

DRUG UTILISATION STUDY IN BRONCHIAL ASTHMA IN A TERTIARY CARE HOSPITAL

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ABSTRACT:

A prospective cross-sectional study was done for 5 months (January- May 2011) in the respiratory medicine outpatient department of SRM Medical College Hospital & Research Center, SRM university, Tamil Nadu to evaluate the drug utilization pattern in patients of bronchial asthma. The prescription data of 125 asthmatic patients was analyzed in this study. Allergic factors have seen to be responsible for precipitating asthma in 48% of patients. All the patients received multiple drug therapy at an average of 3.632 drugs per patient. Short acting β_2 agonists were the most commonly prescribed group of antiasthmatic drugs (68%) followed by methylxanthines (66.4%), antihistaminics (38.4%), leukotriene receptor antagonists (1.6%) and oral corticosteroids (2.4%). Inhalational therapy was prescribed to 50.4% of patients. Antiasthmatic drugs given as inhalational therapy are more beneficial to the patients than systemic therapy. Hence, their maximum utilization in asthmatics will also go a long way in minimizing the incidence of acute asthma as well as the adverse effects of antiasthmatic drugs.

Keywords: Bronchial asthma, short acting β_2 agonists, leukotriene receptor antagonist, corticosteroids, inhalational therapy.

[I] NTRODUCTION

Asthma is a chronic inflammatory disorder of the airways characterized by bronchial hyper responsiveness and airflow limitation [1,2]. The symptoms of asthma include recurrent episodes of wheezing, breathlessness, chest tightness and cough [1]. The characteristic pathophysiological changes in asthma involve several inflammatory cells and mediators that contribute to symptoms. Structural cells of the airways also produce inflammatory mediators, and contribute to the

persistence of inflammation in various ways. Over 100 different mediators are now recognized to be involved in asthma and the key mediators are chemokines, leukotrienes, cytokines, histamine, nitric oxide and prostaglandins [3,4]. The goal of asthma treatment is to achieve and maintain clinical control. 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. Medications to treat asthma can be classified as

controllers or relievers. Controllers are medications taken daily on a long-term basis to keep asthma under clinical control chiefly through their anti-inflammatory effects. They include inhaled and systemic glucocorticoids, leukotriene receptor antagonists, long-acting inhaled β_2 -agonists in combination with inhaled glucocorticoids, sustained-release theophylline, cromones, anti-IgE, and other systemic steroid-sparing therapies [5,6]. Inhaled glucocorticoids are the most effective controller medications currently available.

Relievers are medications used on an as-needed basis that act quickly to reverse bronchoconstriction and relieve its symptoms. They include rapid-acting inhaled β_2 -agonists, inhaled anticholinergics, short-acting theophylline, and short-acting oral β_2 -agonists [3]. Thus these medications that control and relieve asthma can be used for prophylaxis and treatment of acute episodes.

[II] AIM/OBJECTIVE

To evaluate drug utilization pattern in bronchial asthma at a tertiary care hospital in Chennai, India.

[III] MATERIALS & METHODS

Study design- Prospective, observational, cross sectional study.

The study was done in the respiratory medicine outpatient department of SRM Medical College Hospital and Research Centre. A prospective cross-sectional study was done for 5 months (January- May 2011) after getting approval from the institutional ethical committee. The prescriptions of all the patients attending this outpatient department were noted down after taking verbal consent from them.

Inclusion criteria

All adult patients of bronchial asthma attending the respiratory medicine outpatient department were included in this study.

Exclusion criteria

Inpatients and acute severe cases of bronchial asthma, COPD patients and children were excluded from this study.

The collected data was analyzed to calculate the Prescribing indicators & Patient indicators.

Prescribing indicators includes:

- a) Average number of drugs prescribed per patient.
- b) % of encounters (prescription) with an antibiotic prescribed.
- c) % of encounters (prescription) with inhalational therapy prescribed.

Patient indicators:

- a) Average age of men
- b) Average age of women
- c) Average age in years of all patients
- d) Men to women ratio
- e) Average duration of bronchial asthma in years.
- f) Average duration of bronchial asthma in men.
- g) Average duration of bronchial asthma in women.
- h) Precipitating factors for asthma (% of patients).
- i) Grading of asthma severity (% of patients).
- j) % of patients with family history of asthma.
- k) % of patients with occupational history.

[IV] RESULTS

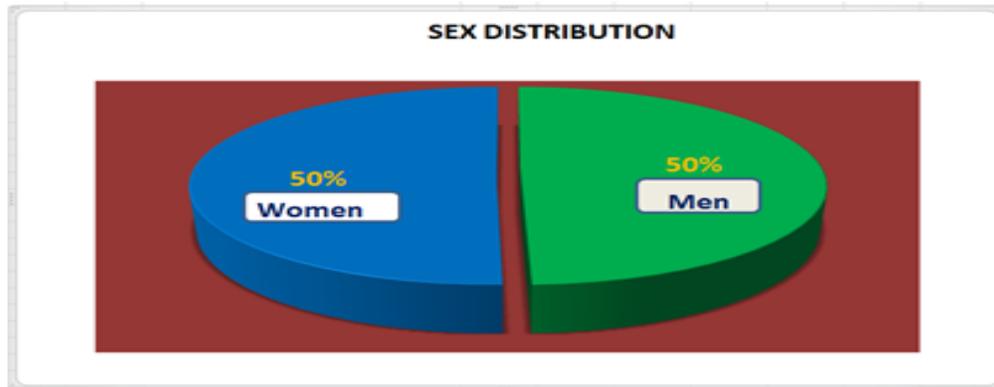
The prescription data of 125 asthma patients was analyzed.

62 (49.6%) of the patients were men and 63 (50.4%) were women. [Table 1] [Figure 1].

Sex	n=125
Men	62 (49.6%)
Women	63 (50.4%)

Table 1: Sex distribution

Figure 1: Sex distribution



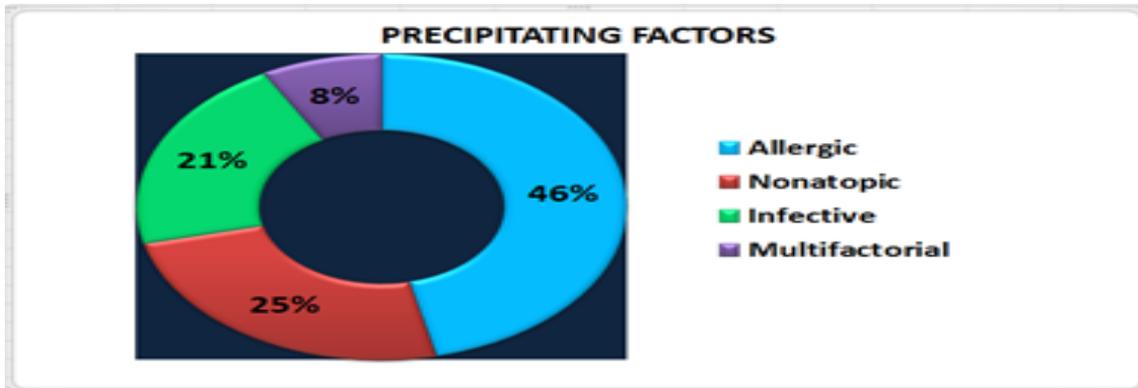
The men to women ratio was 0.98.
 The average age of all patients was 40.69 years.
 Average ages of men and women was 42.34 and 39.06 years respectively.
 The average duration of bronchial asthma in all patients was 5.37 years, being 5.4 and 5.3 years in men and women respectively.

The precipitating factor for asthma was seen to be allergic in 58 (46.4%), nonatopic in 31 (24.8%), infective in 26 (20.8%) and multifactorial in 10 (8%) patients. It was also seen that 9 (7.2%) patients had a family history of asthma and an occupational pre-disposition was present in 8 (6.4%) patients. [Table 2] [Figure 2].

Precipitating factors	n=125
Allergic	58 (46.4%)
Nonatopic	31 (24.8%)
Infective	26 (20.8%)
Multifactorial	10 (8%)

Table 2: Precipitating factors for asthma

Figure 2: Precipitating factors



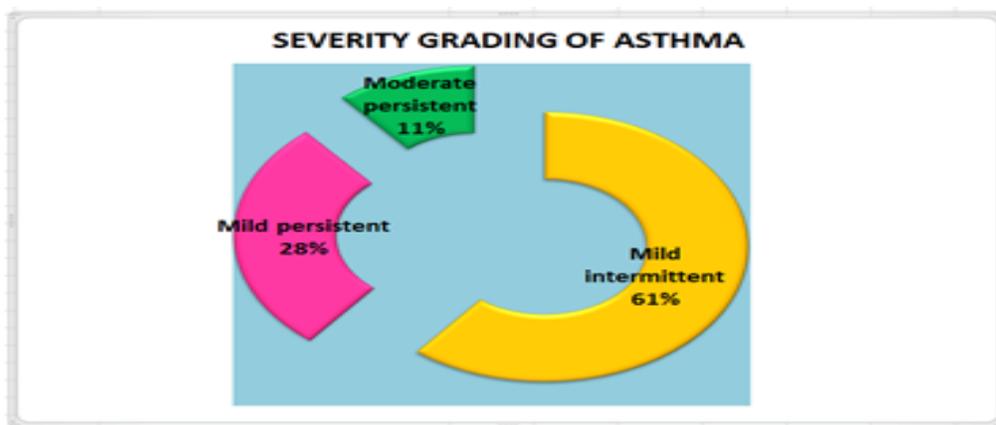
The Global Initiative for asthma (GINA) subdivided asthma by severity based on the level of symptoms, airflow limitation, and lung function variability into four categories: Intermittent, Mild Persistent, Moderate

Persistent, or Severe Persistent. In this study the severity of asthma was mild intermittent in 76 (60.8%) patients, mild persistent in 35 (28%) and moderate persistent in 14 (11.2%) of patients. [Table 3] [Figure 3].

Severity grading of asthma	n=125
Mild intermittent	76 (60.8%)
Mild persistent	35 (28%)
Moderate persistent	14 (11.2%)

Table 3: Severity grading of asthma

Figure 3: Severity grading of asthma



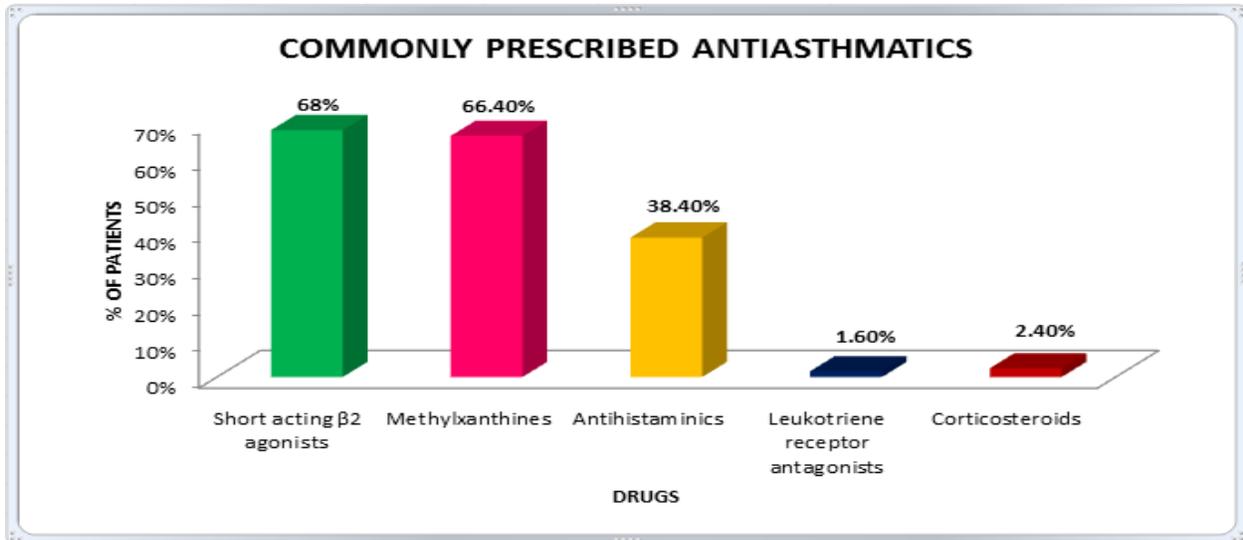
It has been seen that all the patients received multiple drug therapy at an average of 3.632 drugs per patient. Short acting β_2 agonists were the most frequently prescribed group of antiasthmatic drugs (85 patients) followed by

methylxanthines (83 patients), antihistaminics (48 patients), leukotriene receptor antagonists (2 patients) and corticosteroids (3 patients). [Table 4] [Figure 4].

Drug group	n=125
Short acting β_2 agonists	85 (68%)
Methylxanthines	83 (66.4%)
Antihistaminics	48 (38.4%)
Leukotriene receptor antagonists	2 (1.6%)
Corticosteroids	3 (2.4%)

Table 4: Commonly prescribed antiasthmatic drugs

Figure 4: Commonly prescribed antiasthmatic drugs



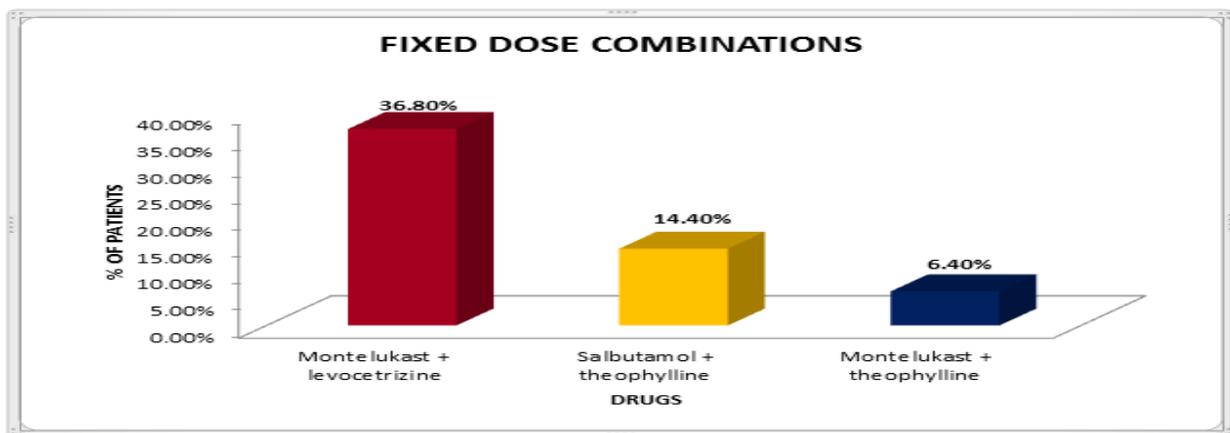
82 (65.6%) patients received antibiotics and 11 patients (8.8%) were prescribed multivitamins as adjuvant therapy. The antibiotics commonly prescribed included amoxicillin (41 patients), levofloxacin (38 patients) and azithromycin (3 patients).

In the fixed dose combinations, montelukast with levocetirizine was prescribed in 46 patients, (36.8%), salbutamol with theophylline in 18 patients (14.4%), and montelukast with theophylline in 8 patients (6.4%). [Table 5] [Figure 5].

Drug combination	n=125
Montelukast + levocetirizine	46 (36.8%)
Salbutamol + theophylline	18 (14.4%)
Montelukast + theophylline	8 (6.4%)

Table 5: Fixed dose combinations

Figure 5: Fixed dose combinations



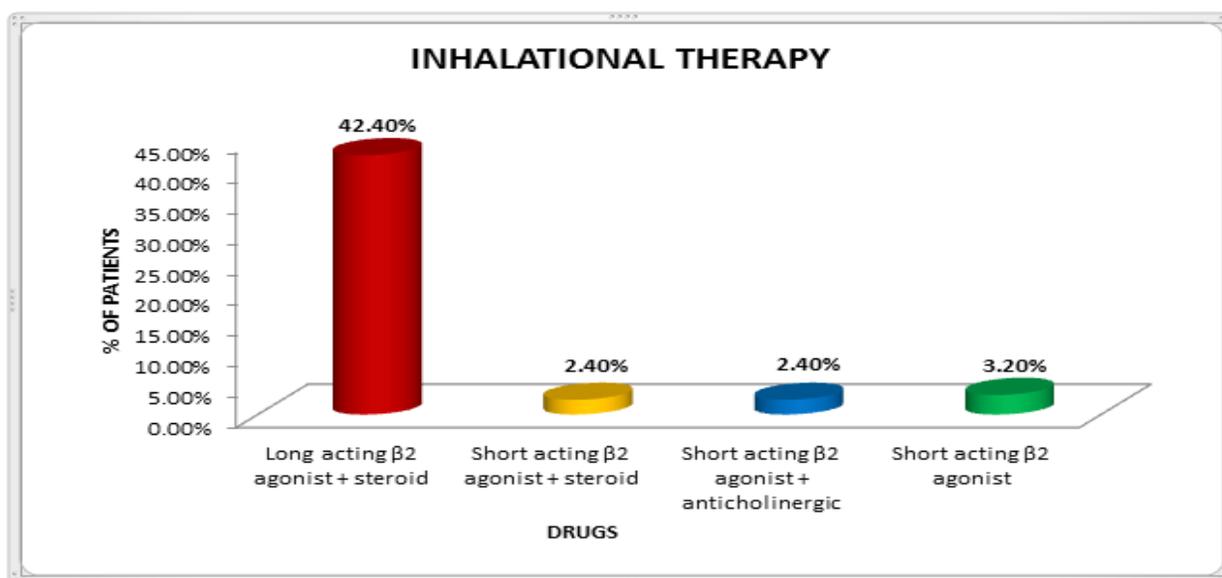
63 patients (50.4%) were prescribed inhalational therapy. It comprised mostly of long acting β 2 agonist with a corticosteroid preparation (53 patients). The other inhalational formulations

included short acting β 2 agonist along with corticosteroids or anti-cholinergic drugs in 3 patients each, and short acting β 2 agonist alone in 4 patients. [Table 6] [Figure 6].

Drug combination	n=63
Long acting β 2 agonist + corticosteroid	53 (42.4%)
Short acting β 2 agonist + corticosteroid	3 (2.4%)
Short acting β 2 agonist + anticholinergic	3 (2.4%)
Short acting β 2 agonist	4 (3.2%)

Table 6: Drugs used in inhalational therapy

Figure 6: Drugs used in inhalational therapy



[V] DISCUSSION

This study showed that all patients with bronchial asthma were prescribed multiple drug therapy at an average of 3.632 drugs per prescription. It is in contrast to a previous study in which only 81% of patients were prescribed multidrug therapy [2]. This prescribing trend may be attributed to the goals of asthma therapy to minimize chronic symptoms, to prevent recurrent exacerbations, to reduce the need for hospitalization and to maintain near normal

pulmonary function [1]. The pattern of drug utilization showed that drugs that provide symptom relief were prescribed more than the asthma controlling agents. Analysis suggested that doctors preferred the oral formulations than the inhalational preparations.

Among the oral preparations, short acting β 2 agonists (68%) were used to the maximum in the form of tablets and syrup. This observation is in par with the previous studies by Anil kumar et al and Awanish Pandey et al. But it is in contrast to

analysis by Arumugam et al and Vijayakumar et al where methylxanthines were frequently prescribed. Short acting β_2 agonists relax airway smooth muscle and inhibit release of bronchoconstricting mediators from mast cells. They may also inhibit microvascular leakage and increase mucociliary transport by increasing ciliary activity [7]. Even in recent times, short acting β_2 agonists are still highly preferred for asthma since they are the most effective bronchodilators which provide quick or “rescue” relief from acute asthma attacks [1,8].

Other than short acting β_2 agonists, methylxanthines (66.4%) antihistaminics (48 patients), leukotriene receptor antagonists (2 patients) and oral corticosteroids (3 patients) were also prescribed frequently. Methylxanthines represent a unique class of drugs for the treatment of asthma. They have demonstrated efficacy in attenuating the three cardinal features of asthma - reversible airflow obstruction, airway hyper-responsiveness, and airway inflammation. At lower serum concentrations, theophylline is a weak bronchodilator but retains its capacity as an immunomodulator, anti-inflammatory and bronchoprotective drug. Hence theophylline's predominant role in asthma treatment is as a controller medication for chronic, persistent disease. Phosphodiesterase inhibition and adenosine receptor antagonism by methylxanthines have both been implicated in promoting airway smooth muscle relaxation and bronchodilation [9,10]. Theophylline serum concentrations need to be monitored closely owing to the drug's narrow toxic-therapeutic range, individual differences in metabolism and the effects of many factors on drug absorption and metabolism [1]. Many clinical studies have shown that theophylline decreases the frequency and severity of symptoms, including nocturnal exacerbations, and decreases the “as needed” use

of inhaled beta-2 agonists. Several clinical studies have demonstrated that adding theophylline to inhaled corticosteroids in uncontrolled mild to moderate asthmatics gives equivalent or better asthma control than doubling the dose of inhaled corticosteroids [10]. Sustained release formulations of theophylline were mostly used in this study as they offer the advantages of less frequent drug administration, more consistent drug levels and are more effective in controlling nocturnal asthma [1,7]. Some patients were also prescribed a fixed dose combination of theophylline and salbutamol.

Second generation antihistaminic like levocetirizine was prescribed as an adjuvant drug in 38.4% patients. Cetirizine improves asthma symptoms, decreases rescue drug use and does not worsen pulmonary function parameters. Short term cetirizine has also some bronchodilatory properties [11]. Montelukast, a leukotriene receptor antagonist which represents an important advance in asthma therapy was prescribed as a fixed dose combination with levocetirizine (36.8%) in this study. Histamine and leukotrienes are released in concert during the early and late phases of allergic reactions. Hence a combination of an antihistaminic and a leukotriene receptor antagonist has impressive additive inhibitory effects on both the early and late bronchoconstrictive reactions seen in bronchial asthma [12]. These leukotriene receptor antagonists are active over a wide range of asthma severity and have both an anti-inflammatory and a bronchodilator property [13]. They cause modest improvement in lung function, reduce asthma symptoms and lessen the need for β_2 agonist rescue therapy [1]. They are active orally, therefore overcoming the potential problems with compliance when using inhalers [13].

Oral corticosteroids were prescribed to a small number of patients (2.4%). As they are potent anti-inflammatory agents, they are effective in achieving prompt control of asthma during exacerbations. They speed the resolution of airflow obstruction and reduce the rate of relapse [1].

This study also showed that antibiotics and multivitamins were prescribed as adjuvant therapy. Among the antibiotics, amoxicillin (32.8%), levofloxacin (30.4%) and azithromycin (2.4%) which are highly effective against respiratory infections were commonly prescribed. These antibiotics favorably affect the bronchial hyper-responsiveness found in asthma and they also helped to improve the breathing & lung function in asthmatic patients with underlying respiratory infection [1,14].

Inhalational form is the most safe and cost effective therapy in bronchial asthma. The advantages being smaller dose, targeted delivery, rapid action and minimal systemic side effects [3,7]. Similar to previous studies, in this study also only 50.4% of patients received inhalation therapy. This could be attributed to low level of acceptance apart from non-compliance and co-ordination associated with the use of inhaler [2]. Fixed dose inhalational therapy with a long-acting beta2 agonist and corticosteroids was most frequently prescribed in this study. Long-acting beta2 agonists should always be used in combination with inhaled corticosteroids as they alone do not treat the underlying chronic inflammation [8]. In combination with corticosteroids they improve symptom scores, decrease nocturnal asthma, improve lung function, decrease the use of rapid-acting inhaled β 2-agonists, reduce the number of exacerbations and achieve more rapid clinical control of asthma [15]. This greater efficacy has led to the development of fixed combination inhalers of corticosteroids and

long-acting β 2-agonist which are more convenient for patients and also increase patient compliance [3].

[VI] CONCLUSION

Allergic factors have seen to be responsible for precipitating asthma in 48% of patients in this study. Leukotriene receptor antagonists, mast cell stabilizers and corticosteroids play a very important role in the prophylaxis of such patients. Montelukast in fixed dose combination and corticosteroids as inhalational therapy have been prescribed to about 50% of patients in this study. Mast cell stabilizers like nedocromil and sodium cromoglycate which when used prophylactically bring down the incidence of acute asthma attacks in allergic asthma patients have not been prescribed to any of the patients. Their inclusion in prescriptions of allergic asthma can alleviate development of acute asthma.

Anti-asthmatic drugs given as inhalational therapy definitely are more beneficial than when given as systemic therapy. Hence, their maximum utilization in asthmatics will also go a long way in minimizing the incidence of acute asthma as well as the adverse effects of anti-asthmatic drugs.

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