



Research Article

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Study of pattern of drug treatment in patients with exacerbations of bronchial asthma in an emergency ward of a teaching hospital: A prospective, cross sectional study

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ABSTRACT

Exacerbations of bronchial asthma is one of the common presenting complaints affecting all age groups. There has been a recent increase in the incidence of asthma with a parallel increase in the number of drugs available for its treatment. The present study was aimed at evaluating prescribing pattern of medications in exacerbations of bronchial asthma and to compare it with National Asthma Education and Prevention Programme (NAEPP) guidelines. This was a prospective, cross sectional, observational study in patients > 18 years of age, reporting with exacerbations of bronchial asthma. The demographic, disease and drug treatment data, was collected from each patient from the Emergency Medicine Ward [EMW] and was analysed descriptively. Total of 400 patients reporting at EMW with exacerbations of bronchial asthma were analyzed for disease profile and drug treatment aspects. Severity of exacerbation, based on NAEPP guidelines, 17% belong to severe, 52% moderate and 30% mild category. After initial treatment at EMW 34% patients were discharged, 64% got shifted to general ward for further treatment and 2% to Intensive care unit. Overall the use of salbutamol and ipratropium by nebulization was 100% and 80% respectively. Patients with severe and moderate exacerbation of asthma, non-responsive to nebulization in addition received systemic steroids with mask oxygen and I.V. theophylline. The use of alternative systems of medicine was seen among 17% and adverse drug reactions in 15% of patients. The drug treatment data was compared with NAEPP guidelines. In the present study drug treatment pattern for exacerbations of asthma did not match completely with NAEPP guidelines. Therefore there is a need to bring awareness among physicians about NAEPP treatment guidelines. Also the influence of concomitant use of alternative systems of medicine will need further evaluation.

Key Words: Bronchial asthma exacerbations, emergency ward, NAEPP guidelines, nebulization, prescribing practices.

INTRODUCTION

Bronchial asthma, a chronic inflammatory disease of airways, is characterized by increased responsiveness of the tracheo-bronchial tree to multiple stimuli manifested as recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night/early morning. From an etiologic standpoint, asthma is considered as a heterogeneous disease with genetic and environmental factors contributing to its initiation and persistence. According to World health organization(WHO) estimates worldwide 300 million people suffer from asthma[1]. In India, 15-20

million people are affected by bronchial asthma. But it is unclear if this is due to an actual increase in the incidence or merely due to the growing size of the overall population [2,3].

Exacerbations of bronchial asthma is one of the common presenting complaints in an emergency medicine ward of a hospital and is a major economic and health burden. Exacerbations of asthma are acute or subacute episodes of progressively worsening shortness of breath, cough, wheezing and chest tightness. Precipitating factors include allergens to which he/she is sensitized, pulmonary infections especially those caused by viruses, cold, physiological stress, exercise and inhaled irritants [4]. Worldwide, approximately 2,55,000 deaths annually are attributable to asthma and are largely preventable, frequently being related to poor management [5].

The expert panel report on the national asthma education and prevention program 2007 has published useful algorithms on the management of acute exacerbations of asthma depending on severity. NAEPP recommend – supplemental oxygen to relieve hypoxemia in moderate and severe exacerbations, short acting beta-2 agonist [SABA]-salbutamol nebulization to relieve airflow obstruction for all patients, addition of ipratropium nebulization in severe exacerbations. Systemic corticosteroids by oral route to decrease airway inflammation in moderate, severe exacerbations and also for patients with mild exacerbations who fail to respond prompt and completely to SABA [6]. Expert panel does not recommend methylxanthine for asthma exacerbations. The use of such standard treatment guidelines for exacerbations of bronchial asthma at the emergency department setting is reported to reduce admissions to both general medical units and at the intensive care unit, decreasing the length of stay, the number of return visits in the next 48 hours, reduce treatment costs and have better prognosis during the post discharge period [7].

The study of prescribing practices as a part of drug utilization studies, has therefore been introduced as a simple tool to assess and evaluate not only rationality in therapeutic practices but to improve use of medications and also to evaluate the cost effectiveness of health and medical care. The quality of medical care requires prescribing to be judicious, appropriate, safe, effective and economical. The aim is to achieve clinical benefit with minimum risk at a cost effective price while respecting the patient choice [8,9].

However, to the best of our knowledge, In India no studies have been conducted in the past to evaluate the prescribing pattern of drugs in exacerbations of bronchial asthma in an emergency ward of a teaching hospital. The present study was therefore designed to examine the same and compare it with NAEPP guidelines for exacerbations of bronchial asthma.

EXPERIMENTAL SECTION

The study was prospective and was carried out at St Johns Medical College Hospital, Bangalore. After obtaining approval from institutional ethics committee, patients admitted to emergency ward with exacerbation of bronchial asthma, above 18 yrs of age, who gave informed consent were considered for the study. Data was collected from patients case sheet details and also by examining the patient wherever necessary. The sample size was 400 patients

Following data relevant to study protocol was collected -

- *Demographic data* – age, sex, address, outpatient / inpatient number, date of admission and date of discharge of the patient.
- *Disease data* - frequency of exacerbations of asthma, severity category of exacerbation of asthma according to NAEPP guidelines [6], coexisting illnesses such as – Gastro-oesophageal reflux disease, allergic rhinitis, respiratory tract infections, diabetes mellitus, hypertension etc.
- *Drug data* - drugs prescribed, dose, frequency, route of administration, duration, both for asthma and coexisting illnesses.
- *Investigational data* - investigations such as routine chest x-ray, ECG, Oxygen saturation by pulse oximetry-SaO₂, Pulmonary Function Tests etc.
- *Immediate Adverse Drug Reactions [ADRs]* - related to Cardiovascular System, Central nervous System, Gastrointestinal tract etc. along with treatment for ADRs.

The data was collected till the patient was discharged from EMW or when shifted to general medical ward.

Statistical analysis

Data was analyzed using descriptive statistics namely mean, standard deviation and percentage. Statistical software SPSS 15.0 was used. Categorical variables were analyzed using Chi square test for gender wise distribution. Microsoft Excel was used to generate graphs and tables.

RESULTS

A total of 400 patients with exacerbation of asthma were analyzed for disease profile and drug treatment aspects. Table 1, shows age and gender wise distribution of patients with exacerbation of asthma admitted to Emergency Medicine Ward. There were more number of males as compared to females across all age groups but with no significant statistical difference ($p = 0.653$), by Chi-square test. Seasonal variation in the number of exacerbations of asthma showed more number (41%) of admissions during June-August.

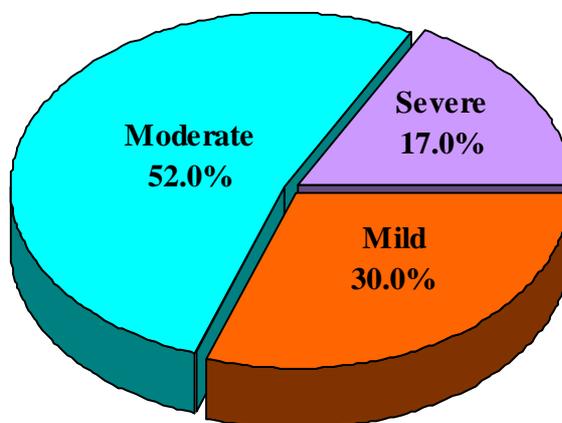
Table 1 : Age and gender wise distribution of percentage of patients with exacerbation of asthma (n=400)

| Age in Yrs | Males (n) | Percentage (%) | Females (n) | Percentage (%) | Total (n) | Percentage (%) |
|--------------|------------|----------------|-------------|----------------|------------|----------------|
| 18-28 | 79 | 35.9 | 61 | 33.9 | 140 | 35.0 |
| 29-38 | 35 | 15.9 | 25 | 13.9 | 60 | 15.0 |
| 39-48 | 44 | 20.0 | 47 | 26.1 | 91 | 22.8 |
| 49-58 | 35 | 15.9 | 29 | 16.1 | 64 | 16.0 |
| 59-68 | 18 | 8.2 | 11 | 6.1 | 29 | 7.3 |
| 69+ | 9 | 4.1 | 7 | 3.9 | 16 | 4.0 |
| Total | 220 | 100.0 | 180 | 100.0 | 400 | 100.0 |

Gender distribution: $p = 0.653$

The distribution of patients based on severity of exacerbations according to NAEPP 2007 guidelines showed 17% severe, 53% moderate and 30% of mild category [Figure 1].

Figure 1: Number and percentage of patients with asthma exacerbations based on severity (n=400)



Most common co-morbid conditions associated with asthma were allergic rhinitis (46%) and gastro-esophageal reflux disease(29%).

The extent and pattern of drugs co-administered with anti-asthma medications for co-existing medical illnesses showed – anti-histaminics for allergic rhinitis(30%), anti-peptic ulcer drugs for GERD(26%), followed by anti-microbial drugs for respiratory tract infections(22%), anti-diabetics(15%), anti-hypertensives(12.5%) and anti-epileptics (1%). The pattern of use of antimicrobials revealed maximum use of third generation cephalosporins in 11% , followed by penicillins in 7% and macrolides in 4% of patients.

While, 34% patients were discharged from EMW, 64% got shifted to the general ward for further treatment and 2% got transferred to the Intensive Care Unit. There were no deaths reported due to exacerbation of asthma while at EMW [Figure 2].

Figure 2: Outcome of initial treatment in patients with acute bronchial asthma at emergency department (n=400)

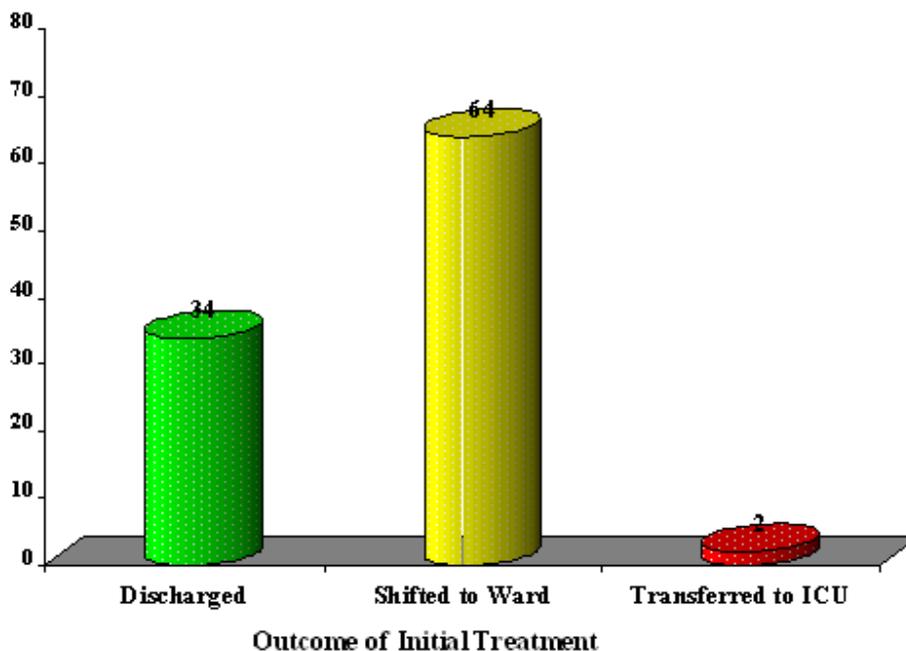


Table-2 shows the anti-asthma drug treatment data for acute exacerbation of asthma

Table 2: Pattern of use of anti-asthma medications in exacerbation of bronchial asthma based on severity (n=400)

| Severity | No of Patients | SAL Neb | IPR Neb | STR IV | THEO Inj | Oxygen |
|----------|----------------|------------|-------------|-------------|----------|--------------|
| Mild | 120 | 120 (100%) | 54 (45%) | 15 (12.5%) | 00 (0%) | 15 (12.5%) |
| Moderate | 212 | 212 (100%) | 198 (93.2%) | 201 (94.8%) | 3 (1.4%) | 212(100%) |
| Severe | 68 | 68 (100%) | 68 (100%) | 68 (100%) | 17 (25%) | 68 (100%) |
| Total | 400 | 400 (100%) | 320 (80%) | 284 (71%) | 20 (5%) | 295 (73.75%) |

SAL-Salbutamol, IPR-Ipratropium Bromide, STR- Steroids, THEO-Theophylline,
Neb-nebulization Inj. -injection IV- intravenous

The use of alternative systems of medicine was acknowledged in 17% of patients in addition to the above anti-asthma medications

The immediate adverse drug reactions[ADRs] were observed in 15% of the patients and the most common reactions reported were - tremors (4%), followed by palpitation (3%), vomiting (3%), dry mouth (2%), nervousness (2%) and the least was ankle edema (1%).

Table 3: Adverse drug reactions profile (n=400)

| Adverse drug reaction | Number of patients | % |
|-----------------------|--------------------|----|
| Tremors | 16 | 4% |
| Palpitation | 12 | 3% |
| Vomiting | 12 | 3% |
| Dry mouth | 8 | 2% |
| Nervousness | 8 | 2% |
| Ankle edema | 4 | 1% |

DISCUSSION

The present prospective, observational drug utilization study [DUS] on pattern of drug use for exacerbation of asthma was carried out for one year among 400 patients admitted to an Emergency Medicine Ward [EMW]. The gender distribution of exacerbation of asthma did not show significant difference between male and female patients. Also, the gender equality was seen when analyzed for age-wise distribution of patients. There were maximum number of patients with exacerbation of bronchial asthma reported during June-August period (42%). This finding correlates well with the fact that 60% of the bronchial asthma exacerbations in adults are due to viral respiratory tract infections which are reported to be the most common among stimuli that evoke exacerbation of asthma [10,11]. It is documented that June-August period being the rainy season, viral respiratory tract infections are more common. The data for evaluation of severity of exacerbation of asthma using NAEPP guidelines [6] revealed, highest number of patients with moderate severity (53%) followed by mild (30%) and severe (17%). Such clinical classification based on the severity of exacerbation of asthma is very important to decide whether the patient can be managed at home or needs to be hospitalized or he/she is to be admitted to an intensive care unit with or without ventilator support and also such analysis of severity of exacerbation of asthma enables the clinician to select appropriate therapy.

In the present study, most common co-morbid conditions associated with asthma were allergic rhinitis 46% followed by gastro-oesophageal reflux disease (GERD) 29%. This observation matches well with established literature wherein epidemiological evidence suggests that about one fourth of the asthmatics have GERD [12,13]. Reflux vagal broncho-constriction secondary to stimulation of sensory nerve fibres in the lower oesophagus and micro-aspiration during sleep are the two proposed mechanisms for such coexistence. Allergic rhinitis and bronchial asthma are considered as one airway and one disease. It is estimated that 40-70% of patients who have asthma also have coexisting allergic rhinitis [14]. In this respect findings of the present study matches to that quoted in literature. Therefore, it is suggested that such coexistence of illnesses could be considered during diagnosis for appropriate monitoring as well as selection of rational drug combinations with anti-asthma medications.

In our study all patients in three categories- mild, moderate, severe exacerbation of asthma received salbutamol nebulization. Salbutamol is the preferred SABA (Short acting beta-2 agonist) because it has an excellent safety profile. Rapid reversal of airflow obstruction is best achieved by repetitive administration of salbutamol nebulisation which is medication of first choice and life saving [15,16]. Expert panel report on the national asthma education and prevention programme 2007 recommends SABA (salbutamol) by inhalation route for all patients irrespective of severity of asthma exacerbations [6].

In our study we found a direct correlation between the use of ipratropium nebulization and severity of exacerbation of asthma. But NAEPP guidelines recommend combined use of ipratropium nebulisation with salbutamol nebulisation only for severe exacerbation of asthma. Adding ipratropium bromide to selective SABA produces additional bronchodilatation particularly in severe exacerbations [17]. The anticholinergics ipratropium nebulisation mainly relax larger airways and facilitate the entry of salbutamol which relax smaller airways [18]. Evidence is lacking for anti-cholinergics producing added benefit in mild and moderate exacerbations [19].

The use of both salbutamol and ipratropium was by nebulisation in the present study. The same seems justified in acute exacerbations as the onset of action by nebulisation is rapid, smaller doses are adequate, less side effects while duration of action is similar to oral therapy [20].

In our study patients with exacerbation of asthma received corticosteroids (hydrocortisone) by intravenous route. But NAEPP guidelines recommend corticosteroids (prednisolone) by oral route to patient who have severe and moderate exacerbations and also for patients with mild exacerbations who do not respond completely to initial SABA therapy. Corticosteroids by oral route is reported to be as effective as intravenous route and is less invasive [21]. Also corticosteroids by nebulization route take seven days for onset of beneficial effect as against four hours by systemic route. Corticosteroids speed the resolution of airflow obstruction and reduce the rate of relapse following an acute exacerbation [22].

In our study we found out that the use of IV methyl-xanthines (theophylline) was least and was mainly used for severe asthma exacerbations. It is reported that there is no added advantage of IV methylxanthines when used in addition to the standard treatment protocol for exacerbation of asthma [23]. Also xanthines are known to have a

narrow margin of safety, increase the frequency of adverse effects and hence their use has significantly declined in the recent past [18]. Further NAEPP guidelines do not recommend use of methylxanthines for exacerbation of asthma.

All patients in severe and moderate category and 12.5% in mild category received mask oxygen. A finding similar to the recent guidelines which recommends oxygen inhalation 1-3 litres/min in severe, moderate exacerbations to achieve SaO₂=90%. Also in mild category when oxygen saturation falls below 90% [24].

In the present study out of 400 patients who were admitted to emergency department with exacerbation of asthma, after initial treatment only 136 patients (34%) were discharged home. The remaining patients are shifted to ward. On the contrary 70 to 80% of the patients in western studies were discharged home after initial treatment at emergency department [25]. The observed difference in our hospital may be because of factors such as inadequate control of concomitant diseases viz diabetes, hypertension when they arrive at emergency department with exacerbation of asthma, fear of relapse, lack of immediate transport and medical facility if relapse occurs may force the patients to continue to be hospitalized. The data on this aspect was not collected in the present study.

The previous studies have documented that patients with asthma use concomitant alternative systems of medicine because of dissatisfaction with conventional medicine, perceived harmful effects of conventional treatment, desire for a more holistic approach and greater philosophical congruence with complementary therapies but have not stood the test of controlled clinical trials [1,26]. The concomitant use of such therapy was acknowledged by 17% of patients in our study. The prevalence of use of complementary therapy for asthma is reported to vary from 6% to 70% depending on the methodology used in the study [27]. There is limited research that has been done on this aspect and explains the paucity of information on outcome of such therapy. It is therefore recommended that the concurrent use of alternative systems of medicine with modern medications should preferably be avoided until further research has been carried out to justify such use. It is not clear if such combination may result in frequent exacerbations of asthma.

The results of the present study showed that none of the patients during treatment for exacerbation of asthma had serious adverse effects requiring prolonged hospitalization or events leading to withdrawal of treatment or increased mortality. The observation that 15% of patients in our study reported drug related ADRs in contrast to most studies that reported a value of 28% [28,29]. Most common ADRs included tremors followed by palpitation, vomiting, dry mouth, nervousness and the least common was ankle edema. These were managed mainly by dosage adjustment as none were serious when compared to acute asthma and were well documented dose dependant reactions.

CONCLUSION

The findings of the present study showed that even though there was no mortality that was encountered with the treatment given, the emergency ward physicians did not fully adhere to NAEPP guidelines for management of exacerbation of asthma. Hence, there is a need to bring awareness about NAEPP guidelines among physicians involved in treatment of exacerbation of asthma. Also larger number of patients were reported to follow concomitant treatment with Alternative Systems of Medicine along with modern medications. It is not clear if this may contribute to exacerbations of acute attacks. It may therefore be suggested that further studies are necessary to investigate into outcome of treatment of such combinations, as this appears to be a poorly explored area from pharmacological view point.

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