

Research Article

Evaluation of Steroid Utilization in Management of Asthma in a Tertiary Hospital in Northern Nigeria

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Background: There are concerns about the rational use of corticosteroids in asthma as they are associated with serious adverse drug reactions, abuse and are rarely evaluated in clinical settings.

Objectives: The study set out to evaluate the drug utilization parameters of corticosteroids in the management of chronic asthma in Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.

Method: A Retrospective study employing structured data collection form to obtain data from randomly selected folders of 120 asthmatic out-patients in a tertiary health care facility between July 2011 and June 2012. Prescribing, facility and complimentary drug use indicators were analyzed using descriptive and Chi-Square statistics.

Results: Females accounted for 80% of study population, mainly housewives (51.6%). While 59.1% were aged 21-50 years. Mean number of drugs per prescription was 4.46 ± 0.098 . Generic prescriptions were 45.5% while antibiotics and injections were 30% and 28.4% respectively. The medications most utilized include inhaled Fluticasone/Salmeterol fixed combination in 71% and inhaled Salbutamol in 77.7% of patients respectively. Oral corticosteroid (prednisolone) was used in 25% of patient. The average cost per prescription was N5080 (\$31). There was no significant association between severity of asthma and use of inhalational steroids (Chi-Square $P > 0.05$), in contrast to a statistically significant difference ($P = 0.01$) in use of oral corticosteroids.

Conclusion: Sub maximal utilization of steroids in asthmatics as inhalational therapy was observed. Recommendations on the use of therapy that suit local conditions with respect to cost will promote adherence and ultimately improve rational drug use and outcomes in patients

Key words: Steroid Utilization, Chronic Asthma, Fluticasone/Salmeterol, Salbutamol

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1. Introduction

Asthma remains a major inflammatory disorder associated with a high cause of morbidity in our society, requiring optimal attention in the healthcare delivery. The prevalence of asthma has increased significantly since the 1970s and as of 2011, approximately 235 million people were affected worldwide (WHO, 2010) with a prevalence of 4.5% in 2011 (To et al, 2012). In

Africa, as at 2010 studies reveal an estimated 119.3 million people been affected (Adeloye et al, 2013). Despite international and national guidelines for the management of asthma, effective control of asthma continues to be a challenge especially in the developing and underdeveloped world. Asthma is a chronic inflammatory disease of the bronchial airways characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. The

burden of asthma affects patients and their families both socially and economically in terms of lost work and school, reduced quality of life, and hospital emergency department visits, hospitalizations, and deaths. However, with improved scientific understanding of the pathophysiology of asthma leading to recent advances in management, significant improvements in asthma care is been recorded.

The goal of asthma treatment is to achieve and maintain clinical control, which is the degree to which the manifestations of asthma are minimized by therapeutic intervention (NAEPP, 2007). According to the Global Initiative for Asthma (GINA), the goals of therapy been commonly assessed by reduced daytime and absence of night-time symptoms, improved level of activities and exercise tolerance, reduction in use of short acting β_2 agonist as reliever and improved lung function (GINA, 2010). Several advances have been made in the pharmacotherapy of asthma over the years and this has contributed to declines in asthma morbidity and mortality. Effective management of asthma requires the development of a partnership between the patient and healthcare professional. This is because adherence to medication plays a key role in asthma management which most times is basically achieved from effective counseling and education of patients about the disease, control of environmental factors and use of inhalational delivery devices. Recommendations for management of asthma also emphasize that care needs be adapted to local conditions, resources and available services (Bateman et al, 2008). However, asthma continues to pose a significant personal and economic burden (GINA 2006; NAEPP 2007). Evidence suggests that persistent airway inflammation is a characteristic feature of asthma and includes infiltration of the airway by inflammatory cells, hypertrophy of the smooth muscle, and thickening of the lumina reticularis. Effective management, therefore requires a correct therapeutic approach, which must interfere with the exaggerated inflammatory response of the airway (Cui, 2006). Clinical studies have shown that asthma can be effectively controlled by intervening to suppress and reverse the inflammation as well as treating the bronchoconstriction and related symptoms. In addition, recommendation states a change in approach to asthma management, with asthma control, rather than asthma severity, being the focus of treatment decisions, further reiterating the importance of control medications

Guidelines emphasize the use of inhaled corticosteroids either singly or in combination with long acting corticosteroids, for the management of chronic persistent asthma and the addition of oral corticosteroids if exacerbation is severe or if patient has history of previous severe exacerbations (Larj and Bleecker 2004; NAEPP, 2007). EPR-3 reaffirms that patients with persistent asthma need both long-term control medications to control asthma and prevent exacerbations and quick-relief medication for symptoms, as needed. Inhaled corticosteroids are considered the most potent and effective long term control treatment across all age groups. They have been documented to reduce asthma severity and symptoms, improve lung function, prevent exacerbation and reduce emergent health services utilization and reduce the risk of death. However concerns exist regarding the chronic use of steroids especially in children because of the

associated side effects. This is also coupled with the fact that poor adherence can be a cause of therapeutic failure. More so, studies have shown that overall adherence to inhaled corticosteroids (ICS) therapy is about 50% (Williams et al, 2004; Walders et al, 2005) and complex or frequent dosing regimens, cost of procuring ICS have also been associated with poor adherence.

The rational use of steroids in clinical setting for the management of asthma is therefore very important as it is employed in patients who may be at high risk of adverse drug reaction and is a critical component of care for asthmatic patient and is also most effective when used in specific ways i.e. as ICS. Its use can be quite expensive leading most times to sub optimal utilization with a consequent negative effect on patient outcome. For the purpose of assisting health care systems to understand, interpret, and improve the prescribing, administration, and use of steroids, drug utilization reviews (DUR) are necessary. In addition the WHO requires that the pharmaceutical sector be monitored and assessed regularly using DUR (WHO, 2010). In view of the above, steroidal medications requires constant monitoring, dose titrations and evaluations when used clinically, with the aim of making interventions to improve rational use for maximal benefit to patients.

The aim of this study was therefore to evaluate the drug utilization parameters associated with use of corticosteroids in the management of chronic asthma in department of medicine in a tertiary health facility.

2. Methodology

2.1 Study site and study design

A retrospective drug utilization evaluation conducted in the medical outpatient clinic in Ahmadu Bello University Teaching Hospital, Zaria, in northern Nigeria over a one-year period between July 2011 to June 2012.

2.2 Study population and eligibility criteria

Both males and females outpatients who had been diagnosed with asthma and attended the respiratory clinic regularly during the one year period were included in the study. Patients who were not regular with scheduled clinic visits were excluded from the study.

2.3 Sample size and sampling procedure

The target sample size was estimated using Slovin's formula. Case files of 120 asthmatic outpatients who met the eligibility criteria were randomly selected.

2.4 Data collection

A structured data collection form was designed and used to obtain data from the case files of the selected patient which included demographics, prescribing, facility and complimentary drug use indicators and details of drug usage. Lung functions as assessed by Peak expiratory flow rates (PEF) and forced expiratory volume (FEV1) were used to group patients into classes of severity of asthma presentation.

2.5 Data Analysis

The WHO recommended procedure for drug utilization evaluation was employed to analyze the drug-use parameters for the disorder (WHO, 1993). All data obtained was entered into the Statistical Package for Social Sciences (SPSS) version 11 soft ware which was used for all the statistical analysis.

Results of the study were expressed as mean and percentage (%). The differences between variables were analysed using Chi-Square test. P values of 0.05 or less were considered statistically significant.

2.6 Ethical Considerations

Ethical approval was obtained from the Department of Medicine of the Ahmadu Bello University, Nigeria.

3. Results

3.1 Demographics of study subjects

In this study, 59.16% of the population was aged 21-50years and 4.2% of patients above 70years. Females accounted for 80% of the patients and were mainly housewives (51.7%), while 16.7% were students and 15% civil servants (**Figure 1**).

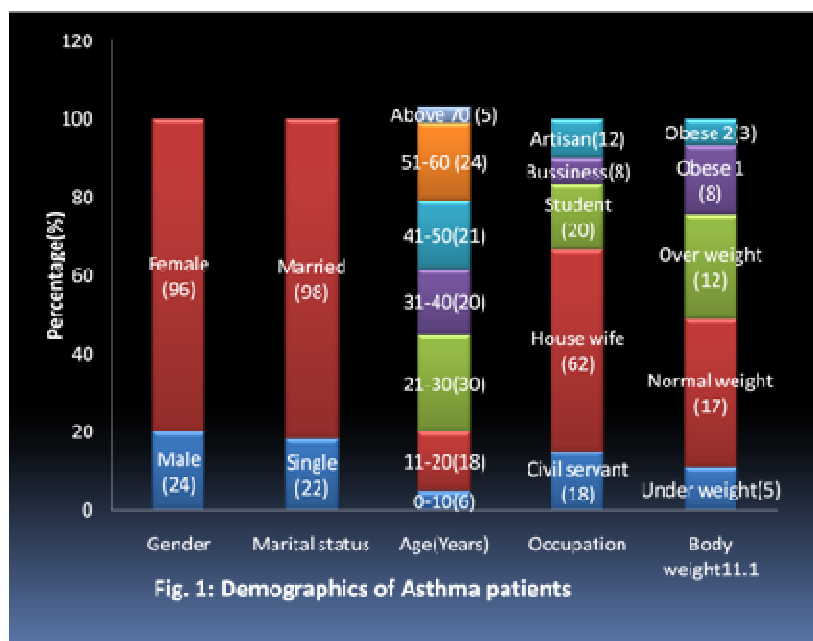


Figure 1: Demographics of Asthma Patients

Table 1: Prescribing indicator data

Core Indicators	N	n (%)
Total number of drugs prescribed	2006	
Average number of drugs per prescription	4.46±0.098	
Number of encounters with an injection		570 (28.4%)
Number of drugs prescribed from EDL		1204 (60%).
Number of encounters with an antibiotic		602 (30%)
Number of drugs prescribed by generic name		9126 (45.5%)
Number of drugs prescribed by Proprietary name		1094 (54.5%)

Table 2: Facility and complimentary indicators

Core Indicators	N	%
Av. Cost per prescription	N5080	
Drugs with dosage form indicated	1526	76.1%
Drugs with frequency of administration indicated	1431	71.3%
Drugs with duration of therapy indicated	1847	92.1%
Availability of EDL	Yes	
Key drugs availability		100%

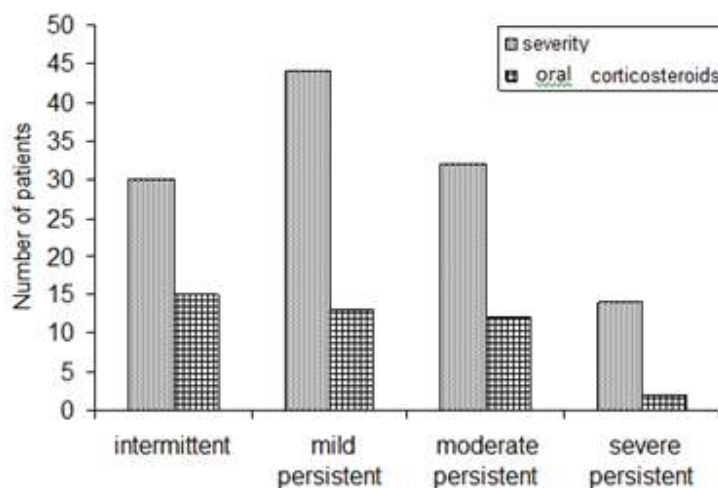


Figure 2: Asthma Severity in Patients and the Use of Oral Corticosteroids

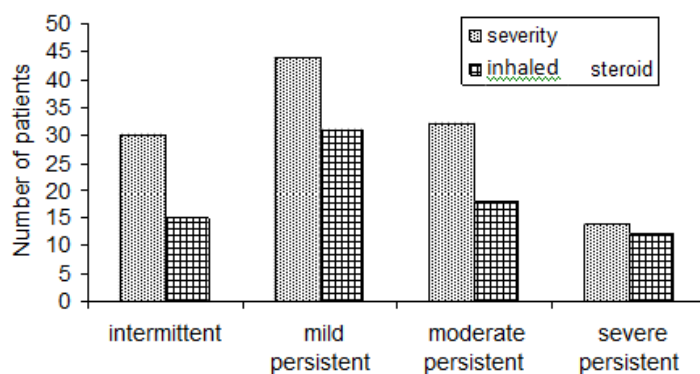


Figure 3: Asthma Severity in Patients and the Use of inhalational Corticosteroids

Table 3: Anti-asthma medications prescribed

Drugs	Number of prescriptions	%
Salmeterol/Fluticasone inhalation	420	71%
Salbutamol inhalation	460	77.7%
Aminophylline injection	33	5.6%
Hydrocortisone injection	33	5.6%
Salbutamol tablets	98	16.6%
Prednisolone tablets	184	31.1%
Antibiotics	29	4.9%
Antihistamines	54	9.1%
Others	29	4.9%

3.2 Prescribing drug Indicators

The average number of drugs per prescription was 4.46 ± 0.098 , with a total of 2006 drugs from 592 prescriptions. Prescriptions for Injections and antibiotics were 28.4% and 30% respectively. Drugs prescribed generically accounted for 45.5% of the prescriptions (Table 1).

3.3 Facility and Complimentary Drug Indicators

The average cost per prescription was N5080 (\$31). The recent copy of the essential drug list was available in this facility, but only 60% of the drugs prescribed were from the EDL. However, all key drugs prescribed were available in this facility (Table 2).

3.4 Medications Prescribed For Asthmatic Patients

Inhaled corticosteroids (fluticasone) and long acting beta 2 agonist LABA (salmeterol) fixed combination accounted for 71% of prescriptions, while short acting beta 2 agonist SABA, (salbutamol) as inhalation was seen in 77.7% of prescription. Parenteral aminophylline and hydrocortisone as emergency medications

accounted for 5.6% of prescriptions respectively. Oral medications prescribed include salbutamol (16.67%), prednisolone (31.1%), antibiotics (4.9%) and antihistamines (9.1%) (Table 3).

3.5 Utilization of Inhalational and Oral Steroids with Respect to Degree of Asthma Severity

Inhaled and oral corticosteroid was prescribed for both patients with intermittent asthma and across the different classes of persistent asthma. No significant difference was seen ($p > 0.05$) comparing the use of inhaled steroids against level of asthma severity across the classes. However about 80% of patients with severe persistent asthma had prescription for inhaled corticosteroid. Conversely there was a significant difference seen ($p = 0.01$) comparing the use of oral corticosteroids in severe persistent asthma against other classes (Figure 2 and 3).

3.6 Co-morbid Diseases in Asthmatic Patients

Co morbid diseases were seen in 69.16% of the studied population, with 41.66%, 18.33%, 9.16% having one, two and three other comorbid diseases respectively. Hypertension was seen in 40% of the patient, chronic obstructive pulmonary disease in 23% and Lower respiratory tract infection (pneumonia) in 10% of the patients (Table 4).

Table 4: Co-morbid Disease(s) in Asthma Patients

Co-morbid Diseases	Frequency	Multiple Co-morbid Diseases (n)	
A. Hypertension	17	A+B (8)	A+B+E (2)
B. Diabetes	5	A+E (4)	A+D+E (4)
C. Peptic Ulcer	4	A+C (4)	A+C+E (3)
D. Pneumonia	4	A+D (3)	A+E+RA (2)
E. COPD	10	D+E (3)	

4. Discussion

During the past two decades, many scientific advances have improved our understanding of asthma and our ability to manage and control it effectively. However, in a current review of studies of asthma management across Europe and the United states, Sims et al (2011) concludes that in spite of international and national guidelines, poor asthma control still remains an issue. In a synopsis of asthma research in Nigeria, asthma care was seen to be inadequate and the level of control sub optimal despite current management guidelines (Ozoh and Bamidele 2012).

Poor asthma control will always hinder activities which ultimately will reduce school time, man-hours and productivity. In this study, the disease was seen to be more predominant in the working class age group. Poor control in this group of patient will definitely have a negative impact on the economy not only in the present but also in the future. With proper management and effective control, restoration of proper lung function is

ensured which improves the quality of life of the patient and increase productivity.

The study also revealed more female patients (80%), mainly housewives (51%) and in their reproductive ages. This confirms reports of asthma prevalence in females than in males as was also seen in a study by (Schartz and Camargo, 2003) were female – male ratio was 65-35 within the age 23-64yrs. Majority of patients could not afford the cost of their medications {average cost of prescription been N5080 (\$31)} especially the inhaled corticosteroid and long acting β_2 agonist (ICS/LABA) combination and resolved most times to oral corticosteroids. Guidelines emphasize the daily use of inhaled corticosteroids (ICS), but ensuring adherence to daily use of ICS continues to be a challenge in developing countries due to cost. It has however been emphasized, due to the diversity of healthcare systems, cost and availability of asthma therapies, that recommendations for asthma care be adapted to local conditions throughout the global community (Bateman et al, 2008).

Mean number of drugs per prescription (4.46 ± 0.098) is similar to observations from previous studies. Pandey and Tripathi (2010) reported multidrug therapy prescription in 81% of patients, with other hospital based studies reporting 3-5 drugs per prescription (Maini et al, 2002). This prescribing trend may be attributed to the presence of other co morbid diseases and the most often use of antibiotics and antitussives in asthma patients. Injections (hydrocortisone) were mostly used in emergency cases to achieve prompt control of asthma attack. About one third of prescriptions included antibiotics, this is evident from the number of patients who were diagnosed with pneumonia and had to be managed effectively as there is mounting evidence concerning the impact of bacterial infection in asthma (Rollins et al, 2010). Price et al (2010) also reported in a matched analysis that 19% of patients with mild to moderate asthma had received antibiotics for a lower respiratory infection in a baseline year this is in comparison to 16% who received ≥ 1 acute courses of oral corticosteroids.

Generic prescriptions for asthma were low (45.5%) although these were mainly prescribed from the essential medicines list (EML). Branded prescription constituted mainly ICS/LABA as a combination device. The assessment group in the Appraisal committee of the NICE technology appraisal guidance 138, considered that in people for whom ICS/LABA treatment is appropriate, the least costly delivery method should be used, which is currently a generic combination device. Generic prescribing allows flexibility of stocking thereby increasing accessibility, availability and affordability of various brands of a particular drug. In addition, generic drugs are most often cheaper and equally effective as proprietary brands.

Prescriptions of salbutamol inhaler as metered dose inhaler (pMDI) were mostly seen in this study closely followed by by salmeterol/fluticasone inhaler as powdered dose inhalers (PDI) and pMDI. The case is similar to the study by Rajathilagam et al (2012) who in a drug utilization study in asthma showed short acting β_2 agonist and Fixed dose inhalational therapy with long-acting Beta2 agonist and corticosteroids as most

frequently prescribed. This result is in line with the stepwise management of asthma (NICE) which recommends the use of inhaled short acting B2 agonist in the management of mild intermittent asthma and as relieve medication in other classes of asthma. More so, inhalational medications are safest in asthma with advantages of smaller doses, targeted delivery, rapid action and minimal systemic side effects (Homer, 2009). The combination of ICS and LABA enables the simplification of the treatment of asthma for both patients and physicians, while effectively improving clinically relevant asthma outcomes such as decreasing asthma exacerbations and improving symptoms and airflow obstruction (Masoli et al, 2005).

The maintenance treatment in patients with asthma over the years has gradually evolved from inhaled corticosteroids alone to combination therapy with LABA instead of increasing the dose of the ICS. The utilization of ICS in this study followed the later pattern and there was no significant difference in the use of ICS/LABA as a combination therapy across the various classes of asthma presentation. Nevertheless, it is worthy of note that about 50% of patients with mild intermittent asthma were still prescribed ICS with LABA. This prescriptions were mainly to control exacerbations in patients but prescriptions continued thereafter and new research has shown that the millions of people who use corticosteroids prescribed daily to control mild asthma do no better than those who use them only when symptoms occur (Calhoun et al, 2012). In another study, investigators expressed the need to combine ICS with as-needed short-acting bronchodilators to increase patient's motivation to take ICS and improve asthma control but emphasized the need to focus ICS therapy on periods when symptoms of asthma are more pronounced (O'Connor and Reibman, 2012). Treatment option for the purpose of reducing patients' pharmacy costs, limit long-term exposure to corticosteroids and enable flexibility in managing the condition is to use the symptoms based assessment (SBA) approach. SBA reduces possible risks of long-term use of ICS, including accelerated cataract development, vocal cord weakness and potential endocrine effects (Calhoun et al, 2012).

Oral corticosteroids (prednisolone) were prescribed in more than one third of patients with mild/moderate persistent asthma and in 50% of patients with mild persistent asthma. The stepwise approach in asthma management (GINA executive report, 2006) indicates that the patient's current level of asthma control determines the selection of pharmacological agents to be used and only introduces oral steroids in the last step 5. Though, oral corticosteroids are very effective in achieving control of asthma in severe cases and during exacerbations by speeding the resolution of airflow obstruction and reducing the rate of relapse (Mark et al, 2010) their chronic use are limited due to systemic side effects. The statistically significant increase seen ($P=0.01$) comparing prescriptions of oral corticosteroids in severe persistent asthma with other classes clearly indicates non compliance to control medications prescribed to patients with mild and moderate persistent asthma. The frequency of severe exacerbations and uncontrolled asthma in these other groups of patients made physicians resolve to oral steroids. The challenges with adherence been largely

due to cost of ICS/LABA therapy as also seen in a study by (Oboh and Bamidele 2012), coupled with incorrect perception/ignorance. Wang et al (2007) in a study in China also reported similarly a poor adherence to ICS/LABA which he attributed to cost, anxiety about the potential side effects and difficulties in using the inhaler device. The burden and the overall cost of controlling asthma is high from the perspective of the patient and the society, but the cost of not treating asthma correctly and the implication is even higher (Accordini et al, 2006, Sullivan et al, 2007).

Hypertension and diabetes coexisted with asthma in 40% and 12.5% of the studied population further driving home the need for the rational use of steroids as these medications are known to be important risk factors in development and also aggravating these diseases. Also contributing to the burden of asthma in the studied population, was the presence of COPD and pneumonia as co morbid diseases and reports from Chen et al 2010 classifies this as major co-morbidities that are significant independent predictor of reduced general health status in the asthma patient. The use of ICS/LABA has also been emphasized in the management of COPD, further reiterating its benefits when used optimally and rationally in asthma/COPD co morbid conditions.

5. Conclusion

Utilization of steroids, following the GINA guideline was seen to be sub maximal. The cost of inhalational ICS/LABA therapy has been the major contributory factor to possible non-adherence in patient. However, outcome of therapy in patients could be enhanced if recommendations that management of asthma care be adapted to suit local conditions throughout the global community especially with respect to affordability and availability in developing nations. Patients' education and awareness about asthma and its management will also go a long way to prevent delays in initiating therapy, overuse of acute relief medications and underuse of maintenance /controller medications. In addition, adequate special patients counseling on use of inhalational devices for effective delivery of medications should be instituted across health care facilities to improve patients' compliance.

Conflict of Interest declaration

The authors declare no conflict of interest.

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