



A Pharmacovigilance Study on Inhaled Bronchodilators in Obstructive Lung Disease

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Abstract

Inhalational Therapy has a wide range of products which are frequently being used for the treatment of Obstructive Lung Disease which generally includes COPD & Asthma. The prevalence of death due to the disease is being found as 3 million each year which is being increasing and at present it is third leading cause of death worldwide. This pharmacovigilance study is a prospective cohort study carried out at SAIMS hospital, Indore. The study is designed to monitor factual clinical trends in the treatment of OLD and to evaluate the correlation between different therapy of inhaled bronchodilator and their outcome. A total of 100 out patients were enrolled in the study after an informed consent, out of which 58 were males and 42 females. Causality assessment was done using the Naranjo's Scale & severity was analysed using Hatwing & Siegel Scale severity scale. 32 % of ADR were attributed in the study cohort of 100 patients. Common ADRs observed with drug treatment were diarrhoea, altered bowel habits, gastritis, tachycardia, headache & muscle cramps. The prevalence of ADR was more in GIT, CVS and other organs. CNS ADRs were less reported. The present study resulted in 60 % of ADR which were observed as mild & 40 % reported to be moderate. No severe ADRs were reported. Out of all ADRs, 37.14 % belongs to Doubtful ≤ 0 category, 25.71 % belongs to possible 1-4 category, 28.57 % belongs to probable 5-8 category and 8.57 % belongs to highly probable ≥ 9 categories. Thus, this study compliance the use of inhaled bronchodilator with no severe ADR at each category (children, adult & elderly) and urges for the use of inhalational therapy.

Keywords: Pharmacovigilance, ADR.

Introduction

Bronchodilators are medication that open or dilate the airways i.e. bronchial tubes of lungs by relaxing bronchial muscles and allow people who have difficulty breathing to breathe better.

Bronchodilators are used for treating:

- Asthma

- Chronic obstructive pulmonary disease (COPD)
- Allergic reactions.
- Related conditions that cause breathing problem¹

Often there are misleads for COPD & asthma, as the symptoms for both correlate each other. Treatment for the one can only be distinguished

on the basis of morbidity of disease. Obstructive Lung Disease (OLD) is progressively irreversible disease. The prevalence of death due to the disease is being found as 3 million each year which is being increasing and at present is third leading cause of death worldwide.² All available pharmacological options are used to improve the quality of life. However none of them is known to reduce the mortality and decline in lung function rather is associated with side effects which further affects the quality of life adversely. To provide symptomatic relief, inhalational therapy is considered as a first choice of drug. The actions of inhaled bronchodilators starts within minutes after you inhale and last up to 2-4 hours. Short acting bronchodilators are used as a “quick relief” or “rescue inhalers” while long acting bronchodilators can be used every day to control the morbidity of disease.³ This study is designed to monitor factual clinical trends in the treatment of OLD and to evaluate the correlation between different therapy of inhaled bronchodilator and their outcome.

Materials and Methods

Prospective cohort study was carried out in the department of respiratory medicine, SAIMS, Indore for a period of three month (April 2013- June 2013). The study protocol had the approval by the Institutional Ethical Committee. Informed written consent was obtained from all participants. Patients diagnosed as OAD & Patients regularly taking inhaled therapy with Dry Powdered Inhaler (DPI) and Metered-Dose Inhalers (MDI) were

included in study. Patients not willing for inhaled bronchodilator, Patients with sputum positive pulmonary TB disease & Patient's extremely critical condition were excluded from study.

Patients were included on 1st follow up visit (2 weeks/1 Month). If newly diagnosed, considered as 1st visit. At first visit, for each patient, current medical history, diagnosis, demographic profile and prescription were noted. If previously diagnosed detailed patient history was taken & monthly follow up was done. On every visit, data regarding symptoms, drug compliance and ADR, if any was recorded. The ADRs were recorded in the specify proforma⁴ designed by the CDSCO for this purpose. Laboratory investigations were done in appropriate cases. At the end of study period, all data were accumulated & reviewed statistically. Causality assessment was done using the Naranjo's Scale.⁵ This scale evaluates the degree of association of an adverse effect with the suspected drug and involves a set of questionnaires, which are ascribed a certain score. Total score for a particular drug-ADR combination is calculated and the association is termed - highly probable, probable, possible or doubtful-depending on the score. & severity was analysed using Hatwing & Siegel Scale severity scale.⁶

Results

The study comprises a cohort to evaluate the correlation between different therapy of inhaled bronchodilator and their outcome. The different therapy used is described in below table:

Table 1: Distribution as per Medicines Administered

S.N.	Group	Drugs	No. of Patients
1.	A	Salbutamol	13
2.	B	Salbutamol + Ipratopium	10
3.	C	Formoterol + Budesonide	32
4.	D	Formoterol + Fluticasone	02
5.	E	Tiatropium	10
6.	F	Taitropium + Formoterol	06
7.	G	Inhaled + Oral Bronchodilator	27
Total			100

A total of 100 out patients were enrolled in the study after an informed consent, out of which 58 were males and 42 females. 32 % of ADR were attributed in the study cohort of 100 patients. Common ADRs observed with drug treatment were diarrhoea, altered bowel habits, gastritis, tachycardia, headache & muscle cramps. The prevalence of ADR was more in GIT, CVS and other organs. CNS ADRs were less reported.⁷

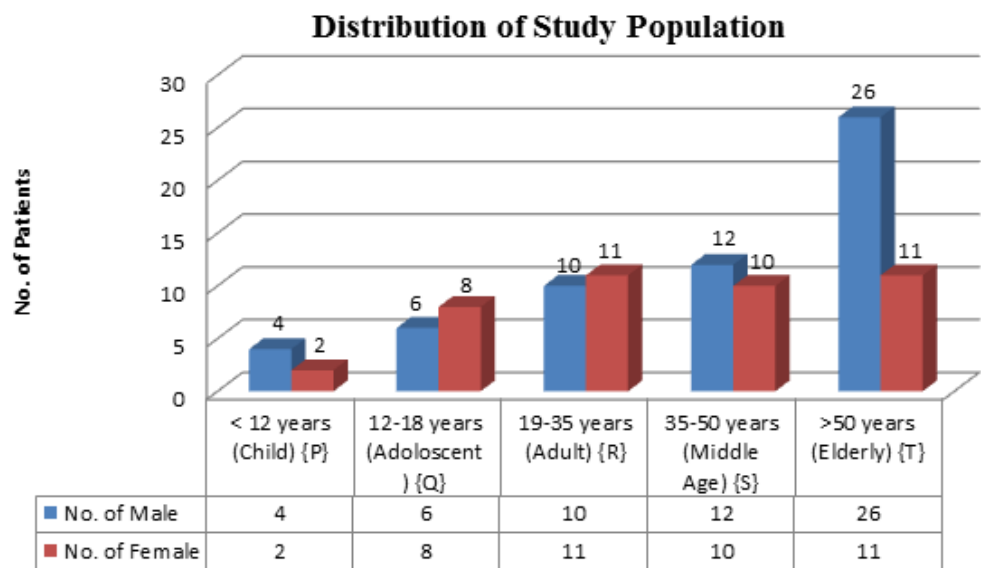
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A] Distribution as per Demography

Table 2: Age Distribution of Demography

S.N.	Age Group	No. of Male	No. of Female	Total
1.	< 12 years (Child) {P}	4	2	6
2.	12-18 years (Adults) {Q}	6	8	14
3.	19-35 years (Adolescent) {R}	10	11	21
4.	35-50 years (Middle Age) {S}	12	10	22
5.	>50 years (Elderly) {T}	26	11	37
6.	Total	58	42	100

Graph 1: Distribution of Patients as per Demograph



B] Distribution of Patients as per Severity of Disease

1. Classification of Asthmatics: (GINA Classification)⁸

Table 3: Severity Classification of Asthma

S.N.	Severity of Disease	FEV ₁ (l/min)	PEFR (l/sec)	N
1.	Mild	78 ± 2	440 ± 50	18
2.	Moderate	54 ± 1	470 ± 38	30
3.	Severe	34 ± 5	320 ± 19	10
Total				58

2. Classification of COPD: (GOLD Classification)⁹

Table 4: Severity Classification of COPD

S.N.	Severity of Disease	FEV ₁	N
1.	Mild	75 ± 2	12
2.	Moderate	56 ± 3	8
3.	Severe	32 ± 4	7
4.	Very Severe	26 ± 1	15
Total			42

Table 5: Medicine Distribution as per Age Group

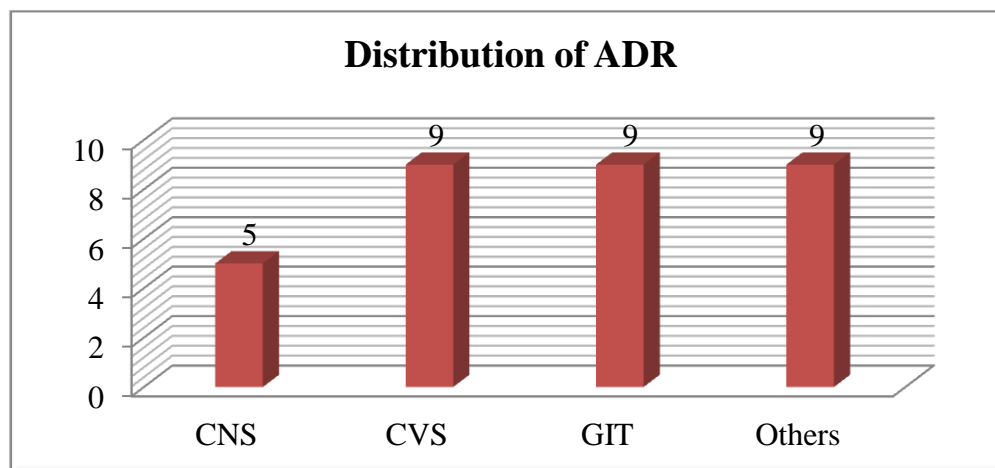
S.N.	Group	P	Q	R	S	T	Total
1.	A	04	04	02	02	01	13
2.	B	-	06	04	-	-	10
3.	C	02	-	12	-	18	32
4.	D	-	02	-	-	-	02
5.	E	-	-	-	10	-	10
6.	F	-	-	-	-	06	06
7.	G	-	02	03	10	12	27
8.	Total	06	14	21	22	37	100

C] Distribution of ADR as per Demography

Table 6: Age Distribution of ADR

S.N.	ADR	P	Q	R	S	T	Total
1.	Yes	01	01	10	04	16	32
2.	No	05	13	11	18	21	68
3.	Total	06	14	21	22	37	100

Graph 2: Distribution of ADR as per Demography

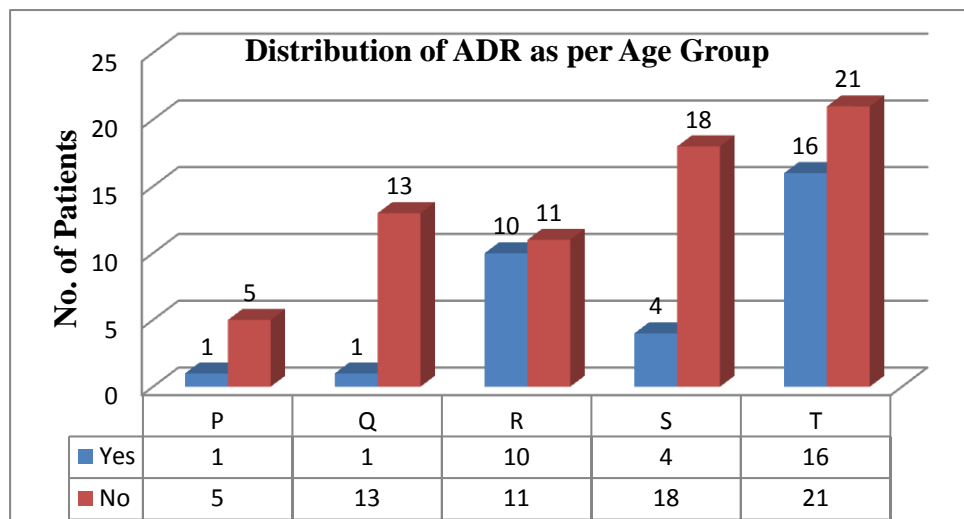


D] Distribution of ADR as per Effects Associated on Different Parts of Body

Table 7: ADR Distribution As per Organs of Body

5S.N.	Organs	A	B	C	D	E	F	G	Total
1.	CNS	2	2	-	-	-	1	-	5
2.	CVS	-	2	7	-	-	-	-	9
3.	GIT	-	2	3	-	4	-	-	9
4.	Others	-	4	1	1	2	1	-	9
5.	Total	2	10	11	1	6	2	-	32

Graph 3: Distribution of ADR on different Organs



E] Classification of ADR’s According to Naranjo’s Scale:

Table 8: Causality Assessment as per Naranjo’s Scale

Assessment Score	No. of ADR	% of ADR
Doubtful ≤ 0	13	37.14
Possible 1-4	9	25.71
Probable 5-8	10	28.57
Highly Probable ≥9	3	8.57
Total	35	99.99

F] Distribution of ADR as per Severity Classification Scale:

Table 9: ADR Distribution as per Severity Scale

Severity	No. of ADR	% of ADR
Mild	21	60
Moderate	14	40
Severe	-	-
Lethal	-	-
Total	35	100

Discussion

Obstructive Airway Disease which requires lifelong treatment. Pharmacotherapy in OAD usually involves poly pharmacy and present study is focused on ADR’s associated with inhaled bronchodilators. Drug safety & occurrence of ADR is cohabiter phenomena. ADR can occur any time whether it is a mono therapy or poly therapy. In present study, the ADR observed were very frequent in the age group of patients > 50 as many biological factors contributes to the risk of developing ADR.

The study focused on the evaluation of effects & ADR observed after administration of inhaled bronchodilator with or without oral administration of other drugs and has found that inhaled bronchodilator always provide symptomatic relief in OAD and found to be the first choice of drug for physician as well as patient adherence. Literature also encompasses, encouraging patients to use inhaled medication¹⁰ as other drugs like theophylline has narrow therapeutic index which can lead to more severe ADR. Oral steroid therapy itself has many adverse event to which

hyperpigmentation of skin has been reported as severe ADR.¹¹

Thus, this study compliance the use of inhaled bronchodilator with no severe ADR at each category (children, adult & elderly) and urges for the use of inhalational therapy.

Limitation

The present work is the open ended base line information about the prevalence of ADRs & their distribution amongst different age groups, genders & organ system affected. The study was of short duration and the no. of study population observed was also small but if the study is elaborated for more time duration and on more number of patients, the ADRs can be better understood.

Implication

The data presented in the study will be useful in future for long term and more extensive ADR monitoring, as the the importance of pharmacovigilance has been on the rise because the frequency of ADRs and the percentage of hospital admissions have been increasing day by day¹². The study also highlights the need for more effective ADR monitoring & also proper counseling is needed to patients regarding the use of different types of inhalers.

In India, there are 150 active ADR monitoring centers¹³ and a lot of effort is required in order to collect ADR data which may generate from safety surveillance of therapeutically active substances either alone or in combinations. Therefore it is important that the use of these medicines is monitored for their ongoing effectiveness and safety.

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