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Review article

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Comparison of the effectiveness of inhaled short-acting β_2 agonist and anti-cholinergic with and without inhaled corticosteroid in improving the pulmonary function in COPD patients

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ABSTRACT

[1] Chronic Obstructive Pulmonary Disease (COPD) is defined as a disease characterized by progressive airflow limitation, that is, not fully reversible. The aim of this study is to compare the effectiveness of inhaled short acting β_2 agonist and anti-cholinergic with and without inhaled corticosteroid in improving the pulmonary function in COPD patients. In this 6 month study, a total of 80 COPD patients were enrolled in which 40 were administering Duolin MDI and the rest were taking Duolin MDI and Budecort MDI. Patient's data collection form was used for recording the demographic details of the patients. Before and after 6 months of study period, the patients were evaluated for improvement in symptoms by using SGRQ and by assessing the 6 Minute Walk Test (6MWT); the improvement in the pulmonary function was evaluated by observing the changes in the FEV1 values in Pulmonary Function Test (PFT). Medication adherence and Quality of Life were analyzed by distribution of questionnaires namely, MMAS-8 and EQ-5D Descriptive System, JSQ respectively. The majority of the patients belong to the 71-75 categories. Out of total patients, each age category has a high medication adherence level. Influences of COPD are more in patients who have a history of cigarette smoking for past several years. Males (86%) are dominated over the female population (14%). There is improvement in the pulmonary function of COPD patients who were taking inhaled corticosteroid with SAMA and SABA than those taking SAMA and SABA alone based on their FEV1 % predicted. The SGRQ score reduction and 6-MWT results evidences shown that inhaled corticosteroid is having greater effect on reducing the symptoms of COPD. Those administering ICS+SAMA+SABA have shown significant improvement in the quality of life and improvement in sleep problems. The results concluded that taking inhaled corticosteroid with inhaled short acting bronchodilators in COPD patients who are initially diagnosed with COPD may reduce fall in FEV1 level, prevent exacerbation of COPD, reduce the number of exacerbations and hospital stay in COPD patients, thus provide better patient care.

Keywords: Forced expiratory volume in 1 second (FEV₁), St George Respiratory Questionnaire (SGRQ) Score, 6 Minute Walk Test (6MWT), Medication adherence, Quality Of Life (QOL).

INTRODUCTION

[1]Chronic Obstructive Pulmonary Disease (COPD) is a major health problem. COPD is defined as a disease characterized by progressive airflow limitation, that is, not fully reversible.

[3]COPD is a preventable and treatable disease that make it difficult to empty air out of the lungs. This difficulty in emptying air out of the lungs (airflow obstruction) can lead to shortness of breath or feeling tired because working harder to breathe. The most common respiratory symptoms include dyspnoea, cough and/or sputum production [3] COPD is a term that is used to include chronic bronchitis, emphysema or a combination of both conditions. A loss of small airways may also contribute to airflow limitation and mucociliary dysfunction, is a characteristic feature of the disease. Airflow limitation is usually measured by spirometry. Chronic bronchitis and emphysema may occur with and without airflow limitation.

REVIEW OF LITERATURE

- [27] Pinar Sarac, et al 2016 conducted a study on *Compare the efficacy and safety of long acting anti-cholinergic and a combination of inhaled steroids and long acting beta -2 agonist in moderate COPD.*
- [25] Huib A M Kerstjens et al 1992 conducted a study on *Comparison of bronchodilator therapy with or without inhaled corticosteroid for obstructive airway disease.*
- [33] Ying Zhu et al (2017) conducted a study on *Discovering the relative efficacy of inhaled medications for of chronic obstructive pulmonary disease: multiple treatment comparisons.*
- [64] P.M .Van Gransven et al (1998) conducted a study on *Long term effects of inhaled corticosteroids in Chronic Obstructive Pulmonary Disease: a meta-analysis*

SIGNIFICANCE AND SCOPE

The newly diagnosed COPD patients are usually treated with SAMA or SABA or combination of both. β_2 agonist and anti-cholinergics work by different mechanisms to

cause bronchodilation. As the disease progresses, the therapy is changed to long acting agents like LABA or LAMA or its combination with ICS (anti-inflammatory effect) which have proven efficacy. This study aims at the effect of adding ICS to initial short -acting therapy of SAMA+ SABA.

Aim

To compare the effectiveness of inhaled short acting β_2 agonist and anti-cholinergic with and without inhaled corticosteroid in improving the pulmonary function in COPD patients.

Objective

- To determine the change in the FEV₁ levels in patients receiving short acting β_2 agonist SABA+ short acting anti-cholinergic SAMA+ Inhaled corticosteroid ICS and SAMA+ SABA.
- To compare the changes in the FEV₁ in the above groups.
- To evaluate the improvement in symptoms in COPD patients by determining the changes in the SGRQ scores and 6-MWT.
- To evaluate the medication adherence by using Morisky Medication Adherence Scale - 8.(MMAS-8)
- To estimate the Quality Of Life in patients using EQ-5D Descriptive System and Jenkins sleep questionnaire (JSQ)

MATERIALS AND METHOD

Methodology

Study Design: Prospective Observational Study.

Study Population: All patients reporting to the Department Of Pulmonary Medicine, Pushpagiri Medical College Hospital, Thiruvalla, who are diagnosed with COPD.

Study Period: 6 months after getting approval clearance from Institutional Ethics Committee.

Sample Size: Assuming that 95% of confidence interval and 80% power based on the mean difference of FEV₁ of group A(ICS+SABA+SAMA) and group B (SABA+SAMA) is 0.11 and standard deviation(S.D) of 0.43 and 0.41 respectively, the required minimum sample size for the study is 80 (40 in each group).

Study criteria

Inclusion criteria

- OP patients in pulmonary department.
- Patients diagnosed with COPD.
- Both female and male patients.
- Age between 45 and 75 years.
- Those who give consent voluntarily to participate in the study.
- FEV1 30-79 % of predicted (moderate and severe COPD).

Exclusion criteria

- Patients who are not willing to give consent.
- Very severe COPD patients.
- Patients who are diagnosed with severe cardiac disease.
- FEV1 < 30 % predicted and > 80% predicted.
- Current smokers.
- Patient diagnosed with asthma.
- Patients diagnosed with chronic kidney disease.
- Patient sensitive to the medications used in the study.
- Patients presenting exacerbation of COPD during the study.

Brief procedure

A prospective observational study was conducted in Department of Pulmonary Medicine at Pushpagiri Medical College Hospital on the topic “The comparison of the effectiveness of inhaled short-acting β_2 agonist and anti-cholinergic with and without inhaled corticosteroid

RESULT AND DISCUSSION

Result

In 6 month study, a total of 80 COPD patients were enrolled as per inclusion and exclusion criteria from out patient department of Pulmonary Medicine, Pushpagiri Medical College, Thiruvalla.

in improving the pulmonary function in COPD patients”. The entire study was carried out only after getting approval from Institutional Ethics Committee. The selection of patients was based upon the inclusion and exclusion criteria. All patients were provided with a brief introduction regarding the study and the confidentiality of the data. A written Informed Consent was obtained from the patient or the care-giver.

Patient’s data collection form was used for recording the demographic details of the patients. It was a 6 month study and follow up was taken 3 months of initiating either Duolin MDI + Budecort MDI or Duolin MDI alone for COPD patients. Before and after the study period, the patients were evaluated for improvement in the symptoms by using SGRQ and the improvement in the pulmonary function was evaluated by observing the changes in the FEV1 values in Pulmonary Function Test (PFT) and by assessing the 6 Minute Walk Test (6MWT). Medication adherence and Quality of Life were analyzed by distribution of questionnaires namely, MMAS-8 and EQ-5D Descriptive System, JSQ respectively.

Materials used

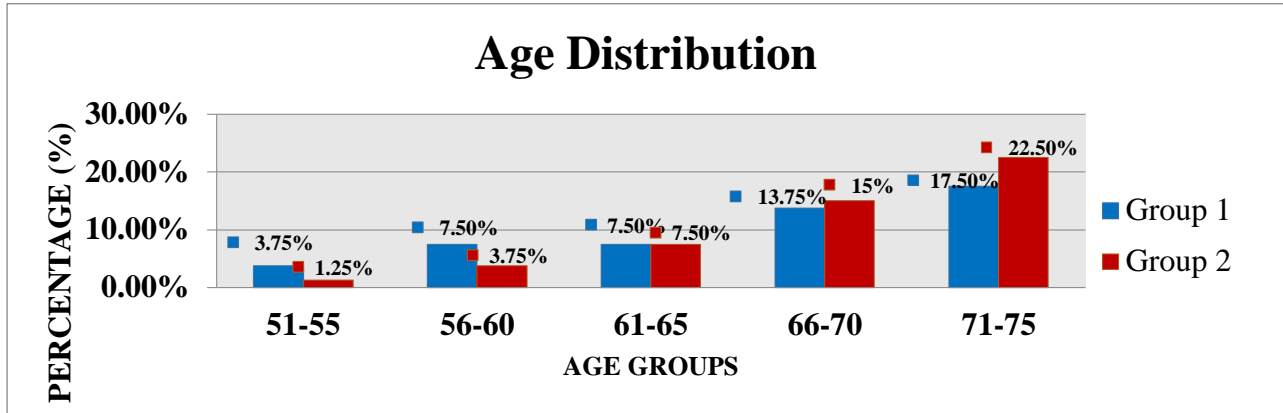
Materials used for the study were FEV1 value from the pulmonary function test (PFT), St. George Respiratory Questionnaire (SGRQ), Six Minute Walk Test (6-MWT) report, EQ-5D-5L Descriptive system, Jenkins Sleep Questionnaire [52] (JSQ), Eight Item Morisky Medication Adherence Scale (MMAS-8) and Medication Diaries.

40 COPD patients who were being administering Duolin MDI and 40 COPD patients who were taking Duolin MDI and Budecort MDI were selected.

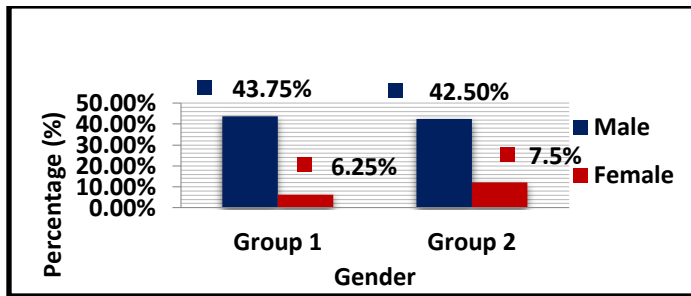
Control (group 1) : Duolin MDI 2-2-2 puff

Treatment (group 2) : Duolin MDI + Budecort MDI

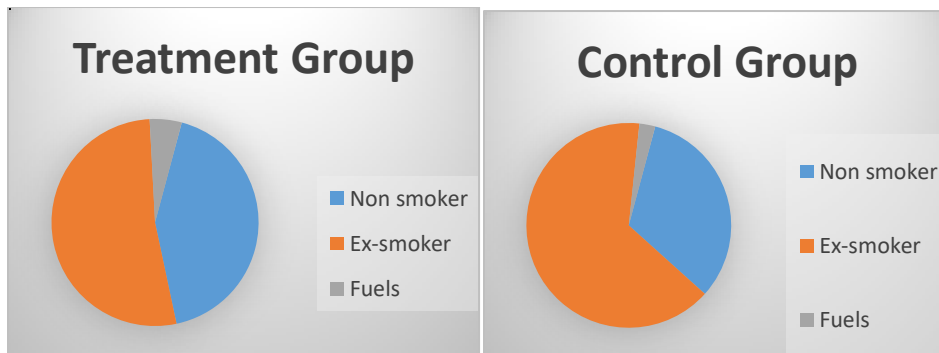
DEMOGRAPHIC DETAILS



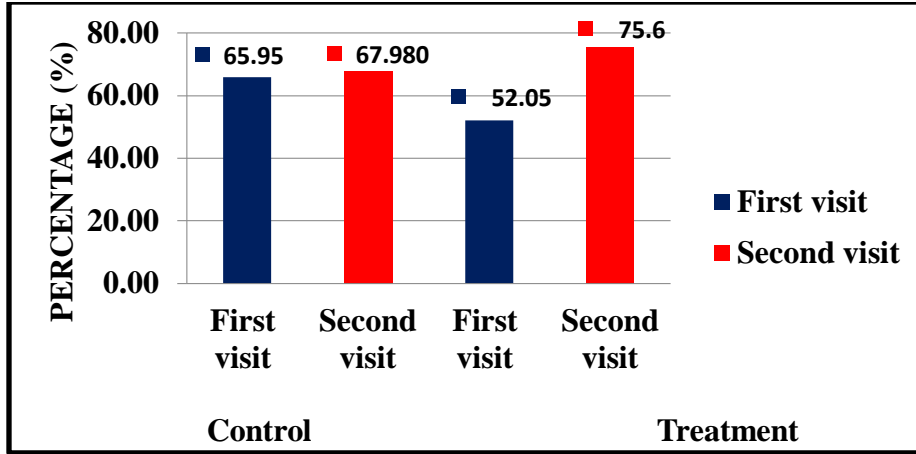
Age categorization: **FIGURE 1: DISTRIBUTION OF PATIENTS BASED ON AGE**



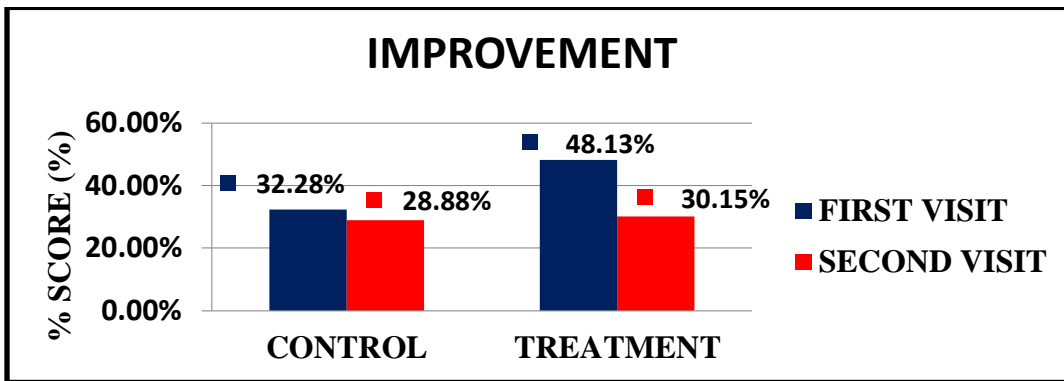
Gender: **Figure 2: distribution of patients in each group based on gender**



ETIOLOGY: FIGURE 3: DISTRIBUTION OF PATIENTS BASED ON ETIOLOGY



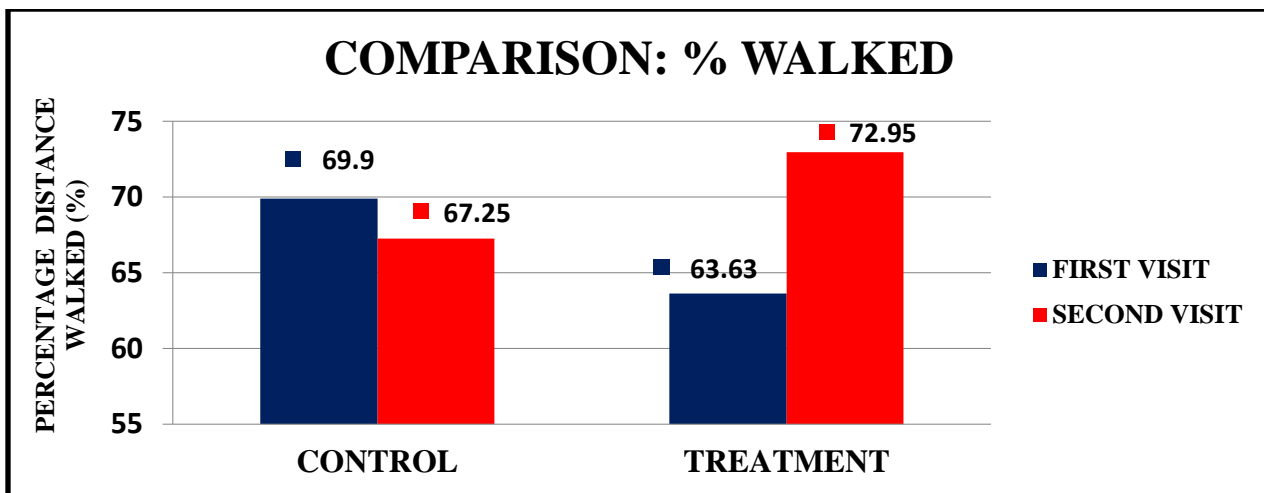
EFFECT OF INHALED CORTICOSTERIOD ON FEV1 VALUE OF COPD PATIENTS
 FIGURE 4: DISTRIBUTION OF FEV1 (% PREDICTED VALUE) AMONG THE PATIENTS



Statistically analysed by Mann-Whitney U Test

IMPROVEMENT IN SYMPTOMS EVALUATED BY SGRQ SCORES

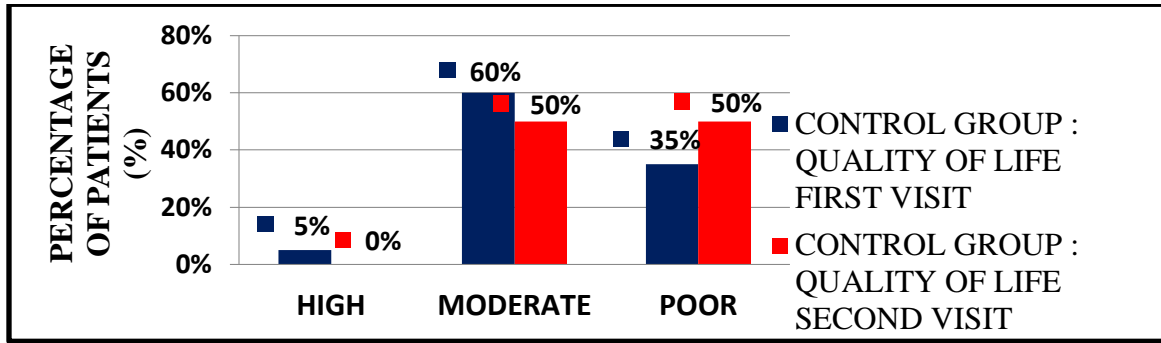
FIGURE 5: IMPROVEMENT IN SYMPTOMS AMONG PATIENTS EVALUATED BY SGRQ SCORES



Statistically analysed by Mann-Whitney U Test

IMPROVEMENT IN SYMPTOMS EVALUATED BY 6 MWT

FIGURE 6: COMPARISON OF OVERALL IMPROVEMENT OF SYMPTOMS AMONG STUDY POPULATION EVALUATED BY 6-MWT



Statistically analysed by Mann-Whitney U Test.

ESTIMATION OF THE QUALITY OF LIFE IN PATIENTS

FIGURE 7: ESTIMATION OF QUALITY OF LIFE IN CONTROL GROUP USING EQ-5D DESCRIPTIVE SYSTEM

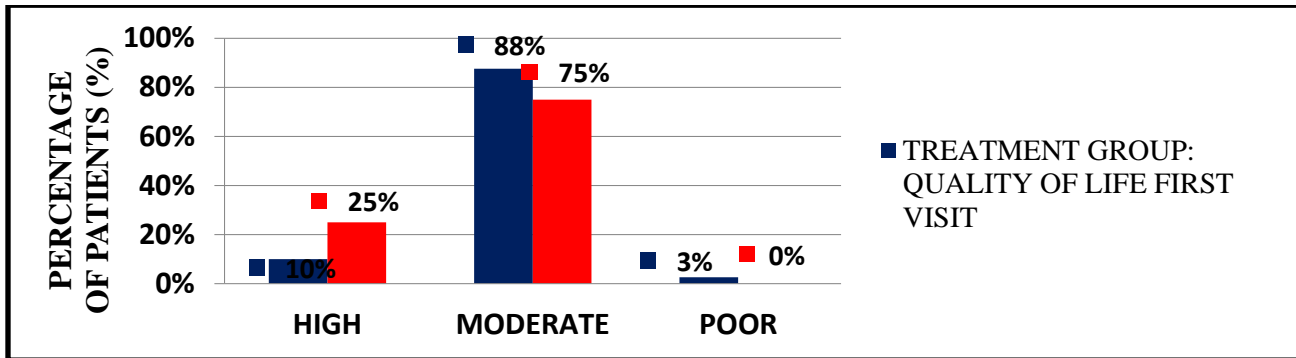
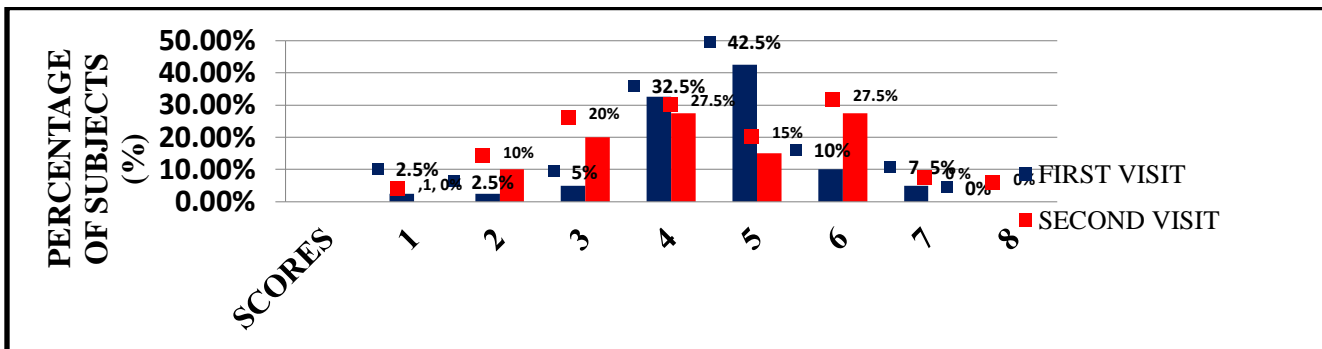


FIGURE 8: ESTIMATION OF QUALITY OF LIFE IN TREATMENT GROUP USING EQ-5D DESCRIPTIVE SYSTEM



• Statistics done by Wilcoxon Signed Rank Test

ESTIMATION OF QUALITY OF LIFE USING JSQ

FIGURE 9: ESTIMATION OF QUALITY OF LIFE IN CONTROL GROUP USING JSQ SCORE

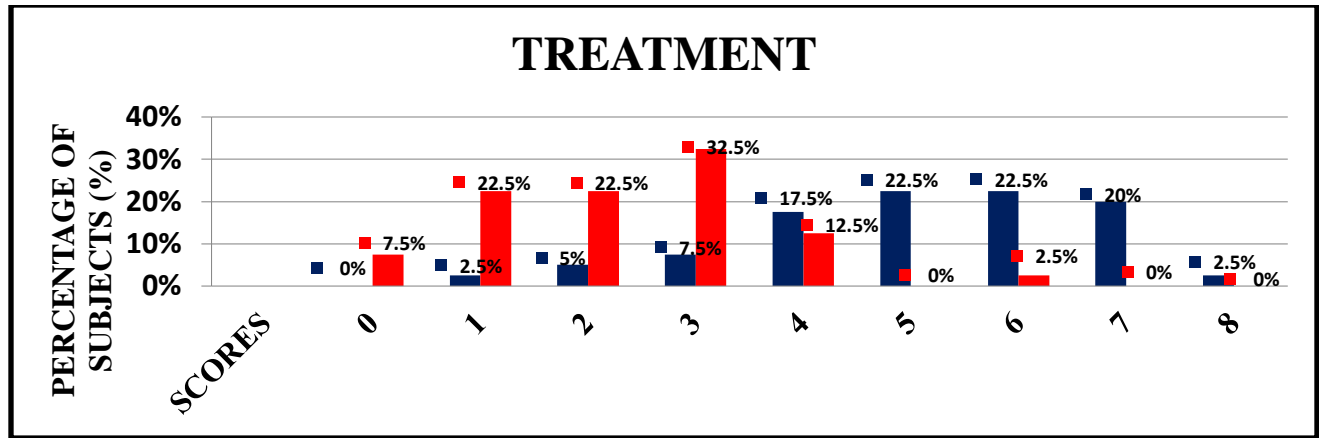


FIGURE 10: ESTIMATION OF QUALITY OF LIFE IN TREATMENT GROUP USING JSQ SCORE
 Statistically analysed by Mann-Whitney U Test.

DISCUSSION

This study was done to compare the effectiveness of inhaled short acting β_2 agonist and anti- cholinergic with and without inhaled corticosteroid in improving pulmonary function in COPD patients. Collected data were organised, tabulated and analysed using statistical methods and described with the help of tables and graphs.

AGE: In this study, the patients of age 50-75 were diagnosed with COPD. The majority of the patients belongs to the 71-75 category, followed by 66-70 category, 61-65 category, 56-60 category and last 50-55 category age group. Among this patients, the occurrence of COPD disease increases with respect to their age proportion.

GENDER: In the study population, 86% were males and 14% were females. Males are dominated over the female population who came for COPD treatment.

ETIOLOGY: From the data collected from 80 patients, it was found that ex-cigarette smokers (65% control and 53% treatment) showed higher percentage of disease occurrence. Therefore, cigarette smoke can be considered to be the main cause of COPD disease.

IMPROVEMENT IN FEV1: The first objective is to determine the change in the FEV1 levels in patients receiving SABA+ SAMA +ICS and SABA+SAMA. In the patients receiving ICS +SAMA+SABA, they showed a more improvement in FEV1 from 52.05% to 75.60% than the patients receiving SAMA+ SABA (from 65.95% to 67.98%).

Control: From the tables and figures, it was found that inhaled SAMA + SABA showed improvement in FEV1 value. The mean FEV1 value change from an average of 65.95% predicted to an average of 67.98% predicted.

Treatment: From the tables and figures, it was found that inhaled SAMA + SABA+ ICS improved the FEV1 value. It was found that the FEV1 value changed from 52.05% predicted to 75.60% predicted.

Comparison between groups: From the tables and figures, it was found that in both treatment and control group, the pulmonary function (FEV1 value) have improved. This proves that ICS +SAMA+SABA and SAMA+SABA are effective in improving the pulmonary function in patients with COPD. The objective is to determine the change in FEV1 levels in patients receiving SABA+SAMA+ICS and SAMA+SABA and compare between the groups. In treatment group, the FEV1 improved from 52.05% predicted to 75.60% predicted. In control group, the FEV1 improved from 65.95% predicted to 67.98% predicted. There is significant ($p < 0.001$) difference in the effect of inhaled corticosteroids on improving the pulmonary function. From this study, it was found that ICS +SAMA+SABA improves the pulmonary function to a greater extend than SAMA+SABA.

SGRQ:

Control:SAMA+SABA reduced the symptom score from 49.13% to 41.83% . SAMA+SABA has

got an effect on symptom score. It reduced the activity score from 33.30% to 32.28% thus, has effect on activity score. It reduced the impact score from 25.85% to 22.95%, showing an effect on impact score.

Treatment: ICS+SAMA+SABA reduced the symptom score from 63.88% to 45.05%. It reduced the activity score from 54.93% to 35.78%. It has got a significant effect on activity score. It has reduced the impact score from 39.45% to 22.53% which shows an effect on impact score.

Comparison of improvement in SGRQ score in both groups

The present study shows that ICS+SAMA+SABA and SAMA+SABA have significant effect on symptom, activity and impact score in COPD patients.

ICS+SAMA+SABA reduced the symptom score from 63.88% to 45.05% whereas SAMA+SABA reduced the symptom score from 49.13% to 41.83%. There is significant ($p < 0.001$) difference in effect of ICS+SAMA+SABA in reducing the symptom score than SAMA+SABA.

ICS+SAMA+SABA reduced the activity score from 54.93% to 35.78% whereas 33.30% to 32.28% by SAMA+SABA. There is significant difference in the effect of ICS+SAMA+SABA in reducing the activity score.

ICS+SAMA+SABA reduced the impact score from 39.45% to 22.53% whereas SAMA+SABA reduced the impact score from 25.85% to 22.95%. There is significant difference ($p < 0.001$) in the effect of ICS+SAMA+SABA in reducing the impact score than SAMA+SABA.

TOTAL SCORE: From the tables and figures, the effects of ICS+SAMA+SABA and SAMA+SABA are determined. ICS+SAMA+SABA reduced the total score from 48.13% to 30.15% and SAMA+SABA reduced the total score from 32.28% to 28.88%. There is significant difference ($p < 0.001$) in effect of ICS+SABA+SAMA than SAMA+SABA. From the study, it is proved that ICS+SAMA+SABA is more effective than SABA+SAMA in improving the symptoms of COPD patients.

6-MWT

Control: SAMA+ SABA increased the SPO2 fall from an average from 2.50% to 4.00%. It has no significant effect on reducing the SPO2 fall. SAMA+SABA reduced the distance walked from 448.80 meters to 427.05 meters. It has no significant effect on improving the distance walked. SAMA+ SABA reduced the percentage walked from 69.90% to 67.25%. It has no significant effect on improving the percentage walked.

Treatment: ICS+SAMA+SABA reduced the SPO2 fall from an average 4.33% to 1.63%. It has a significant effect on reducing the SPO2 fall. ICS+SAMA+SABA improved the distance walked from 406.68 meters to 466 meters. It has a significant effect on improving the distance walked by the COPD patients. ICS+SAMA+SABA improved the percentage walked from 63.63% to 72.95%. It has got significant effect on improving the percentage walked.

Percentage walked: From the tables and graphs, it is found that the ICS+SAMA+SABA has significant effect on percentage walked. ICS+SAMA+SABA improves the percentage walked from 63.63% to 72.95% whereas SAMA+SABA have no significant effect on the improvement in symptoms of COPD patients.

EQ-5D DESVRPTIVE SYSTEM

Control: QOL based on the patients' mobility, their ability of self care and capability to carry out usual activities, discomforts and anxieties and depressions were assessed. From the tables and figures, it was found that among 40 patients in control group, 5% were having high QOL, 60% moderate and 35% poor QOL. This has been changed to 0% high, 50% moderate and 50% poor QOL in the second visit. It is also evident that there is significant reduction in the quality of life of the patients in control group.

Treatment: Among 40 patients in treatment group, 10% of patients were having high QOL, 87.5% moderate and 2.50% poor QOL in their first visit. This has been changed to 25% high, 75% moderate and 0% patients with poor QOL. Thus, it is evident that there is significant rise in the quality of life of the patients in treatment group.

JSQ: From the tables and figure, it is evident that the sleep problems due to COPD have reduced significantly in treatment group than control group patients who have experienced sleep disturbances.

SUMMARY

- The majority of the patients belong to the 71-75 category. Among the patients, the occurrence of COPD increased with respect to their age proportion. The ages have direct relationship with COPD occurrence. Out of total patients, each age category has a high medication adherence level.
- Influences of COPD are more in patients who have a history of cigarette smoking for past several years.
- Males (86%) are dominated over the female population (14%) who came for COPD treatment.
- There is improvement in the pulmonary function of COPD patients who were taking inhaled corticosteroid with SAMA and SABA than those taking SAMA and SABA alone based on their FEV1 % predicted.
- The SGRQ score reduction shown that inhaled corticosteroid is having greater effect on reducing the symptoms of COPD.
- 6-MWT results evidences the significant improvement in symptoms of COPD in those administering ICS+SABA+SAMA, than those taking SAMA+SABA alone.
- Among the 80 patients, those administering ICS+SAMA+SABA have shown significant improvement in the quality of life and improvement in sleep problems.

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CONCLUSION

Chronic Obstructive Pulmonary Disease patients are increasing in the current scenario. This study is an attempt to compare the effect of inhaled corticosteroid in improving the pulmonary function of COPD patients. The current study was conducted in department of pulmonary medicine of Pushpagiri Medical College Hospital, Thiruvalla. Eighty COPD patients, 40 patients who were administering ICS+SAMA+SABA and 40 patients who were taking SAMA+SABA were selected for the study. PFT and 6 MWT were conducted and SGRQ, EQ-5D and JSQ were evaluated, patient counselling on disease, drugs and inhaler use and the patients were provided with medication diaries. These were monitored on the starting day of the therapy and after six months of therapy The obtained parameters were analysed and the results concluded that taking inhaled corticosteroid with inhaled short acting bronchodilators showed significant improvement in the pulmonary function and symptoms of COPD patients when comparing those taking inhaled short acting bronchodilators alone. SGRQ scores showed significant improvement in symptoms of the COPD patients. 6-MWT evidenced significant improvement in the SPO₂ level and capability of the patient to walk without much fall in SPO₂. According to gender, males (86%) are dominated over the female population (14%) who came for COPD treatment. This study offers a new therapeutic approach for the COPD patients who are initially diagnosed with COPD to reduce fall in FEV1 level and prevent exacerbation of COPD. The new therapeutic outcome may reduce the number of exacerbations and hospital stay in COPD patients, thus provide better patient care.

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