADRs). The study was planned to monitor ADRs with intervention of anti-asthmatic drugs in adults visited in medicine outpatient or admitted in inpatient department of a tertiary care teaching hospital.

Methods: A cross-sectional study was conducted among 340 asthma patients in collaboration with Department of Medicine for duration of 12 months. Information of patients was collected with the help of semi-structured case record form ADRs along with interventions given that were also recorded.

Results: Data analysis was done with the help of SPSS version20.0. Fisher exact test was applied. A total of 340 patients were enrolled in the study. The highest numbers of ADRs were observed with Salbutamol (34.78%). The highest ADRs were noted with $Beta_2$ agonists class of drugs. The main ADRs noted were headache followed by tremors and oral thrush. Statistically significant association was found between presence of ADRs and severity of asthma.

Conclusion: Identifying any possible connection between a presenting complaint and drug used is crucial to reduce the risk of ADRs in the future. Appropriate monitoring of ADRs is a key for this. Reduction in ADRs will improve the compliance of patient and ultimately their clinical outcome.

Keywords: Bronchial asthma, Anti asthmatic drug, Adverse drug reactions.

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INTRODUCTION

Bronchial asthma is a clinical syndrome which affects people worldwide of all ages and characterized by recurrent cough, paroxysmal dyspnea, chest tightness, and wheeze due to increase resistance to airflow through the narrowed bronchi. This narrowing is brought by the bronchial hyperactivity and bronchospasm, cellular infiltration, and edema of the bronchial mucosa and blockage of bronchial lumen by inspissated mucus [1]. The global prevalence of asthma, using a definition of clinical asthma or treated asthma, is estimated to be about 4.5% [2]. Asthma cannot be cured, clinical episode can be prevented and controlled by proper management. Medication to treat asthma can be classified as controller or reliever or add on therapy. Controller and relievers can be used for prophylaxis and treatment of acute episodes, respectively [3,4]. According to the WHO: "Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function" [5] is known as adverse drug reaction (ADRs). Monitoring, detecting, evaluating, documenting, and reporting ADRs are needed to as intervening and providing educational feedback to prescribers. According to the European Union legislation, the approval of all new medicines onto the market must now be accompanied by a robust risk management plan from the marketing authorization holder, which may involve the development of specific treatments for managing specific ADRs. We should also try to improve these processes in our country. That is why this study was planned with the primary objective of to assess ADRs of anti-asthmatic medications in adults along with the intervention performed to alleviate these ADRs. Secondary objective was to find out the associates of the ADRs.

METHODS

The study was conducted in the Departments of Pharmacology and Medicine of a teaching hospital. Study protocol was approved by the Department of Pharmacology and Institutional Ethics Committee. Patients attending outpatient department and inpatient department of Medicine Department of Teaching Hospital (tertiary care hospital) were recruited for the study. Adult, who gave written informed consent for participation and known cases of bronchial asthma, already on treatment, irrespective of sex, religion, occupation, and socioeconomic status, were included in the study. Patients with chronic obstructive pulmonary disease, pulmonary T.B, bronchiectasis, cardiac asthma, and tropical eosinophilia or with any other systemic disease/disorder were excluded from the study.

Participants were made to understand the entire purpose of the study, their rights, and the procedure of the study. A prospective, cross-sectional, and observational study design was chosen to fulfill the objectives of study. Data were collected with the help of the case record form which was available in both Hindi and English. Personal information related to the patients such as name, age, sex, occupation, relevant medical history, personal history, past history, family history, and investigations details were obtained from the patient's case file and were recorded in the Case Record Form. Assessment of asthma severity was done on the basis of GINA guidelines [6]. All the drugs used during the treatment of asthma were recorded in details. ADRs observed by investigator or treating physician were recorded in ADR reporting form. In case of any difference of opinion with respect to the drug use, dose, and duration of the treatment or reaction, the treating physician's opinion was considered as final. Age and sex distribution of study patients, severity of asthma, routes of administration, and type of therapy (Monotherapy/Combination therapy) were recorded. All the patients were asked for the occurrence of ADRs which were then subjected to causality assessment. The data were analyzed using Statistical package for the Social Sciences Software (SPSS 20.0). The data were presented using frequencies, percentages along with appropriate statistical diagram. The number of ADRs observed and the prescribed

drugs with which these ADRs were seen and expressed in percentages. Suitable intervention taken for these reactions was also recorded.

RESULTS AND OBSERVATION

Table 1 shows that the most (61%) of the participants were male, 75% participants were below 60 years of age.

Table 2 shows that maximum (73%) participants had moderate asthma followed by mild (23%) and severe (3%) asthma.

Table 3 shows that the most common route of administration of anti-asthmatic (50%) was inhalational followed by oral (45%) and parenteral (5%).

Table 4 shows that maximum participants were (73%) kept on combination therapy.

Table 5 shows ADRs with causative drugs and their respective classes. The most (48%) ADRs were observed with Beta$_2$ agonists class and with Salbutamol drug. Eight ADRs were noted with Salbutamol.

Figure 1 shows that the most common ADRs were headache followed by tremors and oral thrush. Figure 2 shows that the most common ADRs were headache followed by tremors and oral thrush.

Table 6 shows the various ADRs and associated intervention which was given to treat the ADRs.

Table 1: Sociodemographic profile of study participants

Variables	Frequency (%)
Gender	
Male	206 (60.59)
Female	134 (39.41)
Total	340 (100)
Age group	
15–30	25 (7.35)
31–40	54 (15.89)
41–50	70 (20.59)
51–60	105 (30.88)
>60	86 (25.29)
Total	340 (100)

Table 2: Distribution of study participants according to the severity of asthma

Severity of asthma	Frequency (%)
Mild	80 (23.53)
Moderate	248 (72.94)
Severe	12 (3.53)
Total	340 (100)

Table 3: Routes of prescribed anti-asthmatic

Routes	Frequency (%)
Inhalational	432 (49.65)
Oral	396 (45.52)
Parenteral	42 (4.83)
Total	870 (100)

Table 4: Type of therapy given to study participants

Therapy	Frequency (%)
Monotherapy	92 (27.06)
Combination therapy	248 (72.94)
Total	340 (100)

Table 7 shows that a statistically significant association was found between presence of ADRs and severity of asthma. As after applying Fisher exact test, p value was found to be 0.031 (<0.05). The cross tabulation of ADRs was also made between other variables such as age, sex, type of therapy, and route of therapy but only severity of asthma was found to be associated with presence of ADRs. As one cell had <5 count so instead of Chi-square test, we applied Fisher exact test.

DISCUSSION

The objective of this study is to assess the ADRs with management of anti-asthmatic medications in adults. In the present study, prescriptions of 340 adult patients were studied. On analysis of the prescriptions, it was found that asthma was reported more in male patients (60.59%) as compared to females (39.41%). The male female ratio was 1.54:1. However, in a study conducted by Agrawal *et al.* [7] found that female gender has consistently been associated with higher prevalence of asthma in adults. A total of 15 ADRs were reported in a study [8] 13 out of 200 asthmatic patients. Among the 13 patients reported with ADRs, 5 (38.5%) were male and 8 (61.5%) patients were female. Maximum percentage of ADRs (two in 15 prescriptions, 13.3%) observed with montelukast, followed by beclomethasone (one in 12 prescriptions, 8.3%), salbutamol (six in 109 prescriptions, 5.5%), and ipratropium (three in 63 prescriptions, 4.8%). In our study, also higher numbers of ADRs were observed in female patients as compared to male patients. It might be attributed to females being more sensitive to the

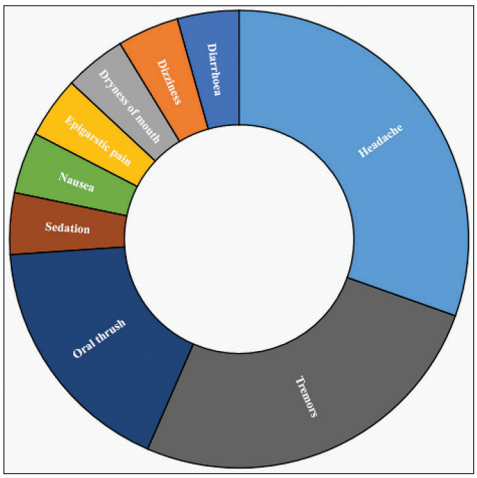

Figure 1: Sunburst diagram showing the various adverse drug reactions

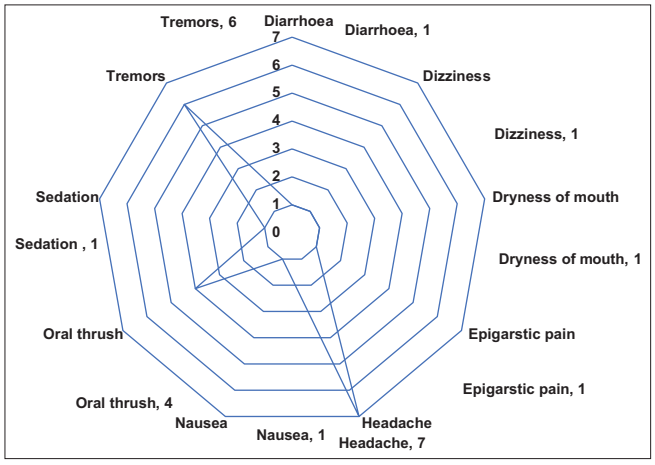

Figure 2: Radar diagram showing various adverse drug reactions

Table 5: Adverse drug reactions and causative drugs with their classes

Class	Drugs	Adverse reaction	Number of ADRs	Percentage
Beta2 agonists	Salbutamol	Tremor	5	47.83
		Headache	3	
	Salmeterol	Headache	1	
	Formoterol	Tremor	1	
		Dizziness	1	
Corticosteroids	Fluticasone	Oral thrush	1	21.74
	Beclomethasone	Oral thrush	3	
	Prednisolone	Epigastric pain	1	
Anticholinergics	Ipratropium	Dryness of mouth	1	4.35
Leukotriene modifiers	Montelukast	Headache	1	4.35
Methylxanthines	Theophylline	Nausea	1	13.04
		Headache	2	
Anti-histaminic	Cetirizine	Sedation	1	4.35
Antibiotics	Amoxicillin+Clavulanic acid	Diarrhea	1	4.35
Total			23	100

ADRs: Adverse drug reactions

Table 6: Adverse drug reaction and interventions

ADR	Intervention given
Tremor	Suspected drug was withdrawn
Headache	Symptomatic treatment (analgesic) was given
Oral thrush	Counseling was done (like use of spacer device, rinsing and spitting out after use, etc.)
Dryness of mouth	Dose of suspected drug was reduced
Diarrhea	Probiotic (sporolac) was given

ADR: Adverse drug reaction

Table 7: Cross table between adverse drug reactions and other factors

Severe asthma	ADRs		df	Exact significant (two-sided)
	Yes	No		
Yes	20	309	1	0.031
No	3	8		
Total	23	317		

ADRs: Adverse drug reactions

effect of drugs as compared to males and we found highest ADRs with salbutamol. Few studies [9,10] also observed more ADRs in female asthmatic patients as compared to male patients. Malmstrom *et al*. [11] reported ADRs that mainly included worsening asthma 48 (19.1%), headache 47 (18.7%), and upper respiratory tract infection 33 (13%) out of 251 patients on beclomethasone therapy. Meltzer *et al*. [12] reported headache in 4 (2%) and sore throat in 1 (<1%) out of 264 patients on montelukast therapy. In a foreign study [13], it was found that the common ADR was tremor (40%), hypokalemia (45.5%), and supraventricular tachycardia (21%); particularly with i.v. infusion, intravenous salbutamol administration. Another study conducted by Gawali *et al*. [14] reported a total 33 ADRs in 23 patients out of 150 bronchial asthma patients. Among the 23 patients reported with ADRs 10 (43.47%) were male while 13 (56.52%) were female as we found in our study also. They also found that oral thrush was the most common ADR (33.33%) followed by palpitation (15.15%), sore throat (12.12%), running nose, tremors (each 9.09%), dry mouth, GI distress, bitter taste (each 6.06%), and headache (3.03%) among the patients of bronchial asthma receiving anti-asthmatic agents. They also observed that the most ADRs were associated with inhalational beclomethasone (58.33%) followed by inhalational budesonide (25%), montelukast (23.07%), salbutamol (18.75%), theophylline (14.29%), ipratropium (7.4%), and salmeterol (02.22%). Bhosale *et al*. [15] found a total of 13 ADRs in 11 out of 50 asthmatic patients. Maximum percentage of ADRs (57.1%) observed with salbutamol, followed by salmeterol (50%), beclomethasone (30%), and tiotropium (25%). A total of 1163 ADRs were reported in a study [16] by patients during the study period with male predominance over female. The average age of the patients in the study was found to be 30–60 years. The most commonly occurred ADRs were beclomethasone-induced seizures, salbutamol-induced tremor, anorexia, and nausea, salmeterol-induced tremor and montelukast-induced angioedema were also common. Padmaja *et al*. [17] reported in a total of 103 patients, nearly 53.40% of patients were male, it indicates that the prevalence of ADRs is more in men than in women. Most commonly identified ADRs were maculopapular skin rashes 28 (27.18%). In a study conducted by Babu *et al*. [18], total 38% of patients taking anti-asthma drugs were encountered ADRs and were more common in elderly females (61–70 years). ADRs were more common in methylxanthine group (48%) compared to Beta 2 agonist group (28%). Headache (38%) was the most common ADR in methylxanthine group and tremors (31%) in Beta 2 agonist group. The most of ADRs were mild (95 %), manageable, and comes under possible (60 %) category of the WHO causality assessment scale.

CONCLUSION

Risk reduction of ADRs is a challenge in clinical practice in setting like India. Causative assessment of ADRS probability is a key to ensure drug safety. If we can identify the association of drug used with complain the risk of ADRs in patients of bronchial asthma can be minimized and the future episodes of ADRs may be prevented. Our objective is to get best outcome from therapy, for achieving this ADRs should be predicted, prevented, detected, and managed appropriately. By preventing ADRs, we can improve the compliance of patient and so that outcome.

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CONFLICT OF INTEREST

There is no conflict of interest provided in this project.

REFERENCES

1. Satoskar RS, Rege NN, Bhandarkar SD. Pharmacology and Pharmacotherapeutics. 24th ed., Vol. 361. India: Elsevier; 2015.
2. Masoli M, Fabian D, Holt S, Beasley R, Global Initiative for Asthma (GINA) Program. The global burden of asthma: Executive summary of the GINA Dissemination Committee report. Allergy 2004;59:469-78.
3. McFadden ER Jr. Harrison's Principles of Internal Medicine. 16th ed. United States: McGraw-Hill; 2005. p. 1508-16.
4. Pascual R, Johnson JR, Peters SP. Fishman's Pulmonary Disease and Disorders .4th ed. United States: McGraw-Hill; 200. p. 815-36.
5. WHO. Requirements for Adverse drug Reaction Reporting. Geneva: World Health Organization; 1975. p. 1039-109.
6. Taylor DR, Bateman ED, Boulet LP, Boushey HA, Busse WW, Casale TB, ***et al.*** A new perspective on concepts of asthma severity and control. Eur Respir J 2008;32:545-54.
7. Agrawal S, Pearce N, Ebrahim S. Prevalence and risk factors for self-reported asthma in an adult Indian population: A cross-sectional survey. Int J Tuberc Lung Dis 2013;17:275-82.
8. Jamali AN, Aqil M, Alam MS, Pillai KK, Kapur P. A pharmacovigilance study on patients of bronchial asthma in a teaching hospital. J Pharm Bioallied Sci 2010;2:333-6.
9. Barranco P, López-Serrano MC. General and epidemiological aspects of allergic drug reactions. Clin Exp Allergy 1998;28 Suppl 4:61-2.
10. Riedl MA, Casillas AM. Adverse drug reactions: Types and treatment options. Am Fam Physician 2003;68:1781-90.
11. Malmstrom K, Rodriguez-Gomez G, Guerra J, Villaran C, Piñeiro A, Wei LX, ***et al.*** Oral montelukast, inhaled beclomethasone, and placebo for chronic asthma. A randomized, controlled trial. Montelukast/Beclomethasone Study Group. Ann Intern Med 1999;130:487-95.
12. Meltzer EO, Lockey RF, Friedman BF, Kalberg C, Goode-Sellers S, Srebro S, ***et al.*** Efficacy and safety of low-dose fluticasone propionate compared with montelukast for maintenance treatment of persistent asthma. Mayo Clin Proc 2002;77:437-45.
13. Habashy D, Lam LT, Browne GJ. The administration of beta2-agonists for paediatric asthma and its adverse reaction in Australian and New Zealand emergency departments: A cross-sectional survey. Eur J Emerg Med 2003;10:219-24.
14. Gawali UP, Deshkar A. Pharmacovigilance study of anti-asthmatic agents in patients of bronchial asthma at a tertiary care centre. Int J Adv Res 2017;5:1867-71.
15. Bhosale U, Jaiswal S, Yegnanarayan R, Godbole G. A pharmacovigilance study of anti-asthmatic agents in patients of bronchial asthma at a tertiary care hospital. J Clin Exp Res 2013;1:26-30.
16. Muthukumar A, Sundara Ganapathy R. A study on adverse drug reactions and their risk factors of anti-asthmatic agents among garments dust-induced asthmatic patients in Manchester of south India. Asian J Pharm Clin Res 2018;11:130-2.
17. Padmaja SY, Palaniswamy S. A study on assessment, monitoring and documentation of adverse drug reactions. Int J Pharm Teach Pract 2012;3:253-6.
18. Babu SN, Kumar CV, Nandini R. Comparative study of adverse drug reaction pattern of two anti-asthma groups of drugs in a tertiary care hospital. Int J Basic Clin Pharmacol 2019;8:788-91.