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ORIGINAL RESEARCH

Assessing the Efficacy of Indacaterol/Mometasone versus Formoterol/Budesonide in Bronchial Asthma Patients

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ABSTRACT

Introduction: Asthma is a chronic inflammatory airway condition. It causes recurrent wheezing, coughing, breathlessness, and chest tightness. It significantly impacts global health. In India, it affects 17.23 million people (2.05% prevalence). Treatment focuses on inhaled corticosteroids and β2-agonists. Combination therapies are recommended for moderate to severe cases.

Aims and Objectives: This study aims to evaluate and compare the effectiveness of Formoterol/Budesonide and Indacaterol/Mometasone as dry powder inhalers (DPI) in asthma patients, specifically in terms of Forced Expiratory Volume in one second (FEV1).

Methods: Fifty-two patients with bronchial asthma were enrolled based on spirometry results and randomly assigned to two groups: Group A (24 patients) received a fixed-dose combination of Indacaterol (150 mcg) and Mometasone (160 mcg) once daily, while Group B (28 patients) received a fixed-dose combination of Formoterol (6 mcg) and budesonide (400 mcg) twice daily, both delivered as DPIs.

Results: Initially, there was no significant difference in FEV1 between the groups at baseline. However, significant differences in post-observation mean FEV1 were observed between Group A and Group B at the 3-month ($p = 0.001$) and 6-month follow-ups ($p = 0.045$). Both groups showed a significant increase in FEV1 from pre- to post-observation at baseline, three months, and six months ($p < 0.001$ for both groups). Significant differences were also noted between the groups when comparing the mean change in FEV1 from pre- to post-bronchodilator (SABA) treatment at baseline ($p = 0.001$), 3-month ($p < 0.001$), and 6-month ($p = 0.015$) follow-ups.

Conclusion: The Formoterol/Budesonide twice daily DPI combination proved to be more effective than the Indacaterol/Mometasone once daily DPI combination in improving lung function, as measured by FEV1.

Keywords: Asthma, Budesonide, FEV1, Formoterol, Indacaterol/Mometasone

INTRODUCTION

Asthma is a persistent inflammatory condition affecting the airways. It leads to sensitive airways and repeated bouts of wheezing, coughing, breathlessness, and chest tightness. These symptoms frequently manifest in the morning or during night-time. The incidents are usually related with variable airflow obstruction. This obstruction can often be relieved with treatment or may resolve on its own.[1] The primary feature of asthma, a heterogeneous condition, is ongoing inflammation of the airways.[2] Asthma is increasingly becoming a global concern, contributing

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to greater illness, a diminished quality of life, and rising healthcare costs.[3]. An Indian study on Epidemiology of Asthma, revealed that 17.23 million people nationwide suffer from asthma, with an overall prevalence of 2.05%.[4]

The defining characteristic of bronchial asthma is the hyperresponsiveness of the tracheobronchial smooth muscle to various stimuli. This leads to airway narrowing, often accompanied by mucus plugging, mucosal edema, and increased secretion.[5] The precise cause of bronchial asthma remains unknown. However, it is widely recognized that its development is influenced by a combination of environmental factors and genetic predisposition.[6] Asthma triggers include pet dander, pollen, and dust. Bacterial, fungal, and parasitic infections can also trigger asthma. Workplace pollutants and food additives are other triggers. The most common triggers are upper respiratory viral infections, particularly rhinovirus.

Bronchial asthma involves a diverse array of immune cells. These cells play crucial roles in the inflammatory responses that characterize asthma. Airway obstruction in asthma results from bronchial smooth muscle contractions, airway wall edema, mucus clogging, and airway remodelling.[6][7]

The primary treatment for asthma revolves around inhaled corticosteroids, complemented by short-acting β2-agonists for rapid symptom relief.[8] According to the Global Initiative for Asthma (GINA), short-duration β2-bronchodilators are recommended as the preferred initial relievers, and low-strength inhaled corticosteroids are suggested as the primary controller option for individuals with persistent asthma.[9]

Global recommendations advise pairing medium doses of inhaled corticosteroids with long-duration β2-agonists when corticosteroids alone fail to sufficiently manage moderate asthma. Utilizing a single inhaler having both ICS/LABA combination enhances adherence to treatment while ensuring safety and effectiveness comparable to using separate inhalers for each medication.[10] According to GINA, long-acting β2-agonists are recommended as the optimal controllers and maintenance treatment when added to inhaled corticosteroid monotherapy for patients experiencing poorly controlled asthma.[9]

As per the asthma guidelines, pairing a moderate or high strength of inhaled corticosteroids with a long-acting β2-agonist (LABA) is advocated as the optimal controller therapy for asthmatics whose asthma remains uncontrolled on corticosteroids alone or a low-strength corticosteroid/β2-agonist mixture. This treatment approach proves superior in enhancing lung function, decreasing asthma exacerbations, and improving overall asthma management compared to using corticosteroids alone in individuals with persistent asthma.[11]

AIM AND OBJECTIVES

This research is done to determine and compare the effectiveness of two dry powder inhaler combinations, Formoterol/Budesonide versus Indacaterol/Mometasone—in patients with asthma, with a focus on FEV1 (Forced Expiratory Volume) in one second.

METHODOLOGY

Study design: This research was conducted as prospective observational research.

Study duration: The research took place over a 12-month period from March 2023 to February 2024.

Study setting: The research was conducted in collaboration with King George's Medical University in Lucknow, specifically involving the Departments of Pharmacology and Therapeutics, as well as Respiratory Medicine.

Approval was granted through the Institutional Ethics Committee (IEC) of the same university (Reference code: XVI-PGTSC-IIA/P58) before the study commenced. Asthmatic patients receiving treatment at the Respiratory Medicine OPD were recruited based on meeting the study's inclusion and exclusion criteria and providing written informed consent.

Inclusion criteria:

- Age between 18 to 60 years.
- Patients with asthma attending the Respiratory Medicine OPD of KGMU, Lucknow.
- Patients who provided written informed consent.
- Both males and females were included.

Exclusion criteria:

- Current smokers.
- History of other chronic lung diseases.
- Recent flare-up of asthma requiring systemic corticosteroids, emergency care, or hospitalization within six weeks of screening.
- Presence of clinically significant comorbidities.
- Patients who refused to give consent or were non-cooperative.
- Pregnant and lactating women.

Study procedure: From March 2023 to February 2024, researchers conducted a prospective observational study involving 60 patients diagnosed with bronchial asthma. Eight patients were excluded during screening due to failure to meet inclusion criteria, withdrawn consent, or recent asthma exacerbations. Ultimately, 52 individuals with confirmed asthma were haphazardly assigned to two various groups: A (24 patients) and B (28 patients).

'A'; group was administered a once-daily fixed-dose of Indacaterol (150 mcg) and Mometasone (160 mcg) using a dry powder inhaler (DPI), while 'B'; group received a twice-daily fixed combination dose of 6 mcg Formoterol and Budesonide (400 mcg) via DPI.

All participants underwent comprehensive history taking, clinical examination, and confirmation of asthma diagnosis based on symptoms and spirometry (Pulmonary Function Test, PFT). A Case Report Form (CRF) captured demographic and clinical data. Initial

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PFTs were conducted, followed by evaluation of bronchoconstriction reversibility using 400 mcg (4 puffs) of inhaled salbutamol after 15 minutes. Salbutamol was used as a bronchodilator for pre and post Pulmonary Function Testing.

FEV1 (forced expiratory volume in one second) was measured at baseline and following bronchodilator use during subsequent 3-month and 6-month follow-ups to assess the efficacy of Indacaterol/Mometasone and Formoterol/Budesonide DPI combinations in improving lung function among asthma patients

Statistical analysis: The data underwent analysis using IBM SPSS version 23 following importation into Microsoft Excel. Descriptive statistics included Mean ± SD for quantitative variables and percentages (%) for categorical variables, assessed using Chi-square tests for categorical data. Quantitative measurements were evaluated using repeated measure ANOVA for time-dependent alterations within groups, paired t-statistic for contrasts within each group, and non-paired t-tests for distinctions between batches. $P < 0.05$ was taken as significant value.

RESULTS

Demographic and clinical characteristics

Age	Group A		Group B	
	No.	%	No.	%
18 - 30 years	14	58.3%	17	60.7%
31 - 40 years	3	12.5%	6	21.4%
41 - 50 years	2	8.3%	2	7.1%
51 - 60 years	5	20.8%	3	10.7%
Mean±SD	33.88±14.86 years		29.82±11.36 years	
Significance	chi square=1.49, p=0.684			

Table 1: Distribution of Age by Groups

Sex	Group A		Group B	
	Total Number	Percentage %	Total Number	Percentage %
Male	17	70.8%	11	39.3%
Female	7	29.2%	17	60.7%
Significance	**chi square=5.18, p=0.023**			

Table 2: Gender wise distribution of patients by Groups

FEV1 (L)		Group A		Group B		unpaired t test	
		Mean	SD	Mean	SD	t-value	p-value
Baseline	Pre	2.14	0.40	2.19	0.36	-0.47	0.641
	Post	2.63	0.43	2.58	0.39	0.46	0.649
	Pre vs Post	t=20.68, **p<0.001**		t=24.86, **p<0.001**			
3 month	Pre	2.52	0.38	2.71	0.40	-1.76	0.084
	Post	2.82	0.38	3.22	0.41	-3.66	**0.001**
	Pre vs Post	t=18.38, **p<0.001**		t=16.47, **p<0.001**			
6 month	Pre	2.84	0.38	2.93	0.33	-0.93	0.358
	Post	3.28	0.50	3.53	0.36	-2.06	**0.045**
	Pre vs Post	t=8.23, **p<0.001**		t=17.16, **p<0.001**			

Table 3: Intergroup & Intra group Comparison of FEV1

At baseline, an absence of notable difference between the groups in prior (t-statistic = -0.47, p = 0.641) and post-data (t-statistic = 0.46, p = 0.649) FEV1 levels, according to the unpaired t-test. Within each group, paired t-tests demonstrated a statistically significant increase in FEV1 from pre- to post-observation in Group A (t = 20.68, p statistic < 0.001) and B (t = 24.86, p < 0.001).

At pre-observation, there was an absence of noteworthy difference between Group A and Group B according to the unpaired t-test (t-statistic = -1.76, p = 0.084). Yet, at the 3-month assessment, there was a notable difference in post-observation mean FEV1 between Group A and Group B (t-value = -3.66, p-statistic = 0.001). Between each cohort, t-tests (paired) highlighted a significant increment in FEV1 from initial to post-observation in both Group A (t = 18.38, p < 0.001) and B, group (t = 16.47, p < 0.001).

At the 6-month follow-up, the unpaired t-test revealed A statistically significant difference in post-observation mean FEV1 among both groups (t-value = -2.06, p-value = 0.045). However, there is no significant difference between the groups at pre-observation (t-value = -0.93, p-value = 0.358).

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Within each cohort, paired t-statistic find out a noteworthy elevation in FEV1 from pre- to post-observation: A Group (t = 8.23, p statistic < 0.001) and B Group (t = 17.16, p statistic < 0.001).

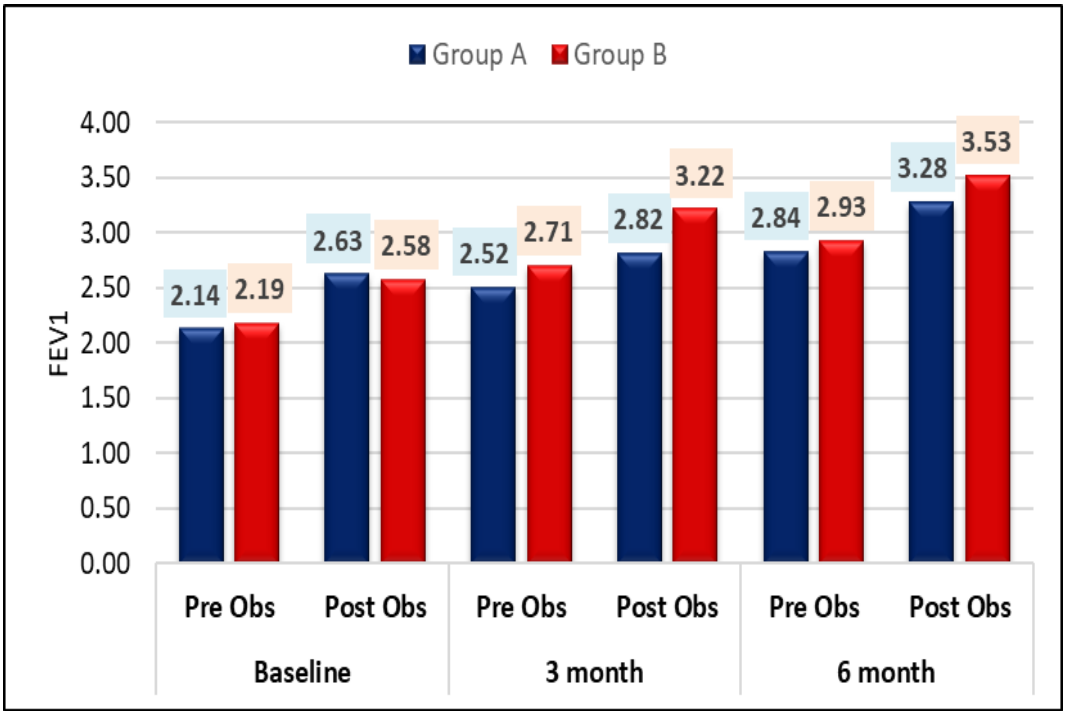

Figure 1: Baseline to 6-month FEV1 Status of A and B groups Observation

FEV1 (Pre - Post Change)	A, group		B, group		t test (unpaired)	
	Mean	SD	Mean	SD	t-value	p-value
Baseline	0.49	0.12	0.39	0.08	3.61	**0.001**
3 month	0.30	0.08	0.52	0.17	-5.77	**<0.001**
6 month	0.44	0.26	0.60	0.18	-2.51	**0.015**
RM ANOVA	F=8.71, **p=0.001**		F=18.6, **p<0.001**			

Table 4: Intergroup & Intragroup Comparison of FEV1 Pre – Post Changes

Baseline:

- Group A: Mean change in FEV1 = 0.49 (SD = 0.12)
- Group B: Mean variation in FEV1 = 0.39 (SD = 0.08)
- Unpaired t-test: Significant difference between groups (t-value = 3.61, p-value = 0.001)

3-month follow-up:

- Group A: Mean change in FEV1 = 0.30 (SD = 0.08)
- Group B: Mean change in FEV1 = 0.52 (SD = 0.17)
- Unpaired t-test: Significant difference between groups (t-value = -5.77, p-value < 0.001)

6-month follow-up:

- Group A: Mean change in FEV1 = 0.44 (SD = 0.26)
- Group B: Mean change in FEV1 = 0.60 (SD = 0.18)
- Unpaired t-test: Significant difference between groups (t-value = -2.51, p-value = 0.015)

Repeated Measures ANOVA:

- Group A: Showed statistically noteworthy changes over time (F = 8.71, p = 0.001)
- Group B: Displayed statistically significant alterations over time (F = 18.6, p < 0.001)

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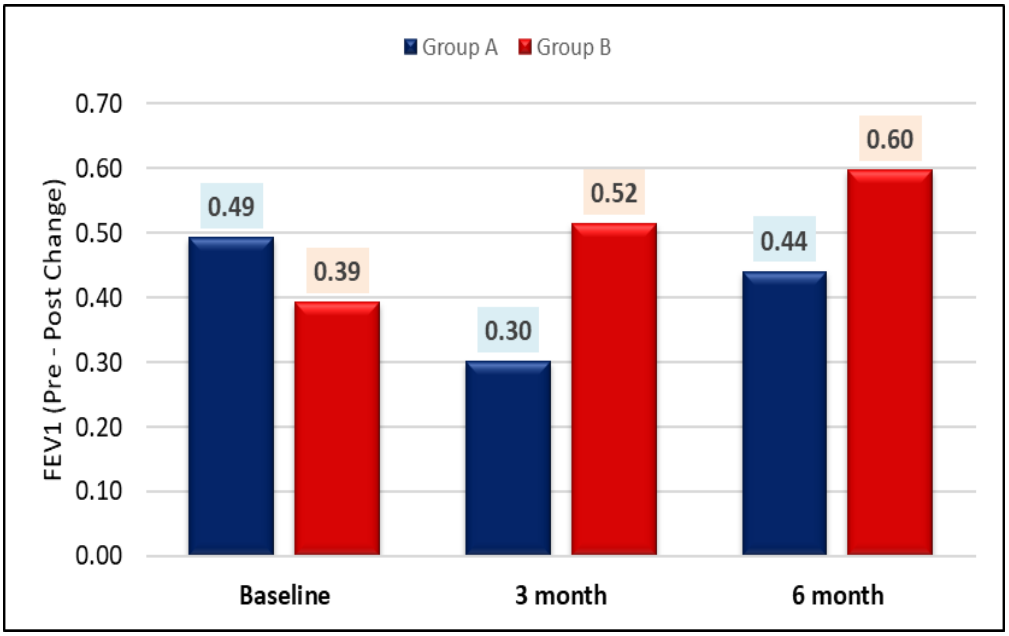

Figure 2: Baseline to 6-month FEV1 Pre-Post changes in A and B groups

DISCUSSION

In the present study comparing the effectiveness of Indacaterol/Mometasone (Group A) and Formoterol/Budesonide (Group B) in bronchial asthma patients, we observed distinct demographic characteristics and participation rates. Group A predominantly consisted of younger individuals, with 58.3% aged between 18 and 30 years, reflecting a mean age of 33.88±14.86 years. This group also had a higher male representation at 70.8%. Conversely, Group B had a similar age distribution, with 60.7% aged 18-30 years and a mean age of 29.82±11.36 years. It notably included a higher proportion of females at 60.7%.

In our study, both Group A (Indacaterol/Mometasone) and Group B (Formoterol/Budesonide) exhibited comparable mean **pre-bronchodilator** FEV1 values **at baseline**: 2.14 L (SD = 0.40) for Group A and 2.19 L (SD = 0.36) for Group B. **Post-bronchodilator** FEV1 values were: 2.63 L (SD = 0.43) for Group A and 2.58 L (SD = 0.39) for Group B. Statistical analysis using **paired t-tests** within each group determines a significant increment in FEV1 from pre- to post-observation in both; A group ($p < 0.001$) and B group ($p < 0.001$). No noteworthy variations were identified among the groups at baseline for either pre-observation (p-value = 0.641) or post-observation (p-value = 0.649) FEV1 values. These findings suggest that both DPI combinations effectively improved lung function in asthma patients, regardless of the initial FEV1 measurements.

At the **3-month follow-up**, Group A exhibited a mean pre-bronchodilator FEV1 of 2.52 L (SD = 0.38), while Group B had a mean of 2.71 L (SD = 0.40). Post-bronchodilator FEV1 measurements were 2.82 L (SD = 0.38) for 'A', group and 3.22 L (SD = 0.41) for B, group. There was no notable distinction between the groups in initial FEV1 assessments ($p = 0.084$). However, a notifiable significant variance emerged in post-observation mean FEV1 between both batches ($p = 0.001$) at the 3-month follow-up. Within each group, **paired t-tests** demonstrated a significant increase in FEV1 from pre- to post-observation ($p < 0.001$) for both Group A and Group B, indicating effective improvement in lung function with treatment over the 3-month period.

After the **6-month**, A group had a mean pre-bronchodilator FEV1 of 2.84 L (SD = 0.38), while Group B had a mean of 2.93 L (SD = 0.33). Post-bronchodilator FEV1 measurements were 3.28 L (SD = 0.50) for A, group and 3.53 L (SD = 0.36) for B group. There was no statistically noteworthy difference between the groups in pre-observation FEV1 (p-value = 0.358). Yet, a notable difference was determined in post-observation mean FEV1 between A and B group (p-value = 0.045) after the 6-month duration. Within each group, **paired t-tests** highlighted a noteworthy increase in FEV1 from prior to after-observation (p statistic < 0.001) for both Group A and Group B, indicating consistent improvement in lung function over the 6-month period with the respective treatments.

At baseline, the mean change in FEV1 before and after bronchodilator (Salbutamol) observation was 0.49 (SD = 0.12) for Group A and 0.39 (SD = 0.08) for Group B, with a statistically notifiable difference between the groups (p-statistic = 0.001).

After three months, Group A exhibited a mean change in FEV1 of 0.30 (SD = 0.08), whereas Group B showed 0.52 (SD = 0.17), revealing a notifiable difference ($p < 0.001$) between the groups.

By the six-month mark, Group A's mean change in FEV1 was 0.44 (SD = 0.26), while Group B recorded 0.60 (SD = 0.18), with a statistically significant difference observed between the groups ($p = 0.015$).

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Analysis of pre-post FEV1 changes over time (baseline, 3-month, and 6-month) displayed statistically significant differences for both A (p statistic = 0.001) and B (p statistic < 0.001) groups, signifying ongoing improvement in lung function throughout the study duration with both treatments.

A comprehensive determination of the IRIDIUM and PALLADIUM trials by Chapman et al. illustrated that high-dose Mometasone/Indacaterol produced superior enhancements in trough FEV1 in comparison to the high-dose Fluticasone/Salmeterol at 26th week (43 mL, p statistic = 0.001) and 52 (51 mL, p statistic < 0.001). Furthermore, the PALLADIUM study by van Zyl-Smit et al.[12] indicated that both high-dose Mometasone/Indacaterol (132 mL, p < 0.001) and medium-dose Mometasone/Indacaterol (211 mL, p < 0.001) demonstrated greater efficacy in improving FEV1 compared to equivalent Mometasone doses at week 26. Although, there was no significant variation in FEV1 improvement between high-dose Fluticasone/Salmeterol and high-dose Mometasone/Indacaterol at week 26 (Δ 36 mL [-7 to 80]; p = 0.101), indicating comparable effectiveness of the former.

REACT Study determines that combination of Budesonide/Formoterol and maintenance therapy led to noteworthy improvements in lung function as measured by FEV1 compared to baseline.[13] Research conducted as per Bodzenta-Lukazyk A et al. demonstrated that the effectiveness of Fluticasone/Formoterol (250/10 µg twice daily) was comparable to Budesonide/Formoterol (400/12 µg two times in a day) in both adolescents and adults with moderate-severe asthma, indicating non-inferiority between the two treatments.[14] On the other hand, research by Kuna P. demonstrated that formoterol and budesonide were equally effective as salmeterol and fluticasone. The FEV1 test did not show any statistically significant differences in lung function between the two treatments.[15]

CONCLUSION

In this study, both Group A (Indacaterol/Mometasone) and Group B (Formoterol/Budesonide) showed significant increment in mean FEV1 from pre- to post-bronchodilator at baseline, three-month, and six-month follow-up visits, indicating substantial improvements in lung function with both treatment regimens. Asthma patients responded favorably to both Indacaterol/Mometasone and Formoterol/Budesonide dry-powder inhaler therapies. At the three-month and six-month follow-ups, there were significant differences in post-bronchodilator mean FEV1 among both groups. Remarkably, the increment in mean FEV1 from pre- to post-observation was significantly higher in Group B (Formoterol/Budesonide) compared to Group A (Indacaterol/Mometasone) at these time point. Therefore, the twice-daily combination of Formoterol/Budesonide was more effective than the once-daily combination of Indacaterol/Mometasone in improving lung function assessed by FEV1 in asthma patients. However, differences in adherence to once-daily versus twice-daily regimens could influence the results but were not controlled for or reported. Further studies are needed to explore the impact of adherence on treatment outcomes and to validate these findings over longer durations.

Conflict of Interest: No conflict of Interest

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