

Loss of Asthma Control in Pediatric Patients after discontinuation of Long - Acting Beta - Agonists

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ABSTRACT

Background: The long-acting beta agonists (LABAs) introduction marked a significant development in the treatment of children suffering from asthma. Nevertheless, the utilization of LABAs has given rise to safety trepidations, particularly regarding the risk of severe asthma exacerbations (SAEs) that could lead to hospitalizations or mortality in extreme cases.

Objective: The purpose of the current study was to assess the immediate clinical effects following the cessation of long-acting β_2 -agonist (LABA) therapy in a cohort of children with asthma whose condition was well-controlled.

Methodology: A retrospective cohort study on 66 pediatric asthma patients at Children Hospital, Lahore, from Nov 2020 to Dec 2021 explored outcomes of transitioning from combination therapy to inhaled corticosteroids. Moderate to severe cases were included. Clinical and physiological data were recorded, reassessed after 8 weeks of monotherapy.

Results: Among 66 patients (57.6% male, 42.4% female), children aged 9.84 years had asthma for 6.8 years. 45.4% used leukotriene receptor antagonists. After 10 weeks, 60.6% maintained asthma control. Those who lost control experienced a significant 7% decline in FEV1 and a 2.9-point drop in asthma control test scores.

Conclusion: The present study observed that children diagnosed with persistent asthma, who ceased long-acting beta agonist (LABA) therapy, faced a 39.4% risk of losing asthma control, necessitating intensified maintenance treatments. Clearly, relying solely on long-acting beta agonist (LABA) therapy as a standalone treatment is not viable. Moreover, the utilization of combination inhaled corticosteroid (ICS) and LABA therapy in a single device is the best alternative for asthma control.

Keywords: Asthma; Children; Long-Acting Beta Agonist (LABAs)

Introduction

Asthma, characterized by chronic inflammation, variable airflow obstruction, and bronchial hyper-responsiveness, stands as the most prevalent chronic lower respiratory ailment among children globally. This condition manifests through recurring episodes marked by wheezing, coughing, breathlessness, and chest tightness.¹ Children dealing with asthma face significant limitations in their daily activities, including sports, school, and even interactions with pets. These limitations significantly diminish their quality of life. Moreover, asthma symptoms can distress them, and they may become frightened during asthma attacks or exacerbations.² Epidemiological studies consistently indicate that asthma in children does not typically resolve completely but later appear in adulthood.^{3,4} International guidelines suggest incorporating LABAs with inhaled corticosteroids (ICS) which effectively control asthma in cases where ICS fails to control asthma.^{5,6} Unlike in adults, enhancing lung function and reducing the use of short-acting β_2 -agonists (SABA) were the benefits of ICS/LABA in children, without a significant decrease in symptoms when compared to using ICS alone.^{7,8}

Pharmacotherapy plays a crucial role in treating pediatric asthma, aiming to control symptoms and prevent exacerbations while minimizing drug-related side effects. Typically, patients start with a low dose (equivalent to 200 μ g of beclomethasone dipropionate) and may increase the dose if control remains inadequate.⁹ There is limited data and clinical practice guidelines available on the optimal approach for discontinuing long-acting β_2 -agonist (LABA) therapy in pediatric patients. Previous studies have indicated that discontinuing LABA results in reduced lung function and less effectively controlled asthma, although these findings are not specific to the pediatric population.^{10,11} Current asthma guidelines recommend reducing the dose of inhaled corticosteroids instead of discontinuing LABA therapy.¹² Therefore, the present study aimed to assess the immediate clinical effects following the cessation of long-acting β_2 -agonist (LABA) therapy in a cohort of children with asthma whose condition was well-controlled.

Objective

The purpose of the current study was to assess the immediate clinical effects following the cessation of long-acting β_2 -agonist (LABA) therapy in a cohort of children with asthma whose condition was well-controlled.

Methodology

This retrospective cohort study was conducted on 66 pediatric asthma patients in the Pediatric Pulmonology

Department of Children Hospital, Lahore from November 2021 to December 2022. All the moderate to severe pediatric asthma patients were enrolled. Patients with concurrent primary pulmonary conditions were excluded. Clinical and physiological outcomes of children experiencing persistent asthma after transitioning from inhaled corticosteroid/LABA (combination therapy) to inhaled corticosteroids (ICS) as a monotherapy were investigated and recorded. Patients underwent reassessment after 8 weeks of therapy. The evaluation also involved spirometry, lung volume measurements, and ACT (Asthma Control Test) scoring. Children with asthma test scores ≥ 20 were identified as an asthma control. Following the discontinuation of LABA, the patients continued to receive equivalent doses of inhaled steroids. Patients underwent reassessment after 10 weeks of therapy. Atopy was determined by either a positive allergy skin test or Immunocap in vitro quantitative assay, the administration of immunotherapy, or a physician's diagnosis of allergic rhinosinusitis. SPSS version 27 was used for descriptive statistics.

Results

Of the total 66 patients, there were 38 (57.6%) male and 28 (42.4%) females. The overall mean age and asthma duration among children was 9.84 ± 4.68 and 6.8 ± 3.92 years respectively. The asthma control test score was 22.8 ± 2.7 . The predicted forced vital capacity (%), forced expiratory volume (%), and forced expiratory flow (%) was 106.2 ± 10.4 , 104.6 ± 10.4 , and 99.2 ± 23.8 respectively. Leukotriene receptor antagonists (LTRA) were used in 30 (45.4%) cases. During the follow-up of 10 weeks, about 40 (60.6%) patients were able to sustain asthma control as determined by symptom monitoring and spirometry results whereas the remaining 26 individuals (39.4%) experienced a loss of asthma control. Among asthma control cases, decrease in FEV1 (forced expiratory volume in one second) by 7% compared to a decrease of 1.8% in those who maintained control was statistically significant. Additionally, the asthma control test scores showed a decline of 2.9 points in the loss of control group, whereas it decreased by 0.7 points in the maintained control group. Patient's demographic details and baseline characteristics are shown in Table 1. Figure 1 illustrates the gender's distribution. Incidence of controlled and uncontrolled asthma children are depicted in Figure 2. Comparison of various parameters in controlled and uncontrolled asthma children are shown in Table 2.

Discussion

Discontinuity of long-acting β_2 -agonists in pediatric patients suffering asthma were mainly investigated in this

Table 1. Patient's demographic details and baseline characteristics

Variables	Value (Mean $\pm$ SD)
Age (years)	9.84 $\pm$ 4.68
Asthma duration (years)	6.8 $\pm$ 3.92
Asthma control test score	22.8 $\pm$ 2.7
Forced vital capacity (%)	106.2 $\pm$ 10.4
Forced expiratory volume (%)	104.6 $\pm$ 10.4
Forced expiratory flow (%)	99.2 $\pm$ 23.8
Leukotriene receptor antagonists (LTRA)	30 (45.4%)
Follow-Up (weeks)	10

retrospective cohort study and found that children diagnosed with persistent asthma, who ceased long-acting beta agonist (LABA) therapy, face a 39.4% risk of losing asthma control. Furthermore, the use of a combination inhaler containing both inhaled corticosteroid (ICS) and long-acting beta agonist (LABA) therapy in a single device represents the most effective alternative for controlling asthma symptoms. It has been observed that

39.4% children had uncontrolled asthma after the discontinuation of LARAs. An earlier trial conducted on 658 asthmatic adults reported that asthma exacerbation decreased after receiving the inhaled corticosteroids (ICS) with formoterol in a time span of one year.¹³ Another study reported similar results according to which decrease in exacerbation and asthma symptoms were associated with clinical advancement. Additionally,

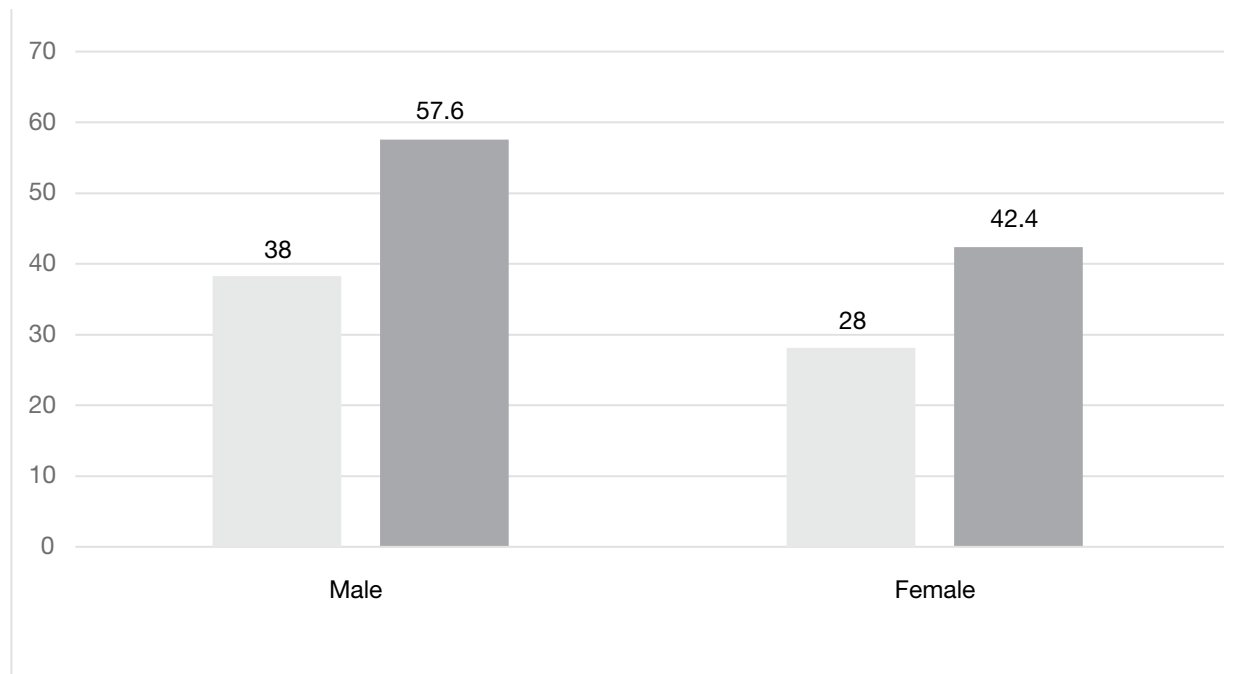


Figure 1. Gender distribution (N=66)

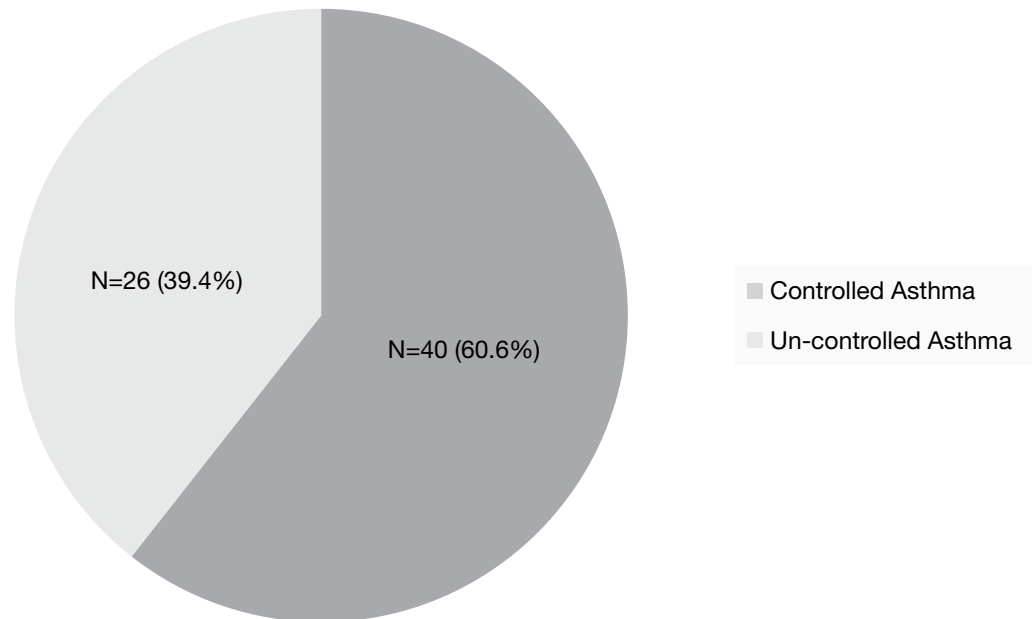


Figure 2. Controlled and un-controlled asthma (N=66)

LABAs therapy improved the pulmonary function.^{14,15} In their study involving pediatric patients, the median duration of 18 months on inhaled corticosteroid (ICS) and long-acting beta agonist (LABA) treatment appears significant. Unlike adult cessation trials where treatment duration prior to discontinuation is often unspecified unless stipulated by the study design.^{16,17}

The successful cessation after 6 months, LABA was effectively discontinued in 83% cases which resemble an earlier study reported 63% children with controlled asthma after 2 months of LABA cessation.¹⁸ The higher rate of success among children as compared to adults could include factors such as reduced airway obstruction and remodeling, shorter duration of the disease, a higher initial dose of inhaled corticosteroids (ICS) to which LABA was added and then withdrawn, a more prolonged period of asthma control before discontinuation of LABA, and a diminished benefit of LABA in children.¹⁹

Pediatric and adolescent patients who need to supplement their inhaled corticosteroid treatment with a LABA should opt for a combination therapy (ICS/LABAs). This choice ensures adherence to both medications, promoting effective asthma management. Currently, several studies are dedicated to investigating the impact of inhaled corticosteroid (ICS) use on adult height, a parameter arguably more crucial than short-term growth rates.^{20,21}

Concerns regarding the safety of asthma medications undoubtedly complicate the treatment process. Furthermore, diagnosing pediatric asthma poses challenges due to overlapping symptoms such as respiratory tract

infections, rhinitis, and sinusitis among children. Co-existing symptoms and asthma could be effectively managed by these conditions.²² In younger children, diagnosis often relies on monitoring the symptoms and severity triggered by persistent cough during colds and allergies.²³ Asthma presents with diverse clinical symptoms over the course of the disease, emphasizing the importance of noninvasive methods for assessing airway inflammation. Ongoing research is offering a promising avenue for understanding and managing the condition.²⁴

Ongoing scrutiny and interpretation of available data regarding safety implications led to significant developments. This culminated in the LABA medications and the initiation of a comprehensive safety study. The changes in label signify the effectiveness of discontinuing LABA use, if feasible, after the control of asthma control.²⁵

Relying solely on symptoms has been proven to underestimate the severity of asthma.²⁶ Asthma control could be indicated by symptoms, they do not always align with lung function. There are cases where patients with objective evidence of poor lung function do not perceive significant symptoms. These individuals, termed "poor perceivers of airflow obstruction," face higher risks of asthma-related complications and even mortality.²⁷

Conclusion

Children diagnosed with persistent asthma, who ceased long-acting beta agonist (LABA) therapy, faced a 39.4% risk of losing asthma control, necessitating intensified

maintenance treatments. Clearly, relying solely on long-acting beta agonist (LABA) therapy as a standalone treatment is not viable. Moreover, the utilization of combination inhaled corticosteroid (ICS) and LABA therapy in a single device is the best alternative for asthma control.

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