**Scholars Journal of Applied Medical Sciences**
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

**Respiratory Medicine**

# Efficacy and Safety of Hydrofluoroalkane Beclomethasone Dipropionate (HFA-BDP) over Chlorofluorocarbon Beclomethasone Dipropionate (CFC-BDP) for the Treatment of Moderate Persistent Asthma: A Randomized Control Trial

Dr. Mohammad Towfique Hasan[1*], Dr. Md. Alauddin[2], Dr. Jalal Mohsin Uddin[3], Dr. Mahfuza Tayeba Yasmin[4]

[1]Assistant Professor, Respiratory Medicine, Sir Salimullah Medical College Dhaka, Bangladesh
[2]Assistant Professor, Respiratory Medicine Sheikh Hasina Medical College Tangail, Bangladesh
[3]Assistant Professor, National Institute of Diseases of Chest and Hospital, Mohakhali, Dhaka Bangladesh
[4]Senior Medical Officer BIHS Hospital, Dhaka Bangladesh

**DOI:** 10.36347/sjams.2022.v10i05.028 | **Received:** 29.03.2022 | **Accepted:** 07.05.2022 | **Published:** 26.05.2022

***Corresponding author:** Dr. Mohammad Towfique Hasan
Assistant Professor, Respiratory Medicine, Sir Salimullah Medical College Dhaka, Bangladesh

**Abstract** **Original Research Article**

***Background:*** Management of moderate persistent asthma is very crucial among the patients. ***Objective:*** The purpose of the present study was to see the efficacy and safety of hydrofluoroalkane beclomethasone dipropionate (HFA-BDP) by comparing the chlorofluorocarbon beclomethasone dipropionate (CFC-BDP) for the treatment of moderate persistent asthma. ***Methodology*:** This randomized clinical trial was carried out at the outpatient department (OPD) of National Institute of diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka from July 2010 to June 2011 for one year. All men and women aged from 18 to 65 years suffering from moderate persistent bronchial asthma attending the OPD of NIDCH, Mohakhali, and Dhaka during the specified period were enrolled after fulfilling the selection criteria. Eligible patients were randomized by odd or even identification numbers divided into group A and group B and they received coded HFA-BDP (400 µg/day) or CFC-BDP (1000 µg/day) respectively for 12 weeks. The patients were evaluated at $4^{th}$, $8^{th}$ and $12^{th}$ weeks after starting the treatment. The outcome parameters were spirometry (FEV1 and PEFR). ***Results:*** All 97 patients were divided into two groups (A & B) by odd or even number. Group A consisted of 49 patients who were treated with HFA-BDP in an amount of 400µg/day and group B consisted of the remaining 48 patients who were treated with CFC-BDP in an amount of 1000µg/day. The mean age of HFA and CFC inhaler group is 27.49 ± 7.04 and 27.98 ± 7.86 (p=0.747) respectively. Baseline PEFR was 65.45 ± 2.26 and 65.00 ± 2.38 in HFA and CFC inhaler group respectively (p=0.343). PEFR at 1st follow up (p<0.001), at 2nd follow up (p<0.001) and at 3rd follow up (p<0.001) in HFA and CFC inhaler group were significant. PEFR difference between baseline and $1^{st}$ follow up, $1^{st}$ and $2^{nd}$ follow up, and 2nd and 3rd follow up found in HFA and CFC inhaler group respectively were statistically significant (p<0.001). FEV1 at 1st follow up (p<0.001), at 2nd follow up (p<0.001) and at 3rd follow up (p<0.001) in HFA and CFC inhaler group were significant. ***Conclusion:*** In conclusion efficacy and safety of hydrofluoroalkane beclomethasone dipropionate (HFA-BDP) is significantly better than chlorofluorocarbon beclomethasone dipropionate (CFC-BDP) for the treatment of moderate persistent asthma.

**Keywords:** Hydrofluoroalkane beclomethasone dipropionate; HFA-BDP; chlorofluorocarbon beclomethasone dipropionate; CFC-BDP; persistent asthma.

**Copyright © 2022 The Author(s):** This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

## INTRODUCTION

Asthma is one of the most common chronic diseases worldwide affecting 300 million people worldwide. It is increasing in prevalence each year [1]. Asthma in Bangladesh appears to be also a substantial public health problem: an estimated 7 million people including 4 million children suffer from asthma related symptoms [2]. According to First National Asthma Prevalence Study [2], in Bangladesh about 7 million people i.e. 5.2% of the population are suffering from current asthma at least three episodes of asthma attack in last 12 months. More than 90% of them do not take modern treatment; however, unfortunately, majority of these people are under 15 years of age group that is 7.4% of the total pediatric population of our country is suffering from asthma [2].

Beclomethasone dipropionate (BDP) is an established corticosteroid for the treatment of asthma and it has now been reformulated using the new HFA propellant, which has provided the opportunity to significantly improve the delivery of inhaled drugs to the respiratory tract [3]. In contrast to current CFC-BDP products, this new formulation is a solution, rather than

a suspension of BDP in propellant with the solution forming an extrafine aerosol of small droplets as the propellant evaporates [4]. Chlorofluorocarbon (CFC) preparations exhibit aerodynamic particle sizes of between 3 to 4 µm, whereas this HFA-BDP formulation has a mass median aerodynamic diameter of approximately 1.2 µm [5].

HFA-BDP extrafine aerosol changes the standard pattern of drug deposition seen with CFC-BDP formulations, delivering most of the inhaled dose to the airways and depositing in much smaller proportion in the oropharynx [6]. Results of direct radiolabeled deposition studies in both healthy volunteers and patients with asthma show ex-actuator lung deposition to be 51% to 60% with HFA-BDP compared with lung deposition of <10% for CFC-BDP [7]. The purpose of the present study was to see the efficacy and safety of hydrofluoroalkane beclomethasone dipropionate (HFA-BDP) by comparing the chlorofluorocarbon beclomethasone dipropionate (CFC-BDP) for the treatment of moderate persistent asthma.

# METHODOLOGY

### Study Settings and Study Population

This was a randomized clinical trial. This study was carried out at the outpatient department (OPD) of National Institute of diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka. This study was carried out during the period from July 2010 to June 2011 for one year. All men and women aged from 18 to 65 years suffering from moderate persistent bronchial asthma attending the OPD of NIDCH, Mohakhali, and Dhaka during the specified period were enrolled after fulfilling the selection criteria. 97 patients were included after taking informed written consent. The diagnosis of moderate asthma was based on Global Initiative for Asthma (GINA) Classification. Patient having daytime symptoms (respiratory distress, cough, wheeze and chest tightness) daily, nocturnal symptoms >1 time a week, diagnosis is confirmed by spirometry. Baseline spirometry showing FEV1 within 60% to 80% and presence of one of the features of severity was sufficient to place a patient in that category were the criteria. Population with moderate asthma (according to GINA classification) who were symptomatic despite current treatment with bronchodilators and inhaled steroid (CFC-BDP) of 500 µg/day, age between 18 to 65 years, nonsmokers were included in this study. Patients with Acute severe asthma attack, refractory asthma, COPD, Acute upper or lower respiratory tract infection within 4 weeks before the start of trial, patients who received any medication other than for asthma, significant diseases other than asthma like Diabetes mellitus, recent history of myocardial infarction (<1 year), heart failure or cardiac arrhythmia requiring drug treatment were excluded from this study.

### Randomization

Eligible patients were randomized by odd or even identification numbers divided into group A and group B. They received coded HFA-BDP (400 µg/day) or CFC-BDP (1000 µg/day) respectively for 12 weeks.

### Intervention

The study was out patients hospital based clinical trial which comprised of 7 day**s** Run-in phase- for confirmation of diagnosis and evaluation of eligibility. Each subject was evaluated with history and symptoms regarding the presentation. They were examined and certain baseline investigations were done. Previous investigation reports and all medical records were evaluated thoroughly. During this period they received 30 mg daily morning dose of oral prednisolone to create a baseline; 12 weeks Clinical and follow-up phase- management of asthma along with either HFA-BDP inhaler, 400µg/day (100µg 2 puffs twice daily) or CFC-BDP, 1000 µg/day (250 µg 2 puffs twice daily) and to see the effect of the drugs.

### Follow Up and Outcomes Measures

The patients were evaluated at 4th, 8th and 12th weeks after starting the treatment. Before entry and the completion of the study, patients had undergone a medical examination and necessary investigations. At each scheduled visit detail of clinical status, adverse events, exacerbations and withdrawals were recorded. The outcome parameters were spirometry (FEV1 and PEFR).

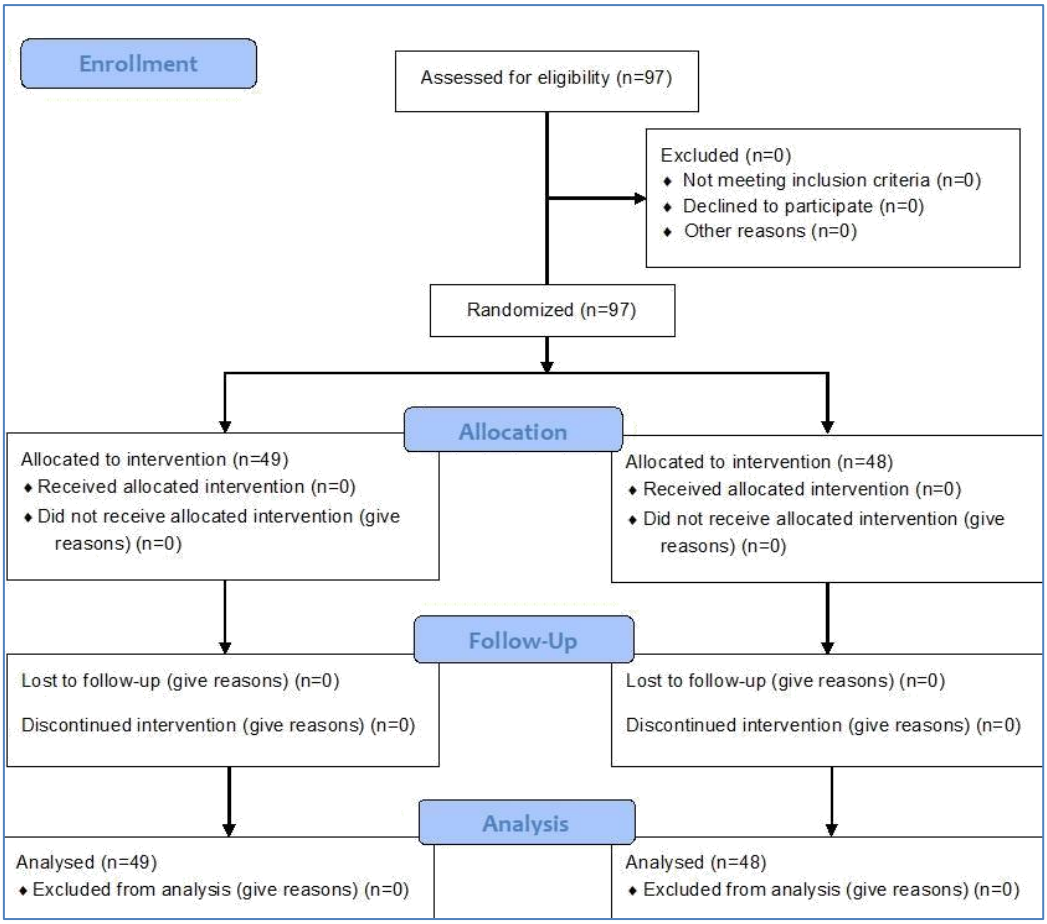


**Fig-I: Consolidated Standards of Reporting Trials (CONSORT) chart of study**

## STATISTICAL ANALYSIS

All data were recorded systematically in preformed data collection form and for quantitative data mean and standard deviation and for qualitative data frequency distribution and percentage was calculated. Statistical analysis was performed by using SPSS (Statistical Package for Social Sciences) for windows version 12.0. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

## RESULTS

All patients were divided into two groups (A & B) by odd or even number. 49 patients were included in group A and 48 patients in group B. Group A consists of 49 patients who were treated with HFA-BDP in an amount of 400µg/day and group B consists of the remaining 48 patients who were treated with CFC-BDP in an amount of 1000µg/day. Among 49 cases in HFA inhaler group majority were in the age group of 26-35 years, 22 (44.9%) followed by less than or equal to 25 years and more than 35 years, 21 (42.9%) and 6 (12.2%) cases respectively. Among 48 cases in CFC inhaler group majority were in the age group of less than or equal to 25 years, 19 (39.6%) followed by 26-35 years and more than 35 years, 17(35.4%) and 12(25.0%) cases respectively. The mean age of HFA and CFC inhaler group is 27.49 ± 7.04 and 27.98 ± 7.86 (p=0.747) respectively (Table 1).

**Table-1: Distribution of age by groups (n=97)**

| **Age (in year)** | **Age (in year)** | | **P value*** | |
|---|---|---|---|---|
| | **Group A (n=49)** | | **Group B (n=48)** | |
| | **(HFA-BDP inhaler)** | | **(CFC-BDP inhaler)** | |
| ≤25 | 21 (42.9) | | 19 (39.6) | |
| 26-35 | 22 (44.9) | | 17 (35.4) | |
| >35 | 6 | (12.2) | 12 (25.0) | |
| **Total** | **49** | **(100.0)** | **48 (100.0)** | |
| Mean ± SD | 27.49 ± 7.04 | | 27.98 ± 7.86 | 0.747 |

*t test was done to measure the level of significance; Figure within parentheses indicates in percentage.

Baseline PEFR was 65.45 ± 2.26 and 65.00 ± 2.38 in HFA and CFC inhaler group respectively (p=0.343). PEFR at 1st follow up was 74.18 ± 3.56 and 71.17 ± 2.98 in HFA inhaler group and CFC inhaler group respectively (p<0.001). PEFR at 2nd follow up was 80.76 ± 3.82 and 77.06 ± 3.12 in HFA and CFC inhaler group respectively (p<0.001). PEFR at 3rd follow up was 88.63 ± 4.64 and 82.58 ± 5.66 in HFA and CFC inhaler group respectively (p<0.001). PEFR difference between baseline and 1st follow up, 1st and 2nd follow up, and 2nd and 3rd follow up found in HFA and CFC inhaler group respectively were statistically significant (p<0.001). Changes of PEFR in the 2nd follow up between two groups were 6.57±3.72 and 5.90±2.28 in HFA and CFC inhaler group respectively which was statistically non-significant (p=0.285). Otherwise, all changes were statistically significant.

**Table-2: Mean ± SD of PEFR by groups (baseline & during follow up) (n=97)**

| PEFR | | Groups | P value* |
|---|---|---|---|
| | HFA inhaler Gr-A(n=49) | CFC inhaler Gr-B(n=48) | |
| **Baseline** | 65.45 ± 2.26 | 65.00 ± 2.38 | 0.343 |
| **1st follow up** | 74.18 ± 3.56 | 71.17 ± 2.98 | 0.001 |
| Difference between baseline and 1st follow up | 8.73 ± 3.85 (#p<0.001) | 6.17 ± 3.01 (#p<0.001) | 0.001 |
| **2nd follow up** | 80.76 ± 3.82 | 77.06 ± 3.12 | 0.001 |
| Difference between 1st and 2nd follow up | 6.57 ± 3.72 (#p<0.001) | 5.90 ± 2.28 (#p<0.001) | 0.285 |
| **3rd follow up** | 88.63 ± 4.64 | 82.58 ± 5.66 | 0.001 |
| Difference between 2nd and 3rd follow up | 7.88 ± 3.39 (#p<0.001) | 5.52 ± 3.78 (#p<0.001) | 0.002 |

*t test was done to measure the level of significance; #Paired t test was done to measure the level of significance; Data was expressed as Mean ± SD.

Table 3 showed the mean ± SD of FEV1 by groups (baseline and after treament). Baseline FEV1 were 65.71 ± 5.6 and 65.75 ± 4.1 in HFA and CFC inhaler group respectively (p=0.972). FEV1 at 1st follow up were 77.04 ± 3.83 and 73.08 ± 4.09 in HFA and CFC inhaler group respectively (p<0.001). At 2nd follow up FEV1 were 83.67 ± 3.28 and 79.19 ± 4.47 in HFA and CFC inhaler group respectively (p<0.001). FEV1 at 3rd follow up were 89.08 ± 4.4 and 83.71 ± 5.97 in HFA and CFC inhaler group respectively (p<0.001). FEV1 differences between baseline and 1st follow up were 11.33. 5.53 and 7.33 ± 3.48 in HFA and CFC inhaler group respectively. They were statistically significant (p<001). But, FEV1 changes between 1st and 2nd follow up, and 2nd and 3rd follow up between the two drugs were statistically not significant (p<0.467 & <0.191). So, both the drugs are equally effective in improving FEV1 in asthma patient.

**Table 3: Mean ± SD of FEV1 by groups (n=97)**

| FEV1 | Groups | | P value* |
|---|---|---|---|
| | HFA inhaler Gr-A(n=49) B(n=48) | CFC inhaler Gr-B(n=48) | |
| **Baseline** | 65.71 ± 5.67 | 65.75 ± 4.12 | 0.972ns |
| **1st follow up** | 77.04 ± 3.83 | 73.08 ± 4.09 | 0.001 |
| Difference between baseline and 1st follow up | 11.33 ± 5.53 (ap<0.001) | 7.33 ± 3.48 (ap<0.001) | 0.001 |
| **2nd follow up** | 83.67 ± 3.28 | 79.19 ± 4.47 | 0.001 |
| Difference between 1st and 2nd follow up | 6.63 ± 3.55 (ap<0.001) | 6.10 ± 3.57 (ap<0.001) | 0.467 ns |
| **3rd follow up** | 89.08 ± 4.42 | 83.71 ± 5.97 | 0.001 |
| Difference between 2nd and 3rd follow up | 5.41 ± 3.55 (ap<0.001) | 4.52 ± 3.06 (ap<0.001) | 0.191 ns |

*t test was done to measure the level of significance; aPaired t test was done to measure the level of significance; Data was expressed as Mean ± SD.

## DISCUSSION

Asthma is a multifactorial and complex chronic disease characterized by variable airflow obstruction and airway hyper-responsiveness [8]. Prevalence of asthma is due to hereditary and changing environmental factors. Asthma exacerbations are episodes of progressively worsening shortness of breath, cough, wheezing, chest tightness or some combination of these symptoms [9].

The use of corticosteroid aerosols to treat asthma and other diseases is increasing dramatically worldwide owing to the ability of steroids to treat more the underlying causes of asthma and to the contrary β-agonists only treat symptoms10. Beclomethasone Dipropionate (BDP) is being formulated as a solution with the propellant HFA-134a. When the propellant evaporates during dosing, it has been found that much smaller aerosol particles are delivered to the patient than with the CFC–BDP suspension products [11]. Therefore, less amount of drug is needed to control asthma. My study supports this too.

In this study among 97 cases in both groups majority were at or below 35 years of age. Similar result was reported by Chen *et al*. [12] and mentioned that younger age group are the most prevalent in asthma attack. Schatz *et al.* [3] also found same result in a similar study.

The mean ± SD of PEFR by groups was shown in the study. Baseline PEFR was 65.45 ± 2.26 in HFA inhaler and 65.00 ± 2.38 in CFC inhaler group (p=0.343) respectively. With therapy PEFR was improved gradually in both groups. PEFR difference between baseline and 1st follow up, 1st and 2nd follow up, and 2$^{nd}$ and 3$^{rd}$ follow up found in HFA inhaler group and CFC inhaler group respectively were statistically significant (p<0.001). Changes of PEFR in the 2nd follow up between two groups were 6.57±3.72 and 5.90±2.28 in HFA and CFC inhaler group respectively. These were the only values statistically non-significant (0.285).

From the above result it was shown that the PEFR gradually increased in both groups almost in an almost equal manner. A similar finding was reported by Woodcock *et al*. [14]. The significant changes of PEFR occured in HFA-BDP inhaler group with a low dose indicated the good efficacy of HFA inhaler.

The mean ± SD of FEV1 by groups was shown. FEV1 differences between baseline and 1$^{st}$ follow up were statistically significant (p<001). But, FEV1 changes between 1st and 2nd follow up, and 2nd and3rd follow up between the two drugs were statistically not significant (p=0.467 & 0.191). So, both the drugs were almost equally effective in improving FEV1 in asthma patient. Woodcock *et al*. [14] was found a similar result. The significant change of FEV1 occurred at a lower dose indicated better efficacy of HFA inhaler. Leach *et al*. [11] also performed a similar study and found that Hydrofluoroalkane Beclomethasone dipropionate was produced better lung performance at a lower dose.

## CONCLUSION

In conclusion, the findings of this study permit to conclude that the effectiveness of Hydrofluoroalkane Beclomethasone dipropionate (HFA-BDP) is better than Chlorofluorocarbon Beclomethasone dipropionate (CFC-BDP) for the treatment of moderate persistent asthma. The improved lung functions are found in Hydrofluoroalkane Beclomethasone dipropionate inhaler group. Therefore, HFA-BDP inhaler can be used as better anti-inflammatory inhaler for the treatment of asthma. HFA- Beclomethasone dipropionate should be used among patietns presented with moderate persistent asthma.

## REFERENCES


1. Litonjua, A. A., Carey, V. J., Burge, H. A., Weiss, S. T., & Gold, D. R. (1998). Parental history and the risk for childhood asthma: does mother confer more risk than father?. *American journal of respiratory and critical care medicine*, *158*(1), 176-181.
2. Hassan, M.R., Bennoor, K.S., Rahman, F. (2005). 'Prevalence of asthma in highly pollulated Dhaka City & low polluted coastal area of Bangladesh.' *International J. Allergy Asthma Immunal*, *19*(2), 85-92.
3. Almqvist, C., G. Pershagen. (2005). 'Low socioeconomic status as a risk factor for asthma, rhinitis and sensitization at 4 years in a birth cohort.' *Clinical & Experimental Allergy, 35*(5), 612-618.
4. Eder, W., Ege, M.J., von, Mutius, E. (2006). 'The asthma epidemic.' *N Engl J Med; 355*; 21, 2226–2235.
5. Rudd, R.E., Zobel, E.K. (2004). 'Asthma: In Plain Language.' *Health Promotion Practice, 5*(3), 334-340.
6. Caldeira, R. D., Bettiol, H., Barbieri, M. A., Terra-Filho, J., Garcia, C. A., & Vianna, E. O. (2006). Prevalence and risk factors for work related asthma in young adults. *Occupational and environmental medicine*, *63*(10), 694-699.
7. Wenzel, S.E. (2006). Asthma: defining of the persistent adult phenotypes. *Lancet; 368*, 9537, 804–13.
8. Borish, L., Chipps, B., Deniz, Y., Gujrathi, S., Zheng, B., Dolan, C. M., & TENOR Study Group. (2005). Total serum IgE levels in a large cohort of patients with severe or difficult-to-treat asthma. *Annals of Allergy, Asthma & Immunology*, *95*(3), 247-253.
9. Anthony, J.F., Helen, E.S. (2001). 'Sublingual immunotherapy.' *J Allergy Clin Immunology*, 104, 441-4.
10. Leach, C. L. (2005). The CFC to HFA transition and its impact on pulmonary drug development. *Respiratory care*, *50*(9), 1201-1208.
11. Leach, C. L., Davidson, P. J., & Boudreau, R. J. (1998). Improved airway targeting with the CFC-free HFA-beclomethasone metered-dose inhaler compared with CFC-beclomethasone. *European Respiratory Journal*, *12*(6), 1346-1353.

12. Chen, Y., Stewart, P., Johansen, H., McRae, L., & Taylor, G. (2003). Sex difference in hospitalization due to asthma in relation to age. *Journal of clinical epidemiology*, *56*(2), 180-187.
13. Schatz, M., Clark, S., & Camargo Jr, C. A. (2006). Sex differences in the presentation and course of asthma hospitalizations. *Chest*, *129*(1), 50-55.
14. Woodcock, A., Williams, A., Batty, L., Masterson, C., Rossetti, A., & Cantini, L. (2002). Effects on lung function, symptoms, and bronchial hyperreactivity of low-dose inhaled beclomethasone dipropionate given with HFA-134a or CFC propellant. *Journal of aerosol medicine*, *15*(4), 407-414.