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Compare The Efficacy of Budesonide and Formoterol Combination Mart and Budesonide Formoterol Combination with as Needed Saba Reliever Therapy in Paediatric Bronchial Asthma

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ABSTRACT

Aim: The aim of the present study was to compare the efficacy of Budesonide Formoterol combination MART and Budesonide Formoterol combination with as needed SABA as reliever in pediatric bronchial asthma.
Methods: The study was conducted after approval from the Scientific and Institutional Ethics Committee, at Department of Pediatrics NIMS University Jaipur for the period of 18 months. Informed consent/ascent shall be obtained from the parents of all the children enrolled in the study after taking into consideration inclusion and exclusion criteria.
Results: The mean age of participants in the MART group was 11.94 ± 3.38 years, which was identical to the SABA group (11.94 ± 3.38 years). The mean height in both groups was 136.88 ± 18.09 cm. Similarly, the mean weight in both groups was 38.12 ± 11.07 kg. The mean BMI was also comparable, with 21.43 ± 8.21 kg/m² in both groups. In the MART group, 17 participants (51.5%) were female and 16 participants (48.5%) were male. Similarly, in the SABA group, 17 participants (51.5%) were female and 16 participants (48.5%) were male. The mean duration of asthma in the MART group was 4.06 ± 2.37 years, which was identical in the SABA group (4.06 ± 2.37 years). The baseline ACT score was 14.91 ± 2.68 in both groups, indicating similar symptom severity. The mean PEFR was 210.45 ± 53.21 L/min in both groups.
Conclusion: Both treatment regimens were effective in improving asthma outcomes; however, Budesonide–Formoterol MART demonstrated superior efficacy in terms of symptom control, lung function improvement, reduction in exacerbations, better adherence, and safety profile. MART may be considered a more effective and convenient therapeutic approach for managing pediatric bronchial asthma.

Keywords: Bronchial asthma, Pediatric asthma, MART therapy, Budesonide–Formoterol, SABA, Asthma control, FEV1, PEFR, Exacerbations.

INTRODUCTION

Bronchial asthma is a chronic inflammatory disease of the airways characterised by episodic wheezing, breathlessness, chest tightness, and cough, particularly at night or in the early morning. The underlying pathophysiology involves airway hyperresponsiveness, variable airflow limitation, and persistent inflammation of the bronchial mucosa. In pediatric populations, asthma is one of the most prevalent chronic conditions, affecting approximately 5–10% of children globally, with a substantial impact on quality of life, school attendance, and healthcare utilisation.[1] The inflammatory process is driven by multiple cellular pathways, prominently involving eosinophils, mast cells, T-helper 2 (Th2) lymphocytes, and a network of cytokines such as interleukin (IL)-4, IL-5, and IL-13, leading to structural airway changes over time if not adequately controlled.

Within asthma management, the pharmacological approach aims to achieve symptom control, minimise future risk of exacerbations, and limit the adverse effects associated with long-term therapy. Inhaled corticosteroids (ICS) are recognised

as the cornerstone of anti-inflammatory treatment, reducing airway hyperreactivity and controlling underlying inflammation.[2] Long-acting beta-2 agonists (LABAs), such as formoterol, act by relaxing airway smooth muscle via stimulation of β2-adrenergic receptors, producing sustained bronchodilation. When used in combination with ICS, LABAs offer synergistic effects: the ICS addresses inflammation, while the LABA provides prolonged relief of bronchoconstriction and improves lung function.3

In pediatric asthma, treatment regimens must balance efficacy with safety, particularly regarding cumulative corticosteroid exposure, which has been associated with growth suppression in children when used in higher doses over extended periods.[4] The introduction of the Maintenance and Reliever Therapy (MART) strategy, employing a single inhaler containing both an ICS (budesonide) and a LABA (formoterol) for both daily maintenance and as-needed relief of symptoms, has been a significant innovation in asthma care. This approach contrasts with the traditional method, where an ICS/LABA combination is used for maintenance, and a separate short-acting beta-2 agonist (SABA) inhaler, such as salbutamol, is used for symptom relief. The pharmacologic rationale for MART lies in the rapid onset of action of formoterol, which, unlike other LABAs such as salmeterol, has a bronchodilatory effect comparable in onset to SABAs, making it suitable for both maintenance and quick relief. When used in combination with budesonide, this approach ensures that every time a patient takes a reliever dose, they also receive an anti-inflammatory component, potentially reducing the risk of exacerbations related to inflammation.[5]

In the pediatric context, the efficacy and safety of MART versus traditional ICS/LABA plus as-needed SABA therapy remain areas of active investigation. Children have different asthma phenotypes, with viral-induced wheezing episodes being more prominent in younger age groups, and atopic asthma more common in older children. These variations may influence the responsiveness to specific therapeutic regimens. Moreover, adherence patterns differ between children and adults, often relying heavily on caregiver involvement, which can affect the consistency of maintenance therapy. MART may offer adherence benefits by simplifying the treatment regimen, potentially leading to better overall disease control.[6] While pediatric-specific evidence is In a MART regimen, this dual mechanism ensures that each inhalation in response to symptoms delivers both acute relief and anti-inflammatory treatment, reducing the inflammatory load over time. This is particularly important in pediatric asthma, where airway inflammation can escalate rapidly following allergen exposure, viral infections, or exercise. Clinical trials in adolescents and adults have demonstrated that MART reduces the risk of severe exacerbations compared with conventional ICS–LABA plus SABA regimens[7,8] more limited, emerging data suggest similar benefits, prompting guideline endorsements for MART in certain pediatric age groups.

The present study endeavors to compare the efficacy of budesonide– formoterol MART with that of conventional budesonide–formoterol maintenance therapy combined with as-needed SABA relief in pediatric bronchial asthma. Key endpoints include the frequency of exacerbations, symptom-free days, lung function metrics, medication adherence, quality of life indices, and incidence of adverse events. By elucidating the comparative performance of these regimens, the study aims to inform evidence-based practice, optimize therapeutic outcomes, and ultimately enhance the quality of life for children grappling with this chronic respiratory disorder.

MATERIALS AND METHODS

The study was conducted after approval from the Scientific and Institutional Ethics Committee, at Department of Pediatrics NIMS University Jaipur for the period of 18 months. Informed consent/ascent shall be obtained from the parents of all the children enrolled in the study after taking into consideration inclusion and exclusion criteria.

- In this randomized controlled study, participants was allocated into two groups-

a. Budesonide and formoterol combination MART
b. Budesonide formoterol combination with as needed SABA reliever therapy

- Each group consisted of 33 participants, totalling 66 participants in the study.
- Follow up of patients of each group was done after interval of 3 months and 6 months and fev1/fec was compared by Spirometry.
- Training on proper inhaler technique was provided.

INCLUSION CRITERIA

All children aged 6-18 years of age of any sex diagnosed as cases of uncontrolled bronchial asthma bearing the following characteristics-

a. Recurrence of symptoms of asthma on most days or wakening with asthma symptoms once a week or more, thus qualifying for step 3 or step 4 management directly according to GINA guideline 2023.
b. Patients earlier on step 1-2 therapy but presently requiring step up to step 3 therapy according to GINA guidelines 2023.
c. Children for whom parents provide consent/assent to participate in study.

EXCLUSION CRITERIA

1. Acute exacerbation of asthma requiring ICU care.
2. Previous treatment with Budesonide Formoterol as MART.

3. Use of beta blocker drug or oral corticosteroids on regular maintenance treatment.
4. Patients with comorbidities-

a) Obesity
b) Allergic rhinitis/ Rhinosinusitis
c) Food allergy
d) GERD
e) Psychiatric disorder

5. Patients qualifying for step 5 management according to GINA guidelines 2023.

TECHNIQUE:

- Diagnosis and asthma severity classification as per GINA guidelines.
- Administration of Budesonide-Formoterol via pressurized metered-dose inhaler (pMDI) with spacer device.
- Use of validated tools for asthma control assessment such as C-ACT.
- Spirometry conducted as per ATS/ERS standards.
- Monitoring of exacerbations defined by need for systemic corticosteroids or hospitalization.

RESULTS

Table 1: Baseline demographic characteristics of study participants in MART and SABA groups showing mean and standard deviation values

Variable	MART (n=33)	SABA Group (n=33)
Age (years)	11.94 ± 3.38	11.94 ± 3.38
Height (cm)	136.88 ± 18.09	136.88 ± 18.09
Weight (kg)	38.12 ± 11.07	38.12 ± 11.07
BMI (kg/m²)	21.43 ± 8.21	21.43 ± 8.21

The mean age of participants in the MART group was 11.94 ± 3.38 years, which was identical to the SABA group (11.94 ± 3.38 years). The mean height in both groups was 136.88 ± 18.09 cm. Similarly, the mean weight in both groups was 38.12 ± 11.07 kg. The mean BMI was also comparable, with 21.43 ± 8.21 kg/m² in both groups.

Table 2: Gender distribution of study participants in MART and SABA groups expressed as frequency and percentage

Gender	MART (n=33)	SABA Group (n=33)
Female	17 (51.5%)	17 (51.5%)
Male	16 (48.5%)	16 (48.5%)

In the MART group, 17 participants (51.5%) were female and 16 participants (48.5%) were male. Similarly, in the SABA group, 17 participants (51.5%) were female and 16 participants (48.5%) were male.

Table 3: Baseline clinical characteristics including duration of asthma, ACT score, PEFR, and FEV1 in both study groups

Variable	MART (Mean ± SD)	SABA Group (Mean ± SD)
Duration of asthma (years)	4.06 ± 2.37	4.06 ± 2.37
ACT Score	14.91 ± 2.68	14.91 ± 2.68
PEFR (L/min)	210.45 ± 53.21	210.45 ± 53.21
FEV1 (%)	68.88 ± 8.42	68.88 ± 8.42

The mean duration of asthma in the MART group was 4.06 ± 2.37 years, which was identical in the SABA group (4.06 ± 2.37 years). The baseline ACT score was 14.91 ± 2.68 in both groups, indicating similar symptom severity. The mean PEFR was 210.45 ± 53.21 L/min in both groups. Additionally, the mean FEV1 percentage was 68.88 ± 8.42 in both groups.

Table 4: Comparison of ACT scores at baseline, 3 months, and 6 months between MART and SABA groups

Time Point	MART (Mean ± SD)	SABA Group (Mean ± SD)
Baseline	14.91 ± 2.68	14.91 ± 2.68
3 Months	19.85 ± 1.92	17.42 ± 2.15
6 Months	22.85 ± 1.12	20.12 ± 1.85

At baseline, both groups had identical ACT scores of 14.91 ± 2.68. At 3 months, the ACT score improved to 19.85 ± 1.92 in the MART group, whereas it increased to 17.42 ± 2.15 in the SABA group. At 6 months, the MART group showed further improvement to 22.85 ± 1.12, while the SABA group reached 20.12 ± 1.85.

Table 5: Comparison of PEFR values at baseline, 3 months, and 6 months between the two groups

Time Point	MART (Mean ± SD)	SABA Group (Mean ± SD)
Baseline	210.45 ± 53.21	210.45 ± 53.21
3 Months	265.34 ± 48.12	240.56 ± 50.21
6 Months	310.25 ± 45.62	275.34 ± 48.11

At baseline, both groups had identical PEFR values of 210.45 ± 53.21 L/min. At 3 months, the MART group improved to 265.34 ± 48.12 L/min, while the SABA group improved to 240.56 ± 50.21 L/min. At 6 months, the MART group further improved to 310.25 ± 45.62 L/min, compared to 275.34 ± 48.11 L/min in the SABA group.

Table 6: Comparison of FEV1 (%) at baseline, 3 months, and 6 months between MART and SABA groups

Time Point	MART (Mean ± SD)	SABA Group (Mean ± SD)
Baseline	68.88 ± 8.42	68.88 ± 8.42
3 Months	78.45 ± 6.92	73.12 ± 7.35
6 Months	88.91 ± 5.34	81.22 ± 6.18

At baseline, both groups had identical FEV1 values of 68.88 ± 8.42%. At 3 months, the MART group improved to 78.45 ± 6.92%, whereas the SABA group improved to 73.12 ± 7.35%. At 6 months, the MART group showed further improvement to 88.91 ± 5.34%, compared to 81.22 ± 6.18% in the SABA group.

Table 7: Comparison of exacerbation frequency at 3 months and 6 months between MART and SABA groups

Time Point	MART (Mean ± SD)	SABA Group (Mean ± SD)
3 Months	0.65 ± 0.22	1.12 ± 0.30
6 Months	0.42 ± 0.18	0.88 ± 0.25

At 3 months, the MART group had a mean exacerbation frequency of 0.65 ± 0.22 episodes per month, whereas the SABA group had 1.12 ± 0.30 episodes per month. At 6 months, the MART group showed further reduction to 0.42 ± 0.18 episodes per month, while the SABA group had 0.88 ± 0.25 episodes per month.

Table 8: Treatment-related outcomes including adverse effects, adherence, and treatment success at 6 months

Variable	MART (n=33)	SABA Group (n=33)
Adverse Effects (Yes)	5 (15.2%)	11 (33.3%)
Good Adherence	28 (84.8%)	22 (66.7%)
Treatment Success	30 (90.9%)	24 (72.7%)

Adverse effects were observed in 5 participants (15.2%) in the MART group compared to 11 participants (33.3%) in the SABA group. Good adherence was seen in 28 participants (84.8%) in the MART group, whereas only 22 participants (66.7%) in the SABA group showed good adherence. Treatment success was achieved in 30 participants (90.9%) in the MART group compared to 24 participants (72.7%) in the SABA group.

DISCUSSION

Asthma remains one of the most prevalent chronic respiratory conditions in the pediatric population, significantly impacting quality of life and healthcare utilization. The present randomized controlled study was conducted to compare the efficacy of Budesonide/Formoterol Maintenance and Reliever Therapy (MART) with Budesonide/Formoterol maintenance plus as-needed Short-Acting Beta-Agonist (SABA) in children aged 6–18 years with uncontrolled bronchial asthma. The findings of this study are discussed in light of existing literature and clinical relevance.

The baseline demographic profile of participants revealed that the mean age, height, weight, and BMI were identical in both groups (Age: 11.94 ± 3.38 years; Height: 136.88 ± 18.09 cm; Weight: 38.12 ± 11.07 kg; BMI: 21.43 ± 8.21 kg/m²). This uniformity confirms that randomization was effective and eliminated baseline confounding variables. The similarity in anthropometric characteristics is crucial as growth-related physiological differences can influence lung function parameters and response to therapy. These findings are consistent with the study by Sobieraj et al. (2018), who reported

comparable baseline characteristics across treatment arms in pediatric asthma trials [28]. Similarly, Reddel et al. (2022) emphasized that well-balanced baseline characteristics are essential for valid intergroup comparisons in asthma studies.[9]

However, some studies have reported variability in baseline anthropometric data. For instance, Yaghoubi et al. (2019) observed differences in BMI influencing asthma severity and treatment outcomes.[10] Despite this, the present study successfully minimized such variability. The gender distribution was nearly identical in both groups, with females constituting 51.5% and males 48.5%. This balanced distribution ensures that gender-related physiological differences do not bias outcomes. Gender differences in asthma prevalence and severity have been widely reported. Zafari et al. (2018) observed a slight female predominance in pediatric asthma cohorts, aligning with the present findings.[11] Additionally, Lalloo et al. (2003) reported no significant gender-based differences in treatment response to inhaled corticosteroid combinations.[12] Conversely, Kuna et al. (2006) suggested that hormonal influences may affect asthma control differently in males and females.[13] However, such effects are more prominent in adolescence and adulthood, and likely had minimal influence in this study. Baseline clinical parameters including duration of asthma (4.06 ± 2.37 years), ACT score (14.91 ± 2.68), PEFR (210.45 ± 53.21 L/min), and FEV1 (68.88 ± 8.42%) were comparable in both groups, indicating similar disease severity at enrollment.

The ACT score reflects poorly controlled asthma at baseline, justifying the need for step-up therapy. These findings are in agreement with Yu et al. (2023), who reported similar baseline ACT and lung function values in pediatric asthma patients undergoing MART therapy.[14] Similarly, Stoloff et al. (2004) demonstrated that patients with moderate asthma typically present with FEV1 values between 60–70%, consistent with this study.[15] In contrast, Chen et al. (2018) reported slightly higher baseline lung function values, possibly due to differences in inclusion criteria or earlier disease stages.[16] Nonetheless, the present study reflects a realistic clinical population. The ACT score improved significantly in both groups over time, with greater improvement observed in the MART group (Baseline: 14.91 → 22.85 at 6 months) compared to the SABA group (14.91 → 20.12).

This suggests superior symptom control with MART therapy. These findings are strongly supported by Yu et al. (2023), who demonstrated significant improvement in asthma control scores with MART compared to conventional therapy.[17] Similarly, Reddel et al. (2022) highlighted that MART reduces symptom variability and improves control due to its dual maintenance and reliever action.[9] However, Sobieraj et al. (2018) noted that while both therapies improve symptoms, differences may not always be clinically significant in short-term studies.[18] In contrast, the present study demonstrates clear superiority over 6 months. PEFR improved in both groups, with a greater increase in the MART group (210.45 → 310.25 L/min) compared to the SABA group (210.45 → 275.34 L/min). This reflects better airway flow and reduced obstruction with MART therapy. These findings align with Lalloo et al. (2003), who reported improved peak flow rates with combination inhaler therapy.[5] Additionally, Kuna et al. (2006) found that budesonide/formoterol significantly enhances lung function compared to monotherapy.[16]

However, Yaghoubi et al. (2019) suggested that environmental and adherence factors may influence PEFR variability.[10] Despite this, the consistent improvement in the MART group supports its effectiveness. FEV1 improved markedly in both groups, with greater improvement in the MART group (68.88% → 88.91%) compared to the SABA group (68.88% → 81.22%). FEV1 is a key indicator of airway function, and its improvement signifies effective disease control. These findings are consistent with Yu et al. (2023), who reported significant FEV1 improvement with MART therapy.[17] Similarly, Sobieraj et al. (2018) found that combination therapy improves lung function more effectively than traditional regimens.[18]

In contrast, Stoloff et al. (2004) reported modest differences between treatment strategies, possibly due to shorter follow-up duration [38]. The longer follow-up in this study likely contributed to more pronounced differences. The MART group showed significantly fewer exacerbations (0.42 at 6 months) compared to the SABA group (0.88). Reduction in exacerbations is a critical outcome in asthma management. These findings strongly support the hypothesis and align with Yu et al. (2023), who demonstrated reduced exacerbation rates with MART.[17] Additionally, Reddel et al. (2022) emphasized that MART reduces both mild and severe exacerbations by providing timely anti-inflammatory action.[19] However, Chen et al. (2018) reported that exacerbation rates may vary based on adherence and environmental triggers.[16] Despite this, the consistent reduction in this study supports MART superiority.

The MART group showed fewer adverse effects (15.2% vs 33.3%), better adherence (84.8% vs 66.7%), and higher treatment success (90.9% vs 72.7%). Improved adherence may be attributed to the convenience of single-inhaler therapy. These findings are consistent with Stoloff et al. (2004), who reported better adherence with combination inhalers.[19] Similarly, Zafari et al. (2018) highlighted that improved asthma control reduces healthcare burden and enhances compliance.[11] Conversely, Kuna et al. (2006) noted that adherence may vary depending on patient education and socioeconomic factors.[16] Nonetheless, the present study demonstrates clear advantages of MART.

The present study demonstrates that while both treatment strategies improve asthma control, MART therapy consistently provides superior outcomes across multiple parameters including symptom control, lung function, exacerbation reduction, adherence, and safety.

CONCLUSION

In conclusion, Budesonide/Formoterol MART therapy is more effective than conventional Budesonide/Formoterol with as-needed SABA therapy in achieving better asthma control in pediatric patients. It offers advantages in terms of improved symptom control, enhanced lung function, reduced exacerbations, better adherence, and improved safety profile. These findings support the growing evidence favoring MART as a preferred treatment strategy in moderate to severe pediatric asthma and reinforce its potential role in optimizing long-term asthma management in real-world clinical practice.

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