Original Article
International Journal of Medical and Dental Sciences, *Vol 10(2), DOI: 10.18311/ijmds/2021/26829, July 2021*
ISSN (Print) : 2454-8952
ISSN (Online) : 2320-1118

A Study to Evaluate the Effectiveness of Inhaled Corticosteroid/Long-Acting Beta Agonist Combination and Assessment of Health-Related Quality of Life Among COPD Patients on this Therapy

Amrit Pal Kaur[1], Vijay Kumar Sehgal[2], Jasbir Singh[3], Surinder Pal Singh[4]* and Meenakshi Raju[1]

[1]Junior Resident, Department of Pharmacology, Government Medical College and Rajindra Hospital, Patiala–147001, Punjab, India
[2]Professor and Head, Department of Pharmacology, Government Medical College and Rajindra Hospital, Patiala–147001, Punjab, India
[3]Associate Professor, Department of Pharmacology, Government Medical College and Rajindra Hospital, Patiala–147001, Punjab, India
[4]Professor, Department of Pulmonary Medicine, Government Medical College and Rajindra Hospital, Patiala–147001, Punjab, India; drsurinderpal09@gmail.com

Abstract

Background: "Do combined inhalers offer additional benefits or harms in people with Chronic Obstructive Pulmonary Disease (COPD) compared with the bronchodilator alone?" The present study was conducted to evaluate the effectiveness of inhaled corticosteroid with long acting ß$_2$ agonist combination and to assess Health Related Quality of Life (HRQoL) among COPD patients. **Methods:** A prospective, comparative study was conducted in department of Pulmonary Medicine, Government Medical College Patiala. Total 80 COPD patients were enrolled, and randomly allocated in two groups with 40 patients in each group. In group 1- budesonide/formoterol (200/6 mcg or 400/6 mcg), and in group 2- fluticasone/salmeterol (250/50 mcg) was prescribed. The effectiveness was evaluated by assessing exacerbation rate, and breathlessness Modified Medical Research Council (mMRC) grade. HRQoL was assessed by "St. George's Respiratory Questionnaire" (SGRQ). All observations were statistically analyzed using suitable tests. **Results:** In present study, male patients (n=63) were more than female patients (n=17). In group 1 significant improvement was observed in mMRC grade between visit 0 and 2nd (x^2 = 8.50, p = 0.004), and between visit 1st and 2nd (x^2 = 7.24, p = 0.007). Similarly, among group 2, significant improvement was seen in mMRC grade between visit 0 and 2nd (x^2 = 8.39, p = 0.004), and between visit 1st and 2nd (x^2 = 5.05, p=0.025). But, no significant difference was seen between group 1 and 2 mMRC grade (p > 0.05). There was no statistically significant difference between group 1 and group 2 exacerbation episodes (x^2 = 2.13, p > 0.05). In SGRQ mean total score, no significant difference was present between group 1 and 2 (p > 0.05). **Conclusions:** 'Budesonide Formoterol' (BFC) and 'Fluticasone Salmeterol' (FSC) belongs to same group of drug class i.e., inhaled corticosteroid with long acting ß$_2$ agonist combination and used to treat exacerbations in moderate to severe COPD patients. BFC and FSC are equally effective in present study.

Keywords: Budesonide formoterol, Breathlessness "Modified Medical Research Council" Grade, Exacerbation Rate, Fluticasone Salmeterol, "St. George's Respiratory Questionnaire"

**Author for correspondence*

1. Introduction

According to World Health Organization, "Chronic Obstructive Pulmonary Disease (COPD) is a leading respiratory disease affecting the length and quality of lives around the globe" [1]. COPD is defined by 'continuous respiratory symptoms and airflow limitation because of airway or alveolar abnormalities caused by serious exposure to noxious particles or gases'[2]. It is currently the fourth leading cause of mortality and morbidity, accounting for 3 million deaths globally[3]. But is expected to be third leading cause of death by 2020. Most people struggle from COPD for years and die prematurely from it or its complications.

The Indian Scenario: The prevalence of total deaths credited to COPD in India was 8.7% (males 8.7% and females 8.6%) and disability adjusted life years were 4.8%[3]. In India, three out of five major causes of mortalities comprise non-communicable diseases while COPD is the second biggest cause of death[4].

The purpose of COPD management includes prevention of disease progression, relieve symptoms, enhance health status and exercise tolerance, rule out and treat complications and exacerbations, minimize mortality, and minimal side effects from treatment[4]. According to several studies, monotherapy with Inhaled Corticosteroid (ICS) neither improve long term decline of FEV1 nor mortality in COPD patients[5]. In patients of moderate or severe COPD and exacerbations, the combination of ICS with Long Acting $ß_2$ Agonist (LABA) has shown better clinical outcomes than either component alone in enhancing lung function, health status and reducing exacerbations[6,7]. However, very scarce information is available on the real-world effectiveness of Budesonide Formoterol Combination (BFC) and Fluticasone Salmeterol Combination (FSC) in COPD patients. Hence, the present study was aimed to evaluate the effect of BFC and FSC maintenance therapies and assess health related quality of life (HRQoL) in COPD patients on this therapy. "HRQoL includes physical and mental health perceptions (e.g., energy level, mood) and their correlates - including health risks and conditions, functional status, social support and socio-economic status" [8].

2. Methodology

Study Design: An observational, comparative, prospective and open labeled study.

Study Site: Department of Pulmonary Medicine in association with Department of Pharmacology, Government Medical College, Patiala.

Study Period: The study was conducted after the approval from Institutional Ethics Committee (approval No.: BFUHS/2K19p-TH/7321). Also, the study was prior registered with CTRI as registration no: CTRI/2020/10/028365.

Study Population: All patients coming to Pulmonary Medicine department were screened. Patients of both genders aged ≥ 40 years with at least 1 Inpatient Department visit with primary diagnosis for COPD (Spirometry: "post bronchodilator- FEV1/FVC < 0.70") or at least '1 emergency department visit with COPD diagnosis', and didn't had an exacerbation for one month prior to study entry and was on inhalational therapy for 2-3 weeks, were taken in the study. Any patient having asthma or other non-COPD respiratory disorder, or past lung volume reduction surgery and/or lung transplantation, or required oxygen therapy for at least 12 hours per day, or co-morbid medical condition (cystic fibrosis, bronchiectasis, respiratory cancer, pulmonary fibrosis, etc.), or any condition expected to cause death within 3 years, or on current use of injectable/oral corticosteroid therapy, or who got ≥ 180 days of Oral Corticosteroids (OCS) in the 12 month pre-index period, or immuno-compromised, or not ready to give written informed consent, was excluded from study. A total of 80 patients were enrolled after taking written informed consent.

Study Procedure: Aim of the study was explained to patients prior to enrollment. Written informed consent was attained from every patient. Total 80 patients were enrolled and randomly categorized into two groups- group I and group II, with 40 patients in each group.

I. Group I (n=40) was prescribed with Budesonide formoterol combination (200/6 mcg or 400/6 mcg)
II. Group II (n=40) was prescribed with Fluticasone salmeterol combination (250/50 mcg).

Data Collection: A standard case proforma sheet was used to collect information on patient's age, sex, occupation, hospital ID no., contact no., address, chief complaints, past history, breathlessness mMRC grade, any acute exacerbation history, personal history (smoking, addiction, habits), family history, and chest radiograph at day 0 (visit-0).

'Breathlessness mMRC grade', 'exacerbation history' and 'St. George's Respiratory Questionnaire' (SGRQ) score were recorded on day 0, 2nd week and then on 4th week (no. of follow up visits - 2). In between the follow up visits, if any exacerbation episode (i.e. COPD-related inpatient hospitalization, or emergency department visit, or history of Short Acting ß$_2$ Agonist (SABA) treatment, or history of SABA+ antibiotics and/or oral corticosteroids treatment, or history of acute respiratory failure) happened, it was recorded in the respective proforma of the patient. Any adverse effect, as reported by the patient, was recorded in the patient proforma and compared. All the recorded data was entered into a computer based excel sheet and the records were assessed to find any missing information.

Prior approval for use of SGRQ was obtained from Professor Paul Jones, developer of SGRQ, St. George's University of London. SGRQ data was entered into score calculator excel sheet, provided by the SGRQ developer. For each subscale and for overall SGRQ questionnaire, score ranges from zero (no impairment) to 100 (max. impairment)[9].

Data Analysis: Data was statistically analyzed by following methods:

a. Breathlessness mMRC grades were compared within each group, and between the two groups (BFC vs FSC). The difference was analyzed using *chi-square test*.
b. Comparison of exacerbation episodes between the two groups (BFC vs FSC) by using *chi-square test*.
c. SGRQ scores were compared within each group, and between two groups (BFC vs FSC). The difference was analyzed using *t-test*.

The statistical program IBM SPSS (Statistical Product and Service Solutions) version 22.0 (2013, Armonk, NY: IBM Corp) was employed in all analyses.

3. Observations

Demographic features of total study population are shown in (Table 1). 'Mean age' of patients was 60.80±12.05 years in group 1, and 61.32±10.06 years in group 2, with higher

Table 1. Demographic features of study population

Domain	Variable	Group 1 (n=40)		Group 2 (n=40)		t-test	p value
		Patients	Percentage	Patients	Percentage		
Age (Years)	40-49	7	17.50%	4	10%	0.212	0.833 (NS)
	50-59	9	22.50%	7	17.50%		
	60-69	15	37.50%	19	47.50%		
	70-79	5	12.50%	8	20%		
	≥80	4	10%	2	5%		
	Mean±SD	60.80±12.05		61.32±10.06			
	Median	60.00		60.00			
	Range	40-90		40-85			
Gender	Female	7	17.50%	10	25%	x^2=1.433	0.230 (NS)
	Male	33	82.50%	30	75%		

Occupation	Govt. Job	1	2.50%	2	5%	x^2=1.222	0.153 (NS)
	Private Job	5	12.50%	1	2.50%		
	Shopkeeper	5	12.50%	1	2.50%		
	Farmer	5	12.50%	7	17.50%		
	Housewife	7	17.50%	10	25%		
	Labourer	8	20%	16	40%		
	Skilled Worker	7	17.50%	3	7.50%		
	Unemployed	2	5%	0	0%		

proportion of males (n=33; n=30) in both group 1 and group 2 study population, respectively.

Past history of study population is depicted in (Table 2). History of exposure to smoke, past history of exacerbation episodes and past history of inhaler use was analyzed. In all three domains (history of exposure to smoke, past history of exacerbation episodes and past history of inhaler use), no significant difference was seen between group 1 and 2.

Breathlessness mMRC dyspnea grade: When mMRC grade was compared between follow up visits (baseline, 2nd week and 4th week: Figure 1) of patients within group

Table 2. Past history of study population

Domain	Variable	Group 1		Group 2	
		Patients	Percentage	Patients	Percentage
Past History of exposure to smoke	No History of smoking	5	12.50%	5	12.50%
	History of smoking	31	77.50%	26	65%
	Exposure to Chulla smoke	4	10%	9	22.50%
	Total	40	100%	40	100%
	x^2	1.51			
	p value	0.219 (NS)			

Past history of Exacerbation episodes	1	13	32.5%	09	22.5%
	2	01	2.5%	01	2.5%
	>2	01	2.5%	02	5.0%
	Total	15	37.5%	12	30%
	x^2	0.60			
	p value	0.438 (NS)			
Past History of inhaler use	No	20	50%	21	52.50%
	Yes	20	50%	19	47.50%
	Total	40	100%	40	100%
	x^2	0.05			
	p value	0.823 (NS)			

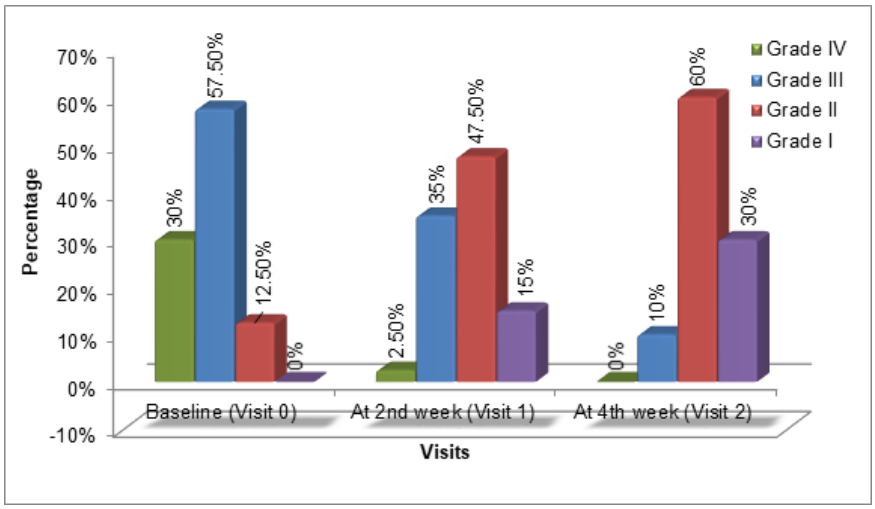

Figure 1. mMRC grade at subsequent follow up visits of patients within Group 1 (BFC).

Table 3. Comparison of mMRC grade between follow-up visits of Patients within Group 1 (BFC)

BLN-mMRC Grade	Group 1	
	x^2	p value
Visit 0-Visit 1	3.89	0.067 (NS)
Visit 0-Visit 2	8.50	0.004 **(S)**
Visit 1-Visit 2	7.24	0.007 **(S)**

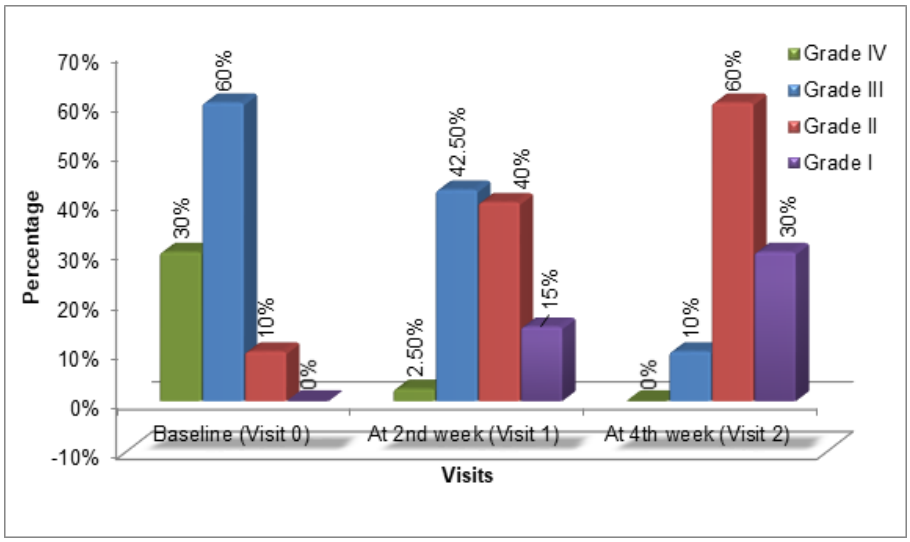

Figure 2. mMRC grade at subsequent follow-up visits of patients within Group 2 (FSC).

Table 4. Comparison of mMRC grade between follow-up visits of patients within Group 2 (FSC)

BLN-mMRC Grade	Group 2	
	x^2	p value
Visit 0-Visit 1	2.38	0.123 (NS)
Visit 0-Visit 2	8.39	0.004 **(S)**
Visit 1-Visit 2	5.05	0.025 **(S)**

1, significant improvement was observed at subsequent visits as shown in (Table 3).

Similarly, mMRC grade was compared between follow up visits (baseline, 2nd week and 4th week) of patients within group 2 (Figure 2). At subsequent visits statistically significant differences was seen among group 2 as shown in (Table 4).

At the end of study, mMRC grade was compared at all the visits (Table 5) and no significant difference was seen between group 1 and group 2 findings.

Exacerbation episodes: During follow-up period, the exacerbation episodes were recorded within both the groups and later on comparison was done between group 1 and group 2 (Table 6). There was no significant difference between the group 1 and 2 exacerbation episodes (p=0.345).

SGRQ score: Health related quality of life was evaluated by 'St. George Respiratory Questionnaire Scale' (SGRQ). It's sensitive, valid and reliable scale containing 50 items with 76 weighted responses which cover three domains:

I. **"Symptom score"** - includes distress due to respiratory features
II. **"Activity score"** – includes disturbances of physical activity
III. **"Impact score"** – involves overall impact on daily life and well being.

In addition to domain score, there is total score[9]. SGRQ score is scaled from zero to 100 (with zero representing

Table 5. Comparison of mMRC grade between Group 1 and Group 2 at different visits

Visit	BLN-mMRC Grade	Group 1		Group 2		x^2	p value
		Patients	Percentage	Patients	Percentage		
Baseline (Visit 0)	Grade IV	12	30%	12	30%	2.99	0.084 (NS)
	Grade III	23	57.50%	24	60%		
	Grade II	05	12.50%	04	10%		
	Grade I	00	0%	00	0%		
At 2nd week (Visit 1)	Grade IV	01	2.50%	01	2.50%	2.72	0.099 (NS)
	Grade III	14	35%	17	42.50%		
	Grade II	19	47.50%	16	40%		
	Grade I	06	15%	06	15%		
At 4th week (Visit 2)	Grade IV	00	0%	00	0%	3.00	0.083 (NS)
	Grade III	04	10%	04	10%		
	Grade II	24	60%	24	60%		
	Grade I	12	30%	12	30%		

Table 6. Comparison of exacerbation episodes between Group 1 and Group 2 after study drug initiation

Exacerbation Episodes	Group 1		Group 2	
	Patients	Percentage	Patients	Percentage
0	19	47.50%	26	65%
1	20	50%	13	32.50%
2	01	2.50%	01	2.50%
Total	40	100%	40	100%
x^2	2.13			
p value	0.345 (NS)			
Odds Ratio	0.55 (0.148-2.046)			

Table 7. Comparison of Mean symptom, mean activity, mean impact and mean total score between group 1 and 2 study population

Domain	Visit	Group	N	Mean	SD	Std. Error Mean	95% confidence interval	t-test	p value
Mean symptom score	Baseline (Visit 0)	Group 1	40	46.38	20.53	3.25	-4.274 - 15.702	1.139	0.258 (NS)
		Group 2	40	40.67	24.20	3.83			
	At 2nd week (Visit 1)	Group 1	40	46.38	20.53	3.25	-4.274 - 15.702	1.139	0.258 (NS)
		Group 2	40	40.67	24.20	3.83			
	At 4th week (Visit 2)	Group 1	40	46.38	20.53	3.25	-4.274 - 15.702	1.139	0.258 (NS)
		Group 2	40	40.67	24.20	3.83			
Mean activity score	Baseline (Visit 0)	Group 1	40	81.42	14.52	2.30	-4.42 - 8.95	0.103	0.918 (NS)
		Group 2	40	79.16	15.48	2.45			
	At 2nd week (Visit 1)	Group 1	40	56.70	16.49	2.61	-6.75 - 7.49	0.675	0.501 (NS)
		Group 2	40	56.33	15.48	2.45			
	At 4th week (Visit 2)	Group 1	40	44.09	14.27	2.26	-7.91 - 3.71	0.721	0.473 (NS)
		Group 2	40	46.19	11.67	1.85			
Mean impact score	Baseline (Visit 0)	Group 1	40	69.32	18.37	2.90	-6.49 - 9.28	0.495	0.622 (NS)
		Group 2	40	67.93	17.01	2.69			
	At 2nd week (Visit 1)	Group 1	40	41.07	20.49	3.24	-11.23 - 6.76	0.352	0.726 (NS)
		Group 2	40	43.31	19.92	3.15			
	At 4th week (Visit 2)	Group 1	40	26.79	12.95	2.05	-7.39 - 3.74	0.653	0.515 (NS)
		Group 2	40	28.61	12.01	1.90			

Mean total score	Baseline (Visit 0)	Group 1	40	69.61	14.43	2.28	-3.85 - 8.36	0.056	0.955 (NS)
		Group 2	40	67.35	12.94	2.05			
	At 2nd week (Visit 1)	Group 1	40	46.82	16.48	2.61	-7.41- 7.01	0.735	0.464 (NS)
		Group 2	40	47.02	15.91	2.52			
	At 4th week (Visit 2)	Group 1	40	35.31	10.92	1.73	-5.41 - 4.16	0.260	0.796 (NS)
		Group 2	40	35.93	10.57	1.67			

Table 8. Statistical analysis of total score in group 1 (BFC) study population

Total Score	Wilcoxon Signed Ranks Test	p value	Significance
Visit 0-Visit 1	-4.986	0.001	**HS**
Visit 0-Visit 2	-5.511	0.001	**HS**
Visit 1-Visit 2	-4.860	0.001	**HS**

Table 9. Statistical analysis of total score in group 2 (FSC) study population

Total Score	Wilcoxon Signed Ranks Test	p value	Significance
Visit 0-Visit 1	-5.066	0.001	**HS**
Visit 0-Visit 2	-5.511	0.001	**HS**
Visit 1-Visit 2	-4.541	0.001	**HS**

best health related quality of life). Mean symptom scores, mean activity scores, mean impact scores, and mean total scores were compared (Table 7) between group 1 and 2 at the subsequent follow-up visits. But, no significant difference was present between group 1 and 2 study population (p value> 0.05).

Total score - Among group 1, significant difference was observed between mean total score at different visits (Table 8). Similarly, in group 2 significant difference was seen between mean total score at subsequent follow-up visits (Table 9).

In group 1, 70% of patients (n=28) reported with certain adverse effects during follow-up period (Figure 3). Also, in group 2, 72.5% of patients (n=29) reported adverse effects during the follow-up period. Most

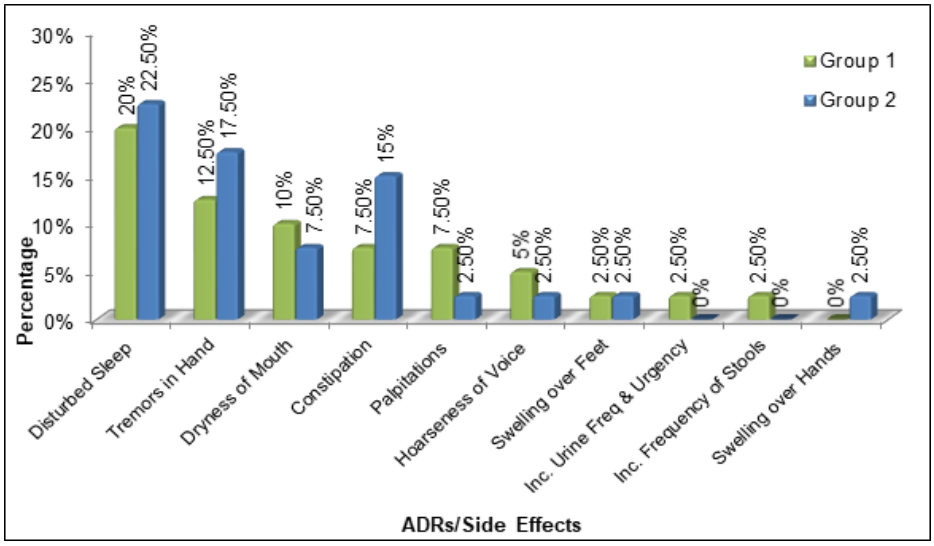

Figure 3. Comparison of adverse drug events between group 1 and group 2 study population.

commonly reported side effect was disturbed sleep, followed by tremors in hand.

4. Discussion

Total 80 patients, diagnosed by spirometry, who fulfilled the inclusion and having none of exclusion criteria, were enrolled in study. Patients were randomly distributed into two groups- group 1 and group 2, with 40 patients in each group. Breathlessness mMRC grade, exacerbation episodes and SGRQ score were recorded at baseline, 2nd week and after 4th week.

Breathlessness mMRC grade improvement: In the present study, patients taking BFC therapy (group 1) and FSC therapy (group 2) had shown improvement in mMRC grade at the subsequent visits. But no significant difference was seen between group 1 and group 2 mMRC grade. An observational study, by Jones PW *et al.,* compared health status scores with MRC grades in COPD patients. mMRC grade 1 was related with significant levels of health status deterioration (SGRQ= 39.415.5; CAT= 15.77.0); even patients with mMRC grade 0 had moderately raised scores (SGRQ= 28.515.1; CAT= 11.76.8). The mMRC grade revealed a clear relationship with health status scores; also, low mMRC grades were associated with health status deterioration[10]. In previous/ past studies, mMRC grade has been observed to assess the quality of life in association with health status scores. The present study is one of a kind where mMRC grade was used to evaluate the effectiveness of combination therapy in COPD patients.

Exacerbation episodes in study population: In our study group 1 (BFC)- 21 patients had exacerbation episodes and 19 patients had no episode of exacerbations during the study period. In group 2 (FSC)- 14 patients had exacerbation episodes and 26 patients had no episode of exacerbation in the study duration. But no significant difference was present between group 1 and group 2 participants for exacerbation episodes ($p = 0.345$). A study done by Blais *et al.,* in a Canadian province in COPD patients showed no significant differences in frequency of COPD exacerbations between participants receiving BFC and FSC (0.63 vs 0.71 exacerbation per patient-year)[11]. Another study, by Roberts M *et al.,* compared the effectiveness of BFC and FSC in US population[12]. The results found no significant difference in clinical outcomes including COPD-related outpatient visits, or exacerbation events. So, the findings of our study were similar to findings from other studies. But, the present study results differ from another observational study done by Perrone

V *et al.,* in Italy in COPD patients. The analysis showed patients receiving fixed combination of Budesonide formoterol had fewer exacerbation episodes than patients treated with Fluticasone salmeterol combination[13].

Health related Quality of life: "St. George's Respiratory Questionnaire" (SGRQ) was used to evaluate health related quality of life among study population. Mean total scores were compared between group 1 and group 2 participants, and there was no significant difference. In a randomized cross-over study, performed by Partridge *et al.,* the effects of BFC vs FSC were assessed on lung function and morning activities in COPD patients[14]. They found SGRQ-C total scores were similar between BFC and FSC treatment groups, with no significant differences between them. Another study done by Zhong N *et al.,* evaluated the efficacy and safety of budesonide/formoterol (BFC) compared with budesonide (BUD) alone in COPD patients, where both were given by dry powder inhaler[15]. Improvement in health-related quality of life was compared between the two groups by using "St. George's Respiratory Questionnaire" (SGRQ). Compared with BUD alone, BFC significantly improved health related quality of life (mean change of total SGRQ score-4.5 points & p = 0.0182). Obaseki DO *et al.,* assessed the health-related quality of life by St. George's Respiratory Questionnaire in a cross-sectional study in fifty COPD patients in Nigeria[16]. The overall mean SGRQ scores were 45.9±26.5, 50.6±29.2, 29.7±19.9, 38.8±22.0 for symptom, activity, impact and total scales, respectively. As compared to this study, group 1 mean SGRQ scores in our study were 46.38±20.53, 44.09±14.27, 26.79±12.95, 35.31±10.92 for the symptom, activity, impact and total scales, respectively. Also, in group 2 of our study, the mean scores were 40.67±24.20, 46.19±11.67, 28.61±12.01, 35.93±10.57 for symptom, activity, impact and total scales, respectively. So, the results of our study were comparable with the outcomes of previous studies. Health status assessment might have a role in risk estimation for COPD patients in routine medical care. Mullerova H *et al.,* estimated the usefulness of St George's Respiratory Questionnaire, to predict the outcomes in patients with COPD. An analysis was conducted using previously collected patient data from several randomized controlled trials. Adverse COPD outcomes included COPD exacerbations, hospital admissions due to exacerbation and all-cause mortality. In COPD patients, health status measured by SGRQ score forecast COPD exacerbations, hospital admissions due to exacerbations and their recurrence and death[17]. Another study by Ayora AF *et al.,* assessed the health-related quality of life by comparative analysis of two questionnaires, SGRQ and CAT (COPD assessment test) in patients having COPD exacerbations. The study showed that SGRQ questionnaire could predict additional changes in HRQoL with a greater number of variables. SGRQ is more precise than CAT in measurement of HRQoL in patients in the hospital setting[18]. The observations of our study have shown significant reduction in SGRQ mean total scores in group 2 (BFC) patients (p=0.001 between visit 0 and 2nd). Similarly, a meta-analysis was done by Tang B *et al.,* in China to evaluate the effectiveness of Budesonide/formotreol (BFC) in COPD patients[19]. BFC was compared with budesonide, formoterol, or placebo. BFC therapy showed significant reduction in total score of SGRQ.

The main limitations of present study were limited sample size and the follow-ups could have been more to look for the long-term effects of combination therapy, as not much research have been done on it. Some patients were taking other respiratory drugs (LAMA) during the study period, so we cannot assign findings solely to initiated ICS/LABA therapy. There was insufficient clinical information and pulmonary function assessment to categorize COPD disease severity.

However, information on past COPD exacerbations were collected which is the best predictor of future exacerbations. Also, smoking status was assessed in the patient history recording.

5. Summary and Conclusion

Both 'Budesonide formoterol' and 'Fluticasone salmeterol' belongs to same group of drug class i.e., inhaled corticosteroid/long acting ß$_2$ agonist combination and are recommended to treat exacerbations in moderate to severe COPD. BFC and FSC are equally effective in present study as no significant difference was seen between group 1 and 2 exacerbations episodes. When health related quality of life was compared between two groups, no significant difference was found in the Mean SGRQ scores.

6. Acknowledgements

We express our sincere thanks to "Dr. Vijay K Sehgal, Professor & Head, Department of Pharmacology, Government Medical College and Rajindra Hospital, Patiala, Punjab" for providing facilities to carry out the work and for his constant encouragement and support.

7. Declarations

Conflicts of interest - No conflicts of interest
Financial support - Nil
Ethical approval - Approved

8. References

1. Chronic Obstructive Pulmonary Disease [Internet]. World Health Organization (WHO): Geneva; 2017 [cited January 2021]. Available from: https://www.who.int/news-room/fact-sheets/detail/chronicobstructivepulmonary-disease-(copd)
2. Global strategy for the diagnosis, management, and prevention of Chronic Obstructive Pulmonary Disease (2020 Report) [Internet]. Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2020 [cited 2020]. Available from: https://goldcopd.org/gold-reports/
3. Ho T, Cusack RP, Chaudhary N, Satia I, Kurmi OP. Under- and over-diagnosis of COPD: a global perspective. Breathe (Sheff). Mar 2019; 15(1): 24–5. https://doi.org/10.1183/20734735.0346-2018
4. Hossain MM, Sultana A, Purohit N. Burden of Chronic Obstructive Pulmonary Disease in India: Status, Practices and Prevention. Int J Pul & Res Sci. Apr 2018; 2(5): 1–4. https://doi.org/10.19080/IJOPRS.2018.02.555599
5. Yang IA, Clarke MS, Sim EH, Fong KM. Inhaled corticosteroids for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012; 7(7): CD002991. https://doi.org/10.1002/14651858.CD002991.pub3
6. Nannini LJ, Lasserson TJ, Poole P. Combined corticosteroid and long-acting beta 2 agonist in one inhaler vs long-acting beta 2 agonist for chronic obstructive pulmonary disease. Cochrane Database Syst. Rev. 2012; 9(9): CD006829. https://doi.org/10.1002/14651858.CD006829.pub2
7. Nannini LJ, Poole P, Milan SJ, Kesterton A. Combined corticosteroid and long-acting beta 2 agonist in one inhaler vs inhaled corticosteroid alone for chronic obstructive pulmonary disease. Cochrane Database Syst. Rev. 2012; 9(9): CD006829. https://doi.org/10.1002/14651858.CD006826.pub2
8. HRQOL Concepts: Health-Related Quality of Life (HRQOL) [Internet]. USA: Centers for Disease Control and Prevention (CDC); 2018 [cited January 2021]. Available from: https://www.cdc.gov/hrqol/concept.htm
9. Jones P. St George's Respiratory Questionnaire Manual: Version 2.3. June 2009; 1–14.
10. Jones PW, Adamek L, Nadeau G, Banik N. Comparisons of health status scores with MRC grades in COPD: implications for the GOLD 2011 classification. Eur Respir J. Sep 2013; 42(3): 647–54. https://doi.org/10.1183/09031936.00125612
11. Blais L, Forget A, Ramachandran S. Relative effectiveness of Budesonide /formoterol and fluticasone propionate/salmeterol in a 1-year, population based, matched-cohort study of patients with chronic obstructive pulmonary disease (COPD): Effect on COPD-related exacerbations, emergency department visits and hospitalizations, medication utilization, and treatment adherence. Clin Ther. 2010; 32(7): 1320–8. https://doi.org/10.1016/j.clinthera.2010.06.022
12. Roberts M, Mapel D, Petersen H, Blanchette C, Ramachandran S. Comparative effectiveness of budesonide/formoterol and fluticasone/salmeterol for COPD management. J Med Econ. 2011; 14(6): 769–76. https://doi.org/10.3111/13696998.2011.622817
13. Perrone V, Sangiorgi D, Buda S, Esposti LD. Comparative analysis of budesonide/formoterol and fluticasone/salmeterol combinations in COPD patients: findings from a real-world analysis in an Italian setting. Int J COPD. 2016; 11: 2749–55. https://doi.org/10.2147/COPD.S114554
14. Partridge MR, Schuermann W, Beckman O, Persson T, Polanowski T. Effect on lung function and morning activities of budesonide/formoterol versus salmeterol/fluticasone in patients with COPD. Ther Adv Respir Dis. 2009; 3(4): 1–11. https://doi.org/10.1177/1753465809344870
15. Zhong N, Zheng J, Wen F, Yang L, Chen P, Xiu Q *et al.,* Efficacy and safety of budesonide/formoterol via a dry powder inhaler in Chinese patients with chronic obstructive pulmonary disease. Curr. Med. Res. Jan 2012; 28(2): 257–65. https://doi.org/10.1185/03007995.2011.636420
16. Obaseki DO, Erhabor GE, Awopeju OF, Obaseki JE, Adewole OO. Determinants of health-related quality of life in a sample of patients with chronic obstructive pulmonary disease in Nigeria using the St. George's respiratory questionnaire. Afr Health Sci. Sep 2013; 13(3): 694–702. https://doi.org/10.4314/ahs.v13i3.25
17. Müllerova H, Gelhorn H, Wilson H, Benson VS, Karlsson N, Menjoge S *et al.,* St George's Respiratory Questionnaire Score Predicts Outcomes in Patients with COPD: Analysis

of Individual Patient Data in the COPD Biomarkers Qualification Consortium Database. Chronic Obstr Pulm Dis. 2017; 4(2):141–9. https://doi.org/10.15326/jcopdf.4.2.2017.0131

18. Ayora AF, Macia-Soler L, Orts-Cortés MI, Hernández C, Seijas-Babot N. Comparative analysis of the psychometric parameters of two quality-of-life questionnaires, the SGRQ and CAT, in the assessment of patients with COPD exacerbations during hospitalization: A multicenter study. Chron Respir Dis. Nov 2018; 15(4): 374–83. https://doi.org/10.1177/1479972318761645
19. Tang B, Wang J, Luo L, Li Q, Huang D. Comparative Efficacy of Budesonide/Formoterol with Budesonide, Formoterol or Placebo for Stable Chronic Obstructive Pulmonary Disease: A Meta-Analysis. Med Sci Monit. 2018; 25: 1155–63. https://doi.org/10.12659/MSM.912033

How to cite this article: Kaur AP, Sehgal VK, Singh J, Singh SP and Raju M. A Study to Evaluate the Effectiveness of Inhaled Corticosteroid/Long-Acting Beta Agonist Combination and Assessment of Health-Related Quality of Life Among COPD Patients on this Therapy. Int. J. Med. Dent. Sci. 2021; 10(2): 1968-1980.