



Original Article

Effectiveness of Pressurized Metered Dose Inhaler (pMDI) Versus Dry Powder Inhaler (DPI) in Delivering Inhaled Corticosteroid and Long-Acting Beta Agonist among Patients with Uncontrolled Asthma in a Tertiary Care Hospital

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ABSTRACT

Uncontrolled asthma remains common in Pakistan despite regular use of inhaled corticosteroid and long-acting beta-agonist combination therapy. Drug delivery may differ according to the inhaler device. Pressurized metered-dose inhalers (pMDIs) and dry powder inhalers (DPIs) are the most frequently prescribed devices, but local comparative evidence remains limited.

Objective: To compare the short-term effectiveness of pMDI and DPI in delivering inhaled corticosteroid and long-acting beta-agonist therapy among adults with uncontrolled asthma in a tertiary care hospital. **Methods:** This parallel randomized controlled trial was conducted at the Department of Pulmonology, Services Institute of Medical Sciences, Lahore. A total of 146 adults with uncontrolled asthma were randomized equally to pMDI (n=73) or DPI (n=73). The primary outcome was the proportion of participants achieving at least a 0.5-point reduction in Asthma Control Questionnaire (ACQ) score at 8 weeks. Secondary outcomes included mean ACQ change, change in forced expiratory volume in one second (FEV₁ % predicted), exacerbations, inhaler technique score, and adverse events. **Results:** Baseline age, sex, body mass index, asthma duration, baseline FEV₁ % predicted, and ACQ score were comparable between groups. Greater mean ACQ improvement was observed in the pMDI group than in the DPI group (4.6 ± 3.1 vs 3.2 ± 2.9; p = 0.006). FEV₁ improvement was also greater with pMDI (p=0.021). Exacerbations occurred in 24.7% of pMDI users and 39.7% of DPI users (p=0.048). Adverse events were mild and similar between groups. **Conclusion:** pMDI use was associated with better short-term asthma control and fewer exacerbations; larger multicentre studies are needed.

INTRODUCTION

Asthma remains one of the critical public health concerns in the world as it influences millions of people and leads to regular hospitalizations. It has been reported by a national survey that about 4.3% of adults in Pakistan live with asthma [1]. It seems that the burden among children and adolescents is even greater. The Global Asthma Network study illustrates that present-day wheeze has reached almost 11% of Pakistani school-going children [2], which

suggests that an appreciable percentage of patients live their lives with a symptom. The prevalence of asthma is reported to be significant in Asia. A survey conducted on a significantly large number of Asians showed that over half of patients report uncontrolled asthma even after medication [3]. Poor outcomes in South Asia can be facilitated by a lack of access to expert care and poor inhaler technique. Most patients use the inhalers

improperly, and this may decrease the amount of drug that goes to the pulmonary system and amplify the side effects at the location [4]. It is estimated that globally, 262 million people suffer from asthma, and that more than 450,000 deaths occur due to asthma per year. Though the mortality rates in high-income countries are reduced, the control rates are below optimal levels. As it has been reported in North America, about 40% of treated adults have uncontrolled symptoms [5]. Regular exacerbations and increased health-care utilization in Europe have been linked with inadequate compliance with inhaled corticosteroid therapy [6]. The combination of inhaled corticosteroid and long-acting beta-agonist therapy is the foundation of the treatment of moderate to severe asthma. Inhaled corticosteroids help in lowering airway inflammation, but long-acting beta-agonists offer prolonged bronchodilation of the respiratory tract. The Global Initiative for Asthma suggests this combination when used in patients who have persisting symptoms [7]. However, there is a significant effect on drug delivery depending on the kind of inhaler device used. The most prevalent respiratory appliances are pressurized metered-dose inhalers (pMDIs) and dry powder inhalers (DPIs). Despite the fact that these two modalities are therapeutically effective when appropriately handled, mistakes made during device handling are common. According to a multinational study, up to fifty percent of patients made at least one critical error in inhaler execution [8]. Another study in Europe implicated critical errors in insufficient control of asthma and a higher rate of exacerbations [9]. It is important to note that the resistance of the device, the actual inspiratory flow needed, and the coordination methods vary between pMDIs and DPIs. These variations can potentially change clinical response. Most of the comparative trials have been conducted in high-income environments with mixed outcomes. Although some of them have shown similar clinical results when sufficient inhalation technique is used [10], some studies have indicated that excessive dependence on devices and their usability could affect adherence and symptom control. The comparison focused on improvement in asthma control measured by Asthma Control Questionnaire (ACQ) score after 8 weeks of treatment. Secondary objectives were to compare changes in forced expiratory volume in one second (FEV₁ % predicted), frequency of exacerbations, inhaler technique performance, and adverse events between the two inhaler device groups.

Limited evidence exists on the use of inhaler technique in Pakistan; the current literature is more focused on the prevalence or educational intervention to achieve this objective. Therefore, there is a dearth of direct comparisons of pMDIs and DPIs in combination therapy in

patients having uncontrolled asthma in a tertiary care setting. This study aimed to compare the effectiveness of pressurized metered-dose inhaler (pMDI) and dry powder inhaler (DPI) in delivering inhaled corticosteroid and long-acting beta-agonist combination therapy among adults with uncontrolled asthma in a tertiary care hospital.

METHODS

It comprised a superiority, parallel, single-centre, randomized, controlled trial which was conducted in the Department of Pulmonology, Services Institute of Medical Sciences, Lahore. The allocation ratio was 1:1. This was a nine-month study (1 February 2025 to 30 November 2025), involving 8 weeks of follow-up of individual participants who had commenced the intervention. The last follow-up of the patient who was last enrolled was done on 30 January 2026. Institutional Review Board approval was obtained under reference IRB/2025/1520/SIMS; dated 27th January 2025, and the trial was post-hoc registered on ClinicalTrials.gov (registration number NCT07372573). Adult patients who had been diagnosed with asthma by a physician and were aged between 18 and 60 years were screened. It had already been diagnosed on the basis of reversible airflow limitation, which is an increase of at least 12% in forced expiratory volume in one second and 200 mL of forced expiratory volume after taking bronchodilators. Only patients with uncontrolled forms of asthma were included; they had to have received inhaled corticosteroid and long-acting beta-agonist treatment at least three months before they were enrolled. Patients who had chronic obstructive pulmonary disease, bronchiectasis, interstitial lung disease, active pulmonary tuberculosis, pregnancy, or severe heart disease were excluded. Those who could not perform spirometry reliably were also excluded. Informed consent was taken in writing before enrollment. The recruitment process was conducted using inpatient clinics, and eligibility was affirmed by a consultant pulmonologist. The sample size was calculated to detect a minimum clinically important difference of 0.5 points in the Asthma Control Questionnaire (ACQ) score between two independent groups. A standard deviation of 0.9 was assumed based on previous adult asthma trials evaluating inhaled corticosteroid and long-acting beta-agonist therapy [11]. Using a two-sided alpha of 0.05 and a power of 80%, the required minimum sample size was calculated. After accounting for possible attrition, 146 participants (73 per group) were enrolled. Participants were selected at random to take either the pressurized metered-dose inhaler or a dry powder inhaler to give them an inhaled corticosteroid and a long-acting beta-agonist. The creation of the random sequences was done via a variable block-based, computer-generated block-randomization scheme. Sequentially numbered, opaque,

and sealed envelopes were used to provide allocation concealment. At the end of the assessment, randomization took place. The study shows the CONSORT diagram of participant inclusion and allocation (Figure 1).

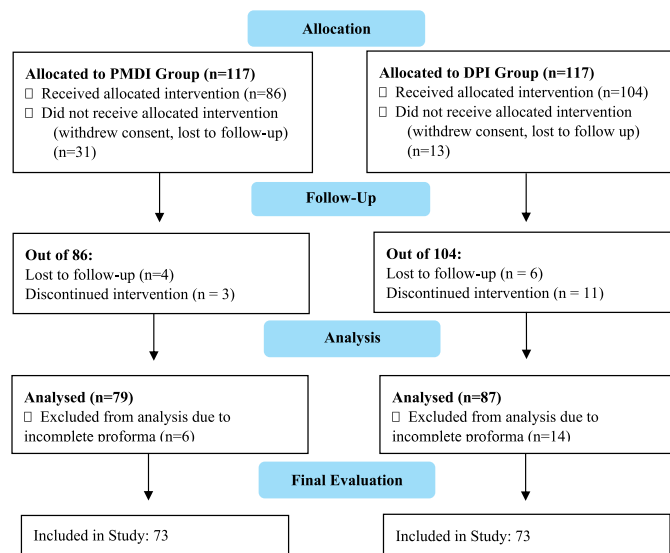


Figure 1: CONSORT 2010 Flow Diagram of the Included Participants

The patients receiving the dry powder inhaler (DPI) group were given 400/12 µg of formoterol-budesonide per day, twice daily, in a single puff. The members of the pressurized metered-dose inhaler (pMDI) cohort were given 200/6 µg of the same formulation, but in two puffs twice daily, so that it yielded an equivalent amount of 800/24 µg each day. This dosing was consistent with previous published literature [12]. Each of the participants was provided with personalized training on inhaler technique, based on a standardized checklist including ten essential steps. The technique was then reviewed at every planned visit. Uncontrolled asthma was operationalized as the use of 400/12 µg of formoterol-budesonide and an Asthma Control Questionnaire (ACQ) score of 3 and above at the time of presentation to the outpatient department. The criterion of treatment effect was a decrease in the ACQ score of at least 0.5 points compared to baseline that was achieved after eight weeks of treatment [13]. Every patient was given a standard dosage of inhaled corticosteroid and long-acting beta-agonist (ICS/LABA), at DPI (400/12 micrograms, 1 puff, twice a day) or pMDI (200/6 micrograms, 2 puffs, twice a day), so that all participants had the same total dose of 800/24 micrograms. The continuous baseline variables included age (years), body mass index (kg m^{-2}), years of asthma (years), baseline forced expiratory volume in one second (FEV1) as percent-predicted, and baseline ACQ score. Spirometry was performed using a MIR Spirobank II Basic spirometer (Medical International Research, Rome, Italy) according to

American Thoracic Society/European Respiratory Society standards. The device was calibrated daily before patient testing, and three reproducible manoeuvres were recorded for each participant. The spirometric tests were performed with a validated spirometer as per the guidelines of the American Thoracic Society; three maneuvers that were reproducible were taken. Body mass index was computed as weight (kg)/height squared (m^2). The categorical variables were gender, smoking status, the existence of allergic rhinitis, exposure to biomass smoke, and previous hospitalization for asthma in the last year. The smoking population was arranged into never smokers, former smokers, and current smokers. Exposure to biomass was categorized as frequent exposure to wood or coal smoke over a duration of more than five years. The major outcome was the difference between baseline and the 4- and 8-week Asthma Control Questionnaire (ACQ) score. Secondary outcomes were the change in forced expiratory volume in one second percent predicted, exacerbations during follow-up, and inhaler technique score. Exacerbation was considered to be symptoms that worsened to the extent that they required systemic corticosteroids during a period of at least three days or an emergency department visit. The score on the inhaler technique was assessed using a 10-point checklist; a value of 8 and above was deemed as correct technique [14]. A random selection of consenting participants already taking the baseline dose of DPI (400/12 micrograms of Formoterol-Budesonide) was put into either formulation of inhaled corticosteroid (ICS) and long-acting beta-agonist (LABA) (Budesonide and Formoterol), either by the use of a pressurized metered-dose inhaler (pMDI) or the use of a dry powder inhaler (DPI). The study indicates that both of the devices that the asthma patients were using (Figure 2)

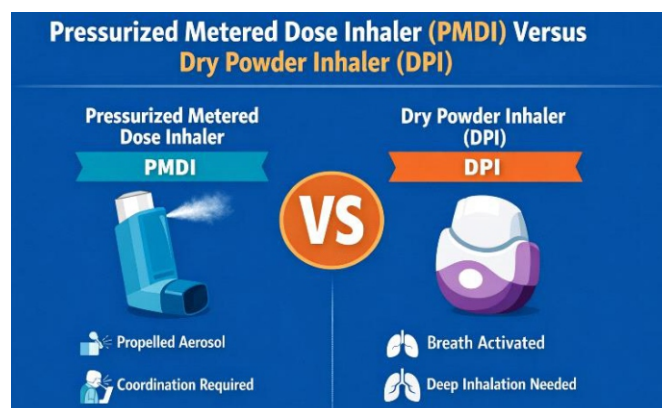


Figure 2: PMDI and DPI Devices Used by Asthma Patients

The Asthma Control Questionnaire (ACQ) at 8 weeks was prespecified as the primary outcome. Secondary outcomes were analysed as supportive exploratory endpoints; therefore, no formal adjustment for multiple comparisons was applied, and secondary outcome p-

values were interpreted cautiously. SPSS version 26.0 was used in statistical analysis. Means and standard deviations represented continuous variables, and frequencies and percentages represented categorical ones. The primary analysis was performed using analysis of covariance (ANCOVA), with 8-week Asthma Control Questionnaire (ACQ) score as the dependent variable, treatment group as the fixed factor, and baseline ACQ score as a covariate. A similar ANCOVA approach was used for FEV₁ % predicted at follow-up, adjusting for baseline FEV₁. Between-group adjusted mean differences with 95% confidence intervals were reported. Categorical outcomes were compared using the chi-square test or logistic regression, where appropriate. An independent consultant who had no part in the allocation of patients performed safety monitoring. Every protocol deviation was noted. There was no planned interim analysis. The trial was conducted in accordance with the Declaration of Helsinki [13]. Each participant provided written informed consent. The analysis of the data was in line with a prespecified statistical plan, ensuring transparency and methodological rigor.

RESULTS

A total of 146 participants were randomized equally to the pressurized metered-dose inhaler (pMDI) group (n=73) and the dry powder inhaler (DPI) group (n=73). All participants completed 8 weeks of follow-up and were included in the final analysis. No crossover between treatment groups occurred during follow-up. At 8 weeks, a clinically meaningful improvement in ACQ score (≥ 0.5 -point reduction from baseline) was achieved by 61 participants (83.6%) in the pMDI group compared with 49 participants (67.1%) in the DPI group. The study presents the demographic and exposure characteristics of participants at baseline. Continuous variables are expressed as mean $\pm$ standard deviation or median (interquartile range), while categorical variables are reported as frequencies and

percentages. No baseline demographic variable showed a statistically significant difference between the two treatment groups (Table 1).

Table 1: Baseline Demographic and Exposure Characteristics

Variables	pMDI Group (n=73)	DPI Group (n=73)	Test Statistic	p-value
Age (years)	40.3 $\pm$ 10.9	39.2 $\pm$ 11.5	t (144) = 0.61 ^a	0.540
Male Gender	42 (57.5%)	40 (54.8%)	χ^2 (1) = 0.13 ^c	0.710
Body Mass Index (kg/m ²)	27.6 $\pm$ 4.3	26.9 $\pm$ 4.7	t (144) = 1.08 ^a	0.280
Duration of Asthma (years)	6 (3-10)	6 (3-10)	Mann-Whitney U ^b	0.470
Current Smoker	16 (21.9%)	18 (24.7%)	χ^2 (1) = 0.29 ^c	0.590
Biomass Exposure	19 (26.0%)	22 (30.1%)	χ^2 (1) = 0.60 ^c	0.440
Allergic Rhinitis	31 (42.5%)	32 (43.8%)	χ^2 (1) = 0.02 ^c	0.890

Data were presented as mean $\pm$ SD, median (IQR), or n (%). Statistical significance set at p<0.005. ^aindependent sample t-test; ^bMann-Whitney U test; ^cchi-square test. Baseline clinical and pulmonary function parameters were also similar between groups. Mean baseline forced expiratory volume in one second (FEV₁ % predicted) and Asthma Control Questionnaire (ACQ) scores showed no statistically significant differences. These findings suggest that both treatment arms had similar initial asthma severity before intervention. The study summarizes baseline lung function and asthma symptom burden in both groups. All variables are presented as mean $\pm$ standard deviation. Statistical comparison confirmed no significant difference in baseline clinical severity (Table 2).

Table 2: Baseline Clinical and Lung Function Variables

Variables	pMDI Group (n=73)	DPI Group (n=73)	Test Statistic	p-value
FEV ₁ % predicted	62.4 $\pm$ 8.7	61.8 $\pm$ 9.1	t (144) = 0.41 ^a	0.680
ACQ score at presentation	4.3 $\pm$ 0.8	4.1 $\pm$ 0.9	t (144) = 0.33 ^a	0.740

Data are presented as mean $\pm$ SD. Statistical significance set at p<0.005. ^aindependent sample t-test. FEV₁ = forced expiratory volume in one second; ACQ = Asthma Control Questionnaire

Both treatment groups showed improvement during follow-up, although greater improvement was observed in the pMDI group at 8 weeks. A clinically meaningful reduction in ACQ score was achieved more frequently among pMDI users. Improvement in lung function and lower exacerbation frequency also favored pMDI. The study presents the primary and secondary clinical outcomes measured at 4 and 8 weeks. Continuous outcomes are shown as mean $\pm$ standard deviation, and categorical outcomes are shown as frequencies and percentages. Significant between-group differences were observed mainly at 8 weeks (Table 3).

Table 3: Clinical Outcomes at 4 and 8 Weeks

Variables	pMDI Group (n=73)	DPI Group (n=73)	Test Statistic	p-value
Change in ACQ Score at 4 Weeks	1.9 $\pm$ 0.8	1.7 $\pm$ 0.9	t (144) = 1.38 ^a	0.170
Change in ACQ Score at 8 Weeks	2.9 $\pm$ 1.1	2.3 $\pm$ 1.0	t (144) = 2.79 ^a	0.006
≥ 0.5 -Point ACQ Improvement at 8 Weeks	61 (83.6%)	49 (67.1%)	χ^2 (1) = 5.31 ^c	0.021
Change in FEV ₁ % Predicted at 4 Weeks	5.2 $\pm$ 4.6	4.5 $\pm$ 4.4	t (144) = 0.99 ^a	0.320
Change in FEV ₁ % Predicted at 8 Weeks	8.4 $\pm$ 6.2	6.1 $\pm$ 5.8	t (144) = 2.33 ^a	0.021

≥1 Exacerbation During Follow-Up at 4 Weeks	6 (8.2%)	12 (16.4%)	$\chi^2 (1) = 2.65^c$	0.100
≥1 Exacerbation During Follow-Up at 8 Weeks	18 (24.7%)	29 (39.7%)	$\chi^2 (1) = 3.91^c$	0.048
Correct Inhaler Technique at 4 Weeks	55 (75.3%)	47 (64.4%)	$\chi^2 (1) = 2.96^c$	0.090
Correct Inhaler Technique at 8 Weeks	61 (83.6%)	52 (71.2%)	$\chi^2 (1) = 3.11^c$	0.080

Statistical significance set at $p < 0.005$

Adverse events were infrequent and mild in both groups. No serious treatment-related complications were observed during follow-up. Improvement in inhaler technique showed a moderate positive correlation with improvement in symptom control. The results present safety outcomes and correlation analysis. Local adverse effects were similar between groups, while correlation analysis demonstrated a statistically significant relationship between inhaler technique improvement and ACQ reduction (Table 4).

Table 4: Safety Outcomes and Correlation Analysis

Variables	pMDI Group (n=73)	DPI Group (n=73)	Test Statistic	p-value
Oral Candidiasis	6 (8.2%)	9 (12.3%)	$\chi^2 (1) = 0.69^c$	0.410
Dysphonia	4 (5.5%)	6 (8.2%)	$\chi^2 (1) = 0.43^c$	0.510
Any Local Adverse Effect	10 (13.7%)	9 (12.3%)	$\chi^2 (1) = 0.06^c$	0.810
Correlation Between Inhaler Technique Improvement and ACQ Score Change	—	—	$r = 0.34$, $t (144) = 4.32^f$	<0.001

Data are presented as n (%) or correlation coefficient (r). Statistical significance set at $p < 0.005$. ^cchi-square test; ^fPearson correlation

DISCUSSION

The findings of the present study should be interpreted in the context of prior literature on asthma burden, inhaler technique, and treatment control. World Medical Association highlighted the persistent global burden of asthma, emphasizing that asthma remains a major public health problem across regions and healthcare systems [13]. This broader context supports the clinical relevance of our findings, as even modest improvements in controller therapy delivery may translate into meaningful gains in disease control. In our trial, patients using pMDI achieved greater improvement in ACQ score and FEV₁, with fewer exacerbations than those using DPI, suggesting that device choice may contribute to better short-term outcomes in uncontrolled asthma. Melani *et al.* reported that incorrect inhaler technique is common among asthma patients in Pakistan, which is consistent with our observation that inhaler technique performance improved over follow-up and was positively correlated with improvement in symptom control [14]. The current results extend their findings by showing that, despite training in both groups, the pMDI group achieved better clinical outcomes, indicating that device-related differences may remain important even under supervised conditions.

Similarly, Zhang *et al.* found that poor asthma control persists in a substantial proportion of treated adults, suggesting that pharmacologic treatment alone does not guarantee adequate disease control [15]. This aligns with our results, where both groups received equivalent budesonide-formoterol doses, yet the pMDI group demonstrated superior improvement, reinforcing the importance of delivery efficiency in addition to medication selection. Irfan *et al.* showed that inhaler-use errors remain frequent across devices and are associated with poorer outcomes [16]. However, the greater gains observed in the pMDI arm suggest that, when patients are properly instructed, pMDI may offer a practical advantage in drug delivery and clinical response in this setting. Collectively, these studies support our conclusion that inhaler device selection, together with structured education, can meaningfully influence asthma outcomes. Biological plausibility is worthy of consideration. Airway inflammation is reduced by inhaled corticosteroids, which inhibit eosinophilic activity and cytokine secretion. An effective anti-inflammatory effect demands proper pulmonary deposition. The condition may lead to chronic inflammation and relapsing current symptoms [17]. Various empirical studies have revealed that non-adherence and incorrect methods are linked to increased eosinophil counts and reduced disease control [18]. The correlation observed between enhanced technique and improvement in symptom scores may hence indicate this mechanistic pathway [19,20].

The strengths of the study are random allocation, standardization, and the variability of dosing and objective lung function (spirometry). Follow-up was done for all subjects, and symptom scores, as well as lung function, were measured. However, there were some limitations. The research was done at one tertiary care unit and not at a rural or primary care setting. The sample size was not large, despite the fact that it was calculated correctly. The maximum follow-up period was eight weeks, and the patterns of long-term adherence were not determined. Biomarkers like fractional exhaled nitric oxide were not measured.

CONCLUSIONS

In this single-centre randomized study, the pressurized metered-dose inhaler was associated with greater improvement in asthma control and lung function compared with the dry powder inhaler over 8 weeks of follow-up among adults with uncontrolled asthma. These

findings suggest that device selection and structured inhaler education may influence short-term asthma outcomes in similar tertiary care settings.

Authors' Contribution

Conceptualization: SS

Methodology: MH, SA², LQB

Formal analysis: SA¹

Writing and Drafting: XQ

Review and Editing: XQ, MH, SA¹, SS, SA², LQB

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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