ORIGINAL RESEARCH PAPER

Volume-8 | Issue-7 | July - 2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ADVERSE DRUG REACTIONS IN PEDIATRIC ASTHMA PATIENTS ATTENDING A TERTIARY CARE TEACHING HOSPITAL

Pharmacology

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ABSTRACT

Background of the study: Adverse drug reactions (ADR) are an unfortunate burden on the society, both financially as well as in terms of human suffering. As compared to adults, ADRs in children can have a relatively more severe effect. As such, study of ADRs in pediatric patients of bronchial asthma can play a significant role in systemized ADR monitoring and protect the patients from preventable harm.

Materials and Methods: An observational, non-interventional and cross-sectional study was conducted in pediatric patients of bronchial asthma at a tertiary care teaching hospital for a period of 16 months. All the adverse drug reactions (ADRs) occurring during the therapy (either spontaneously reported or identified by the investigator) among the outpatient as well as inpatient departments were examined for relevant data like type of ADR, drug suspected to cause ADR, body system affected by the ADR. Adverse drug reactions were then assessed for causality by WHO-UMC scale and Naranjo's scale & their severity were also assessed by modified Hartwig and Siegel's scale

Results: During the study period, a total of 35 ADRs were reported among 330 patients. The incidence rate of ADRs was found to be 10.6%. The percentage of ADRs was the highest (37.14 %) in patients aged between 5 to 8 years. The most commonly reported ADRs were palpitations (11.42%), dryness of mouth (11.42%), tachycardia (8.57%), headache (8.57%), sore throat (8.57%) and diarrhea (8.57%). There were no severe reactions, 29 (82.85 %) accounted for mild reactions and 6 (17.14 %) were moderate reactions in the severity scale. Causality analysis revealed that about 42.5 % of ADRs were probable, 54.28 % were possible and 2.85 % were certain. None of the reported ADRs were found to be fatal, life threatening or needed hospital admission for management.

Conclusion: Adverse drug reactions associated with anti-asthmatic drugs are quite common. Increased awareness regarding these ADRs, among children, their parents and physicians may result in early detection of ADRs, their early reporting and minimize risk of ADR related harms. This demands necessity of rigid ADR monitoring in pediatric population.

KEYWORDS

Adverse drug reactions, Asthma, Pediatrics, Anti-asthmatic drugs, causality

INTRODUCTION

Asthma is a common heterogenous disorder of airways in children and imposes a significant impact on health care system. It is characterized by variable expiratory airway narrowing clinically presented by symptoms of wheezing, shortness of breath, chest tightness and cough.[1]

As per World Health Organization (WHO) estimates, it has been reported that 300 million people suffered from asthma causing death of 255,000 people in 2005. Moreover, 80% of these deaths occurred in low and lower-middle income countries.[2]

The prevalence of bronchial asthma in pediatric population is variable across the countries ranging from 4 to 32% for 6-7 years of age, as well as for 13 and 14 years. Globally, highest prevalence of severe bronchial asthma has been reported in UK.[3] Among the Indian children, a median prevalence of about 4.75% has been estimated so far.[4]

Adverse drug reactions (ADR) are an unfortunate burden on the society, both financially as well as in terms of human suffering. They are associated with almost every drug and may range from mild to serious and even life threatening. WHO (1975) defines an 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 the physiological function".[5]

As compared to adults, ADRs in children can have a relatively more severe effect. They not only result in hospital admissions or prolonged hospitalization but also may lead to permanent disability or even death. Since pre-marketing clinical trials are done mostly in adults, the information regarding the frequency, severity and types of drugs most frequently involved in adverse reactions in the pediatric age group is of particular interest. Adverse drug reactions in children constitute a reported incidence of 9.5%, including 2.1% of hospital admissions, with 39.3% of them being life-threatening.[6] Therefore, Pharmacovigilance plays a significant role in detecting, treating and preventing the likely ADRs and thus reduce the harm to the patients. Hence, this study was planned to observe the occurrence of the adverse drug reactions associated with pharmacotherapy of pediatric bronchial asthma in a tertiary care hospital.

MATERIALS AND METHODS

It was an observational, non-interventional and cross-sectional study that was conducted in Department of Pediatrics, MGM Medical college & Hospital at Aurangabad. The study commenced following the approval of the Institutional Ethics Committee.

Pediatric patients of bronchial asthma (both acute and chronic cases) of either gender between the age group of 1-17 years who attended outpatient department (OPD) as well as in patient department (IPD) from November 2017, willing to fill informed consent and assent forms were included in the study. Patients with other co-morbid conditions like TB, Diabetes/renal failure or any other systemic disorders, or who were immunocompromised were excluded.

All information pertaining to the patient, such as patient's demographic details was obtained from the patient's case files. All the adverse drug reactions that occurred during the therapy (either spontaneously reported or identified by the investigator) were noted. All information pertaining to the adverse drug reaction such as the type of reaction, onset, duration, culprit drug, system affected were also recorded. Further they were subjected for causality assessment using the WHO-UMC and Naranjo's scale and the severity of the reactions were analyzed using modified Hartwig and Siegel's scale.

OBSERVATION AND RESULTS

During the study period, a total of 35 ADRs were reported among 330 patients. The incidence rate of ADRs was found to be 10.6%. Our study revealed that out of 35 reported cases of ADR, 19 (54.28 %) occurred in males and 16 (45.71%) in females as shown in Table 1. The pediatric patients enrolled in the study were grouped into 4 subgroups based on their age. It was observed that the percentage of adverse drug reactions was the highest (37.14 %) in Group II patients aged between 5 to 8 years followed by group III patients of age group of 9 to 12 years, who showed 28.57% ADRs. Patients of group IV (13-17 years) exhibited 25.71% ADRs, while minimum ADRs (5.71%) were reported in group I having children of 1-4 years of (Figure 1). Also, all 35 ADRs were found to be of type A reactions i.e. predictable.

It was observed that 7 (20%) ADRs were associated with each of the

following systems cardiovascular system, gastro-intestinal system and ENT whereas 6 (17.14%) ADRs affected skin and mucus membranes. However, only 4 (11.42%) ADRs were found associated with respiratory system and to central nervous system as indicated in figure 2.

The most commonly reported ADRs were palpitations (11.42%), dryness of mouth (11.42%), tachycardia (8.57%), headache (8.57%), sore throat (8.57%) and diarrhea (8.57%). The percentages of other adverse drug reactions were comparatively less which can be seen in figure 3.

On causality assessment by WHO-UMC method, it was observed that 15(42.5 %) were probable, 19 (54.28 %) were possible and only 1 (2.85 %) was certain ADR. (Figure 4) Similarly, causality assessment by Naranjo's scale displayed that 15 (42.85) ADRs were probable, 19 (54.28%) were possible and only 1(2.85%) was definite, as indicated in figure 5.

Assessment of severity of recorded adverse drug reactions with the help of Hartwig and Siegel scale showed that 29 (82.85 %) accounted for mild reactions and 6 (17.14 %) were moderate reactions. No severe ADR were recorded during the study period. (Figure 6)

Of the recorded 35 cases of the ADRs, in 26 (85.42 %) patients, despite the occurrence of ADR, the suspected drug was continued with or without utilizing medical treatment to overcome the reaction. In 2 (5.71%) cases of reported ADRs, the dose of the suspected drug was decreased. Further, 4 (11.42 %) of the suspected drugs, that caused ADR were discontinued from use and symptomatic treatment was given to manage ADR. On the other hand, suspected drug was discontinued without involving any medical treatment for ADR management in 1 patient (2.85%). In the remaining 2 (5.71%) cases, the treatment with suspected drug was discontinued and was replaced by another suitable drug to treat the condition.

Table -1: Gender of patients and adverse drug reaction (n = 330)

Gender	Number of patients		Total
	With ADR (%)	Without ADR (%)	
Male	19 (54.28)	151 (51.18)	170 (51.51)
Female	16 (45.71)	144 (48.81)	160 (48.48)
Total	35 (100)	295 (100)	330 (100)

Figures in parentheses show percentage

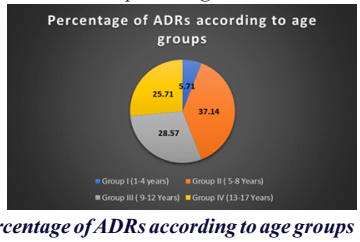

Figure 1: Percentage of ADRs according to age groups

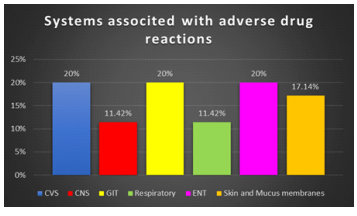

Figure-2: Systems associated with adverse drug reactions

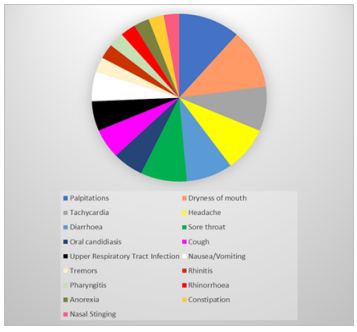

Figure-3: Percentage of various reported adverse drug reactions

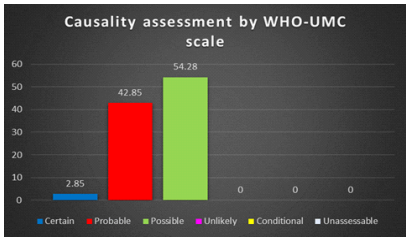

Figure-4: Causality assessment of ADRs according to WHO-UMC scale

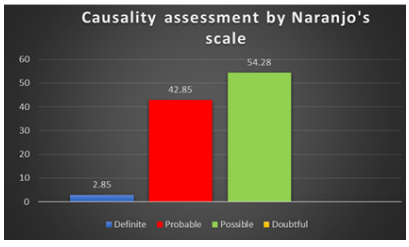

Figure-5: Causality assessment of ADRs according to Naranjo's scale

DISCUSSION

In the present study, we observed that in a period of 16 months, total 35 ADRs occurred affecting patients of either ender but the number was higher in males as compared to females. This does not comply with the statement that females are more sensitive to the effect of drugs as in comparison to males.[7] During the course of pharmacotherapy administered to the patient, short acting beta 2 agonist (levosalbutamol) as well as leukotriene receptor antagonist (montelukast) were found to be responsible for causing highest number of ADRs i.e. 10 (28.57%). These were followed by corticosteroids (budesonide) causing 17.14% and anticholinergics (ipratropium bromide) causing 14.28% of ADRs. Administration of antibiotics (amoxicillin) also resulted in 8.57% ADRs whereas only 2.85% ADRs were caused by alpha agonist (xylometazoline).

In our study, it was observed that administration of levosalbutamol by inhalational route in children resulted in palpitations, tremors, tachycardia, nausea/vomiting and rhinitis out of which palpitations were the most frequently accounted ADRs. Dose was decreased in one case of palpitations where as in case of rhinitis, metered dose inhaler (MDI) levosalbutamol was discontinued and a combination of levosalbutamol and ipratropium, bromide was administered via nebulization.

With the use of montelukast, pediatric patients reported headache as the most common ADR for which symptomatically treatment was given. These findings are consistent with a review article by Haarman et al (2017), which stated that headaches were most frequently reported to the Dutch database for both the whole population and children.[8] Other ADRs encountered due to administration of montelukast include cough, nausea/vomiting, upper respiratory tract infections, rhinorrhea and anorexia.

It was observed that administration of inhalational budesonide in children majorly resulted in sore throat and oral candidiasis. Anti-fungal therapy was given to manage oral candidiasis whereas for sore throat, patients and their parents were counselled to ensure oral hygiene after every inhalation.

Similarly, the most common ADR encountered with the use of ipratropium bromide was dryness of mouth (11.42%). Out of these 4 cases, 3 were mild reactions where as 1 was of moderate severity and was managed by discontinuation of ipratropium bromide. 3 cases of diarrhea were reported with the use of Amoxicillin, two of which were of moderate severity and resulted in discontinuation of amoxicillin. However, the milder reaction was only symptomatically managed by rehydration.

All drug related ADRs were evaluated for causality in accordance with Naranjo's scale as well as WHO-UMC scale. 42.5 % were found to be probable ADRs and 54.28 % as the possible ADRs. None of the reported ADRs were found to be fatal, life threatening or needed hospital admission for management.

CONCLUSION

Adverse drug reactions associated with anti-asthmatic drugs are quite common. This study highlights the incidence and pattern of ADRs associated with pharmacotherapy of pediatric bronchial asthma. As such, increased awareness regarding the occurrence of the adverse drug reactions among parents and the Health care professional may result in early detection of ADRs, their early reporting and minimize risk of ADR related harms.

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