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A PROSPECTIVE OBSERVATIONAL STUDY ON THE EFFICACY OF FORMOTEROL / BUDESONIDE VERSUS FORMOTEROL / GLYCOPYRRONIUM & TO ASSESS THE QUALITY OF LIFE IN PATIENTS WITH COPD

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ABSTRACT:

BACKGROUND:

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable chronic lung disease which affects men and women worldwide. Formoterol is a LABA, decreases resistance in the respiratory airway and increases airflow to the lungs. Budesonide is a corticosteroid, has a potent anti-inflammatory activity.Glycopyrronium is a LAMA, competitively blocks muscarinic receptors thus inhibiting cholinergic transmission.

Spirometry is the essential test to assess how well your lungs work by measuring how much air you inhale, how much you exhale & how quickly you exhale.St. George Respiratory Questionnaire (SGRQ) is a disease-specific instrument designed to measure impact on overall health, daily life & perceived well-being in patients with obstructive airways disease.

METHODS:

The study was carried out in 50 patients with COPD. The study was conducted by categorising them into two groups, 25 patients taking Formoterol/Budesonide and 25 patients taking Formoterol/Glycopyrronium.The efficacy of drugs are assessed using spirometry and health related QOL is assessed using SGRQ-C

RESULT:

By using spirometry, it was found that Formoterol/Glycopyrronium showed improvement in patients. A significant increase in the QOL was found in patients taking Formoterol/Glycopyrronium using SGRQ-C.

CONCLUSION:

It was concluded that, Formoterol/Glycopyrronium is slightly more efficient than Formoterol/Budesonide. There is a significant improvement in the QOL scoring in patients taking Formoterol/Glycopyrronium when compared to that of patients taking Formoterol/Budesonide.

KEYWORDS:

Formoterol, Budesonide, Glycopyrronium, Spirometry, SGRQ, FEV1/FVC ratio.

INTRODUCTION

CHRONIC OBSTRUCTIVE PULMONARY DISEASE: [3]

Chronic Obstructive Pulmonary Disease (COPD) is a respiratory disease of inflammation. It is used to describe a progressive and irreversible decrease in lung function. This decline in lung function results in decreased airflow and obstruction. The term COPD can be used to describe the more specific terms, emphysema and chronic bronchitis. The primary risk factor for COPD is smoking. Other risk factors including air pollution, second-hand smoking, occupational exposure to toxins, and frequent respiratory infections. At present time there is no known cure for COPD, however with treatment progression of the disease can be controlled and quality of life improved.

EPIDEMIOLOGY: [5]

- In developed countries, cigarette smoking accounts for 90% of cases.
- COPD is currently the fourth leading cause of death in world.
- More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally.

CLASSIFICATION:[10]

COPD includes two types:

a) EMPHYSEMA

b) CHRONIC BRONCHITIS

a. EMPHYSEMA:

Abnormal permanent enlargement of air spaces distal to terminal bronchioles, accompanied by destruction of their walls, without obvious fibrosis.

TYPES OF EMPHYSEMA: [11]

1. CENTRIACINAR EMPHYSEMA:

- Begins in the respiratory bronchioles and spreads peripherally.
- Also termed centri-lobular emphysema.
- Predominantly involves the upper half of the lungs.

2. PANACINAR EMPHYSEMA:

- Cause homozygous α_1- Antitrypsin deficiency.
- Destroys the entire alveolus uniformly.
- Predominant in the lower half of lungs.

3. PARASEPTAL EMPHYSEMA:

- There is scarring & damage affecting the lung parenchyma which is patchy.
- Preferentially involves the distal airway structure ,alveolar ducts alveolar sacs
- Localized around the septae of lungs or pleura.

b. CHRONIC BRONCHITIS:

- It is a condition with chronic or recurrent excessive mucus secretion into bronchial tree with cough that is present on most days for at least 3 months of the year during at least 2 consecutive years.
- It is a chronic inflammation of the lower respiratory tract characterized by excessive mucous secretion, cough & dyspnoea associated with recurrent infections of the lower respiratory tract.

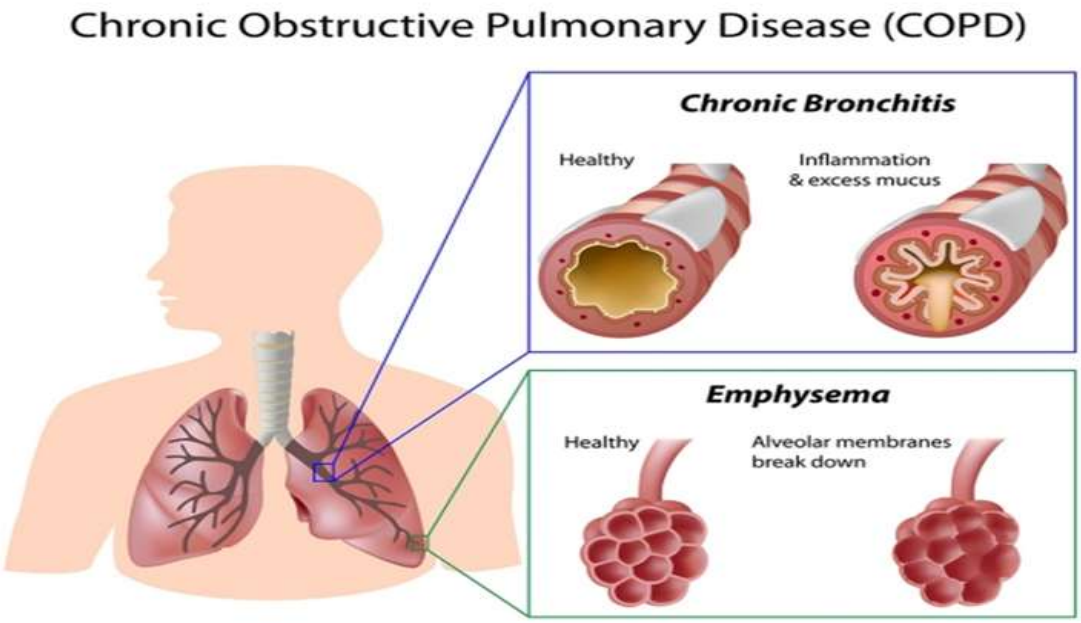


FIGURE: 1 CLASSIFICATION OF COPD[61]

RISK FACTORS: [3]

a) Environmental factors:

- Tobacco smoke
- Indoor air pollution
- Occupational exposures, such as coal dust, silica & cadmium
- Low birth weight
- Lung growth: childhood infections or maternal smoking may affect growth of lung during childhood
- Low socio-economic status
- Cannabis smoking

b) Host factors:

- Genetic factors: alpha-1-antitrypsin deficiency, other susceptility genes are likely to be identified
- Airway hyper-reactivity

CLINICAL FEATURES: [3]

- Chronic bronchitis
- Breathlessness
- Cough & associated sputum production
- Hemoptysis
- Presence of edema
- Morning headaches
- Breath sounds
- Bronchiectasis
- Cor pulmonale
- Fatigue, anorexia & weight loss
- Pink puffers
- Blue bloaters

PATHOPHYSIOLOGY: [11]

COPD has both pulmonary & systemic components. The presence of airflow limitation combined with premature airway closure leads to gas trapping & hyper-inflation, adversely affecting pulmonary & chest

wall compliance. Pulmonary hyper-inflation also results, which flattens diaphramic muscles and leads to an increasingly horizontal alignment of the intercostal muscles, placing the respiratory muscles at a mechanical disadvantage.

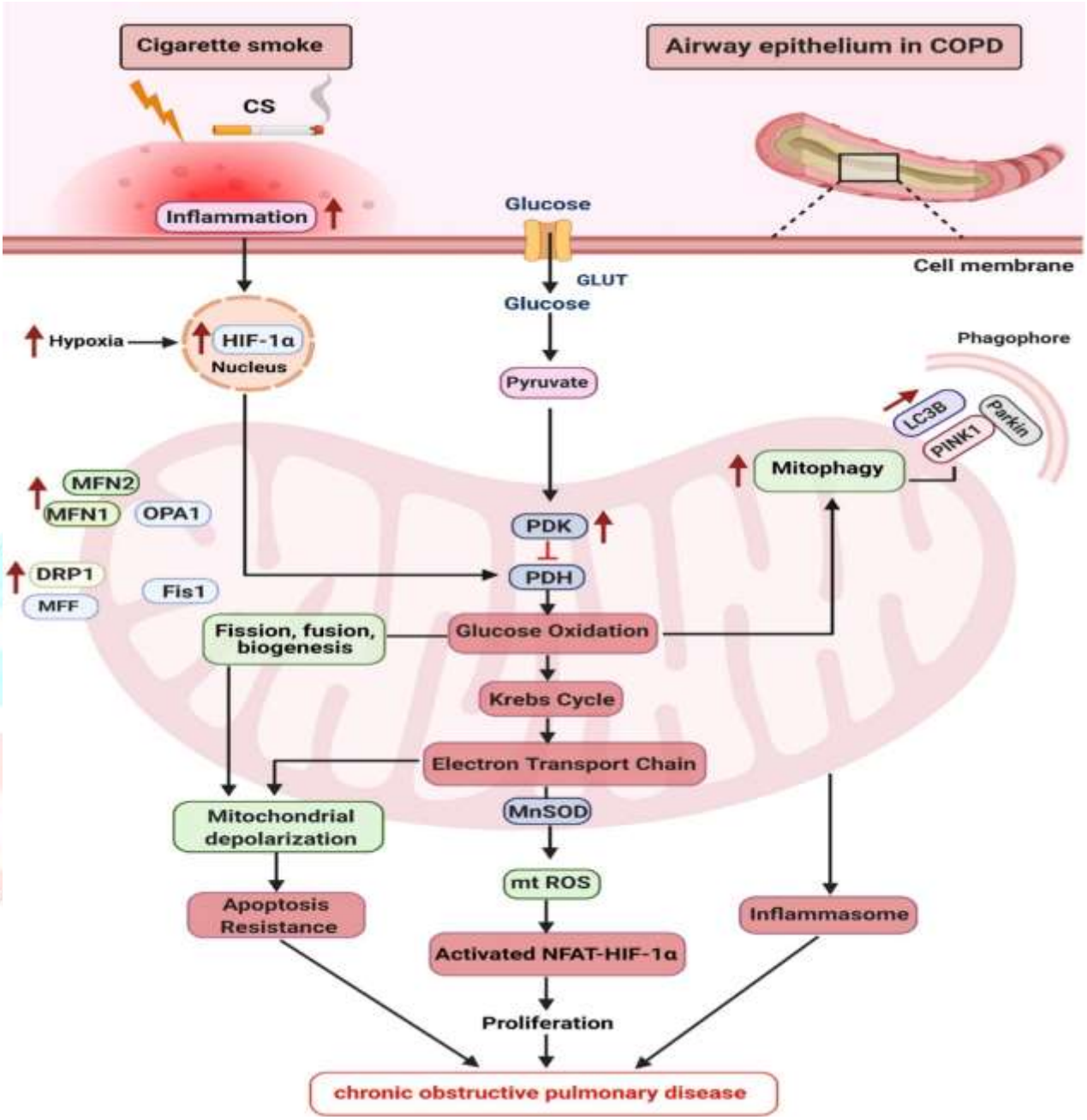


FIGURE: 2 PATHOPHYSIOLOGY OF COPD [61]

INVESTIGATIONS: [1, 13]

- A chest [illegible]re, lung cancer & the presence of bullae.
- All patients should be tested for alpha-1-antitrypsin deficiency.
- The diagnosis requires objective demonstration of airflow obstruction by spirometry and is established when the post-bronchodilator FEV_1/ FVC is 70%.
- Measurement of lung volumes provides an assessment of hyperinflation.
- Body plethysmography is preferred to estimate lung volumes.

- Exercise & rehabilitation programmes.
- Pulse oximetry may prompt referral for a domiciliary oxygen assessment if less than 93%.
- High Resolution Computed Tomography (HRCT) allows the detection characterization & quantification of emphysema.

MANAGEMENT: [13,14]

The main aim is to improve a patient's functional status and quality of life by preserving optimal lung function, improving symptoms, and preventing the recurrence of exacerbations, reduce mortality, improve exercise tolerance.

NON PHARMACOLOGICAL TREATMENT: [12]

- Smoking cessation.
- Pulmonary rehabilitation.
- Pneumococcus and influenza vaccination.
- Non-invasive positive pressure ventilation (NPPV).
- Long-term oxygen therapy (LTOT).
- Surgery and bronchoscopic lung volume reduction.
- Respiratory muscle training can be beneficial, especially when combined with general exercise training.

SURGICAL MANAGEMENT:

- Bullectomy:
  - Resection bulla allow expansion of the surrounding lung tissue.
- Lung volume reduction surgery:
  - FEV_1 < 35%.
- Lung transplant:
  - Age < 65 years
  - FEV < 35%
  - PaO_2 < 55mmHg, PaO_2 > 55mmHg
  - Secondary pulmonary HTN, absence of IHD.

PHARMACOLOGICAL MANAGEMENT:[23]

COPD CLASSIFICATION OF DRUGS:

1. Anti-inflammatory medications:

a) Corticosteroids:

- Inhaled corticosteroids:

- Fluticasone
- Budesonide
- Mometazone

- Systemic corticosteroids:

- Prednisolone
- Methyl prednisolone

b) PDE inhibitors:

- Non selective inhibitors:

- Theophylline

- Selective inhibitors:

- Roflumilast

2. Inhaled bronchodilators:

a) Inhaled beta agonists:

- Short Acting Beta Agonists(SABA):

- Albuterol
- Terbutaline

- Long Acting Beta Agonists (LABA):

- Salmeterol
- Formoterol
- Indacterol

b) Inhaled anticholinergics:

- Short acting anticholinergics(SAAC):

- Ipratropium bromide

- Long acting anticholinergics (LAAC):

- Tiotropium bromide

- Glycopyrronium bromide

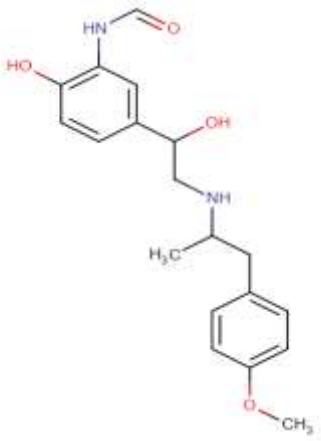
3. Miscellaneous:

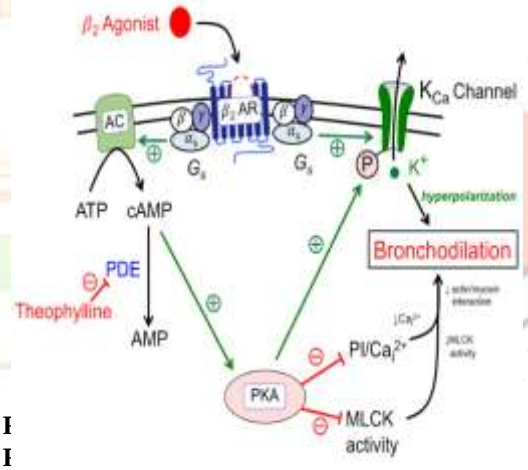
- Smoking cessation medications
- Immunization
- Oxygen therapy

DRUGS & TOOLS USED IN THE STUDY:

FORMOTEROL:

Formoterol, a long-acting beta 2-selective adrenoceptor agonist, produces dose-proportional bronchodilation in patients with obstructive airways disease with a reversible component.





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BUDESONIDE:

Budesonide is an inhaled corticosteroids that suppresses airway inflammation by activating anti-inflammatory genes, switching off inflammatory gene expression, and inhibiting inflammatory cells.

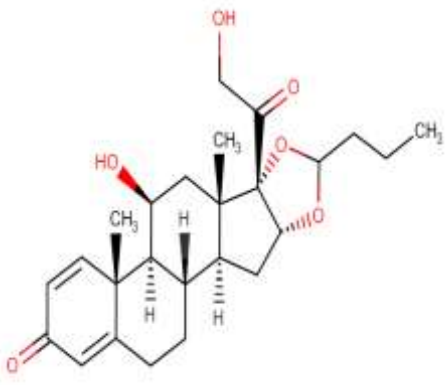


FIG: 5 CHEMICAL STRUCTURE OF BUDESONIDE[65]

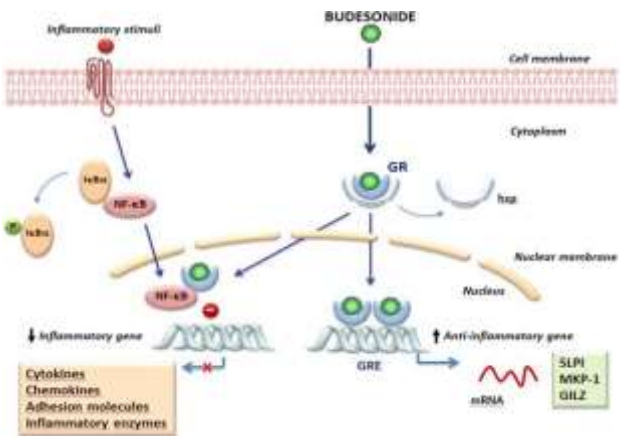
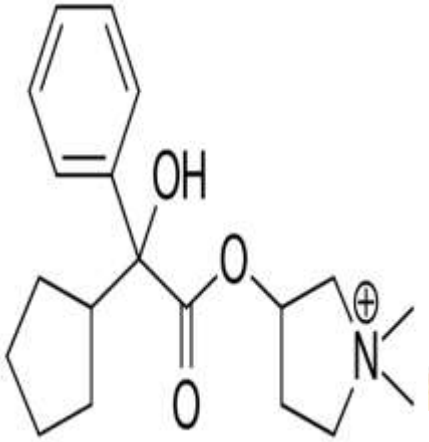


FIG: 6 MECHANISM OF THE DRUG BUDESONIDE [68]

Glycopyrrolate, or glycopyrronium bromide, like other LAMAs, inhibits para-sympathetic nerve impulses by selectively blocking the binding of acetylcholine to muscarinic receptors & helps to prevent the formation of secretions that can cause problems in the respiratory tract.



OF GLYCOPYRRONIUM [64]

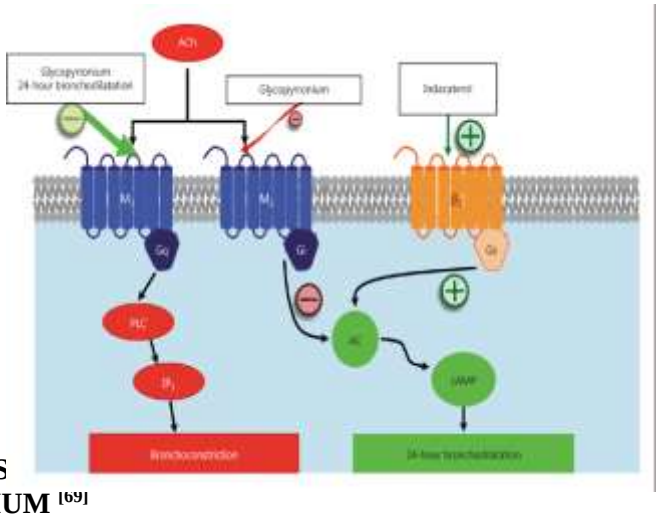


FIG: 8 MECHANIS
GLYCOPYRRONIUM [69]

Spirometry is a method of assessing lung function by measuring the volume of air that the patient can expel from the lungs after a maximal inspiration. The indices derived from this forced exhaled maneuver have become the most accurate and reliable way of supporting a diagnosis of COPD. When these values are compared with predicted normal values determined on the basis of age, height, sex, and ethnicity, a measure of the severity of airway obstruction can be determined. It is on these values that COPD guidelines around the world base the assessment of mild, moderate, and severe disease levels. Spirometry is however only one way of interpreting COPD disease severity.

Major uses of spirometry in COPD:

• Confirm the presence of airway obstruction

• Confirm an FEV_1 / FVC ratio < 0.7 after bronchodilator

• Provide an index of disease severity

• Help differentiate asthma from COPD

• Detect COPD in subjects exposed to risk factors, predominantly tobacco smoke, independently of the presence of respiratory symptoms

• Enable monitoring of disease progression

• Help assess response to therapy

• Aid in predicting prognosis and long-term survival

• Exclude COPD and prevent inappropriate treatment if spirometry is normal

Types of Spirometers:

i. **Bellows or rolling seal spirometers**

- These are large and not very portable, and are used predominantly in lung function laboratories.
- They require regular calibration with a 3-liter syringe and are very accurate.

ii. **Electronic desktop spirometers**

- These are compact, portable, and usually quick and easy to use.
- They have a real-time visual display and paper or computer printout.
- Some require calibration with the 3-liter syringe; others can be checked for accuracy with the syringe but require any changes to be performed by the manufacturer.
- Generally they need little attention other than cleaning.
- They maintain accuracy over years and are ideal for primary care.

iii. **Small, inexpensive hand-held spirometers**

- They provide a numerical record of blows but no printout.
- It may be necessary to look up predicted values in tables, but some include these in their built-in software.
- Recent models allow pre-programming of patient details so that the spirometer also gives percent predicted values.
- These are good for simple screening and are accurate for diagnosis if the more expensive desktop form is impractical or too expensive.

Information provided by the Spirometer: [22]

The standard spirometry maneuver is a maximal forced exhalation (greatest effort possible) after a maximum deep inspiration (completely full lungs). Several indices can be derived from this blow.

- **FVC (Forced Vital Capacity**) - the total volume of air that the patient can forcibly exhale in one breathe.
- **FEV_1 (Forced Expiratory Volume in One Second**) - the volume of air that the patient is able to exhale in the first second of forced expiration.
- **FEV_1 / FVC** - the ratio of FEV_1 to FVC expressed as a fraction (previously this was expressed as a percentage).

- Values of FEV_1 and FVC are measured in litres and are also expressed as a percentage of the predicted values for that individual.
- The ratio of FEV_1 / FVC is normally between 0.7 and 0.8.
- Values below 0.7 are a marker of airway obstruction, except in older adults where values 0.65 - 0.7 may be normal.
- Caution particularly needs to be taken in patients over 70 years, where the use of predicted values extrapolated from the younger population may result in over-diagnosing COPD.
- In people over 70 years old, the FEV_1 / FVC ratio may need to be lowered to 0.65 as a lower limit of normal.
- Conversely, in people under 45, using a ratio of 0.7 may result in under-diagnosis of airway obstruction.
- To avoid both of these problems, many experts recommend use of the lower limit of normal for each population.
- Predicted values are calculated from thousands of normal people and vary with sex, height, age and ethnicity.

❖ **Flow-Volume Measurement**:

- Many electronic desktop spirometers and spirometers used in lung function laboratories utilize a pneumotachograph measuring gauge, which measures airflow and integrates the signal to derive volume.
- This allows the spirometer to plot traces of flow rate against the volume of air exhaled, producing a flow-volume curve.
- On many spirometers such curves provide the main initial visual real-time display when patients are performing their blows.

❖ **FEV_6 (Forced Expiratory Volume in Six Seconds):**

- This is a more recently derived value which measures the volume of air that can forcibly be expired in 6 seconds.
- It approximates the FVC and in normal people the two values would be identical.
- Using FEV_6 instead of FVC may be helpful in patients with more severe airflow obstruction who make take up to 15 seconds to fully exhale.
- As they find this difficult and often stop before full exhalation, the FVC, and hence the severity of airway obstruction, may be under estimated.

- Some new hand-held spirometers from vitalograph use the FEV_6 instead of FVC and have predicted tables to match.
- The FEV_1 / FEV_6 is well validated and is an acceptable alternative to FEV_1 / FVC.

❖ **Slow VC (Slow Vital Capacity)**:

- The patient takes a full breath in as before but exhales slowly in their own time.
- In patients with COPD with more marked airway obstruction and dynamic compression, the slow vital capacity may exceed the FVC by > 0.5 litres.
- This index is not used routinely in primary care.
- However, ATS / ERS guidelines are increasingly suggesting FEV_1 / Slow VC as the preferred ratio.

Diagnosis of Airway Obstruction:

The spirometric criterion required for a diagnosis of COPD is an FEV_1 / FVC ratio below 0.7 after bronchodilator.

TABLE:1 GOLD SPIROMETRIC CRITERIA FOR COPD SEVERITY

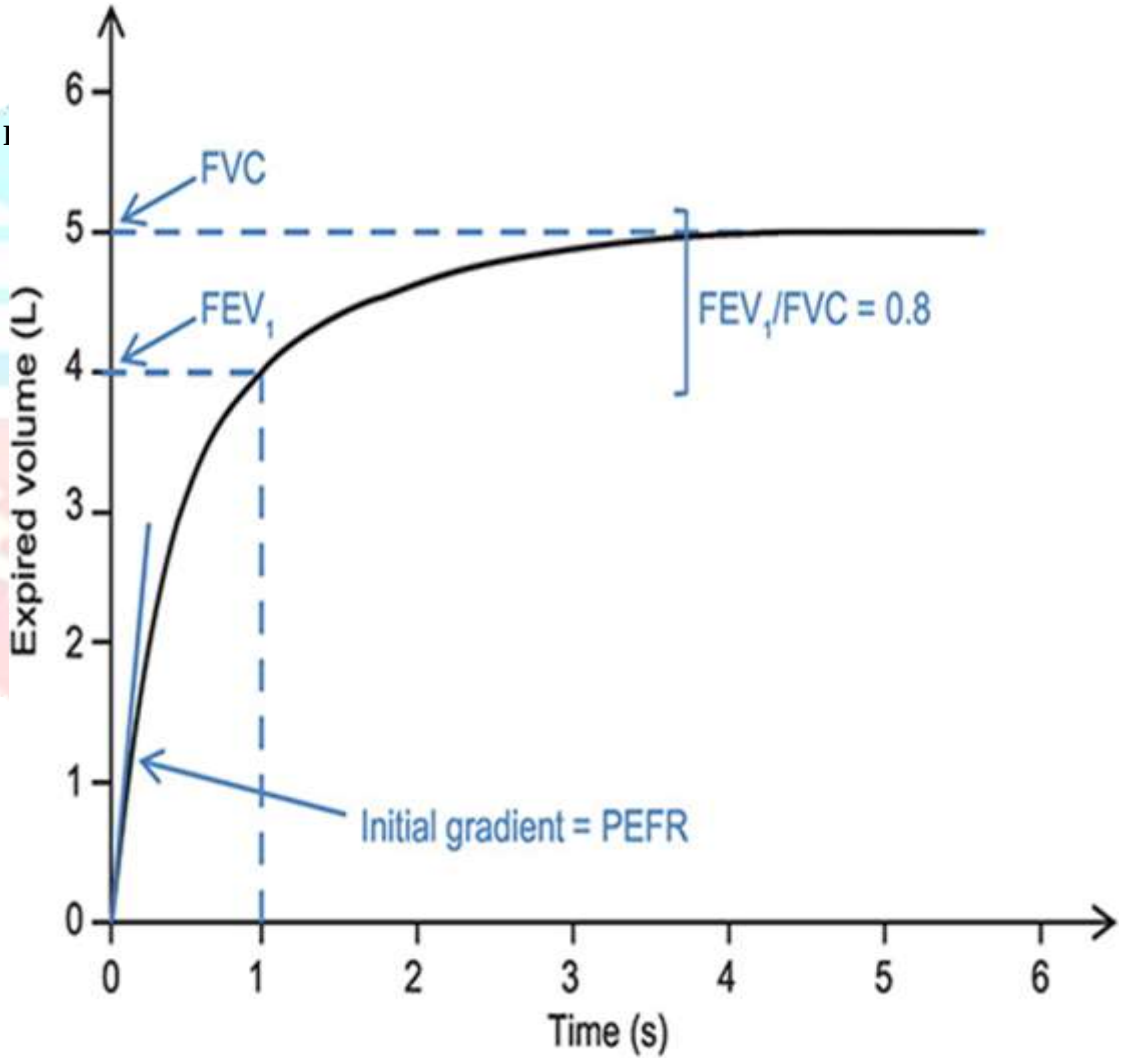
I: Mild COPD	• FEV_1 / FVC < 0.7 •$FEV_1 \geq 80\%$ predicted	At this stage, the patient may not be aware that their lung function is abnormal.
II: Moderate COPD	• FEV_1 / FVC < 0.7 • $50\% \leq FEV_1 < 80\%$ predicted	Symptoms usually progress at this stage, with shortness of breath typically developing on exertion.
III: Severe COPD	• FEV_1 / FVC < 0.7 • $30\% \leq FEV_1 < 50\%$ predicted	Shortness of breath typically worsens at this stage and often limits patients daily activities. Exacerbations are especially seen beginning at this stage.
IV:Very Severe COPD	• FEV_1 / FVC < 0.7 •$FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$	At this stage, quality of life is very appreciably impaired and

	predicted plus chronic respiratory failure	exacerbations may be life threatening	**SPIROGRAM**

INTERPRETATION:

Normal Lung Function:

Interpretation of spirometry involves looking at the absolute values of FEV_1, FVC, and FEV_1 / FVC, comparing them with predicted values, and examining the shape of the spirograms. Patients should complete three blows that are consistent and within 5% of each other many electronic spirometers automatically provide this information.



In a patient with normal lung function, the volume - time curve should rise rapidly and smoothly and plateau within 3 to 4 seconds. With increasing degrees of airway obstruction it takes longer to blow out the air upto 15 seconds and the upward slope of the spirogram is much less steep.

PERFORMING SPIROMETRY: [21]

A. Preparing the Patient:

- It is important to explain the purpose of the test and describe clearly what the patient will be asked to do.

- Before starting the patient's age, sex, and height need to be recorded and entered into the spirometer so that predicted curves and values can be calculated by the spirometer.
- Inquire and record the time of last bronchodilator inhaler use, particularly if performing a reversibility test.
- Ideally, they should be seated for the procedure as there is a small risk of syncope, which is greater if standing.

B. **Measuring FEV_1, FVC, and Flow-Volume Curves:**

FIGURE: 10 DIAGRAMMATIC REPRESENTATION OF PERFORMING SPIROMETRY [63]

- Attach a clean, disposable, one-way mouthpiece to the spirometer.
- Instruct the patient to breathe in fully until the lungs feel full.
- The patient should hold their breath long enough to seal their lips tightly around the mouthpiece.
- Blast the air out as forcibly and fast as possible until there is no more air left to expel.
- The operator should verbally encourage the patient to keep blowing and keep blowing during this phase.
- Watch the patient to make sure a good mouth seal around the mouthpiece is achieved.
- Check that an adequate trace has been achieved. Sometimes with electronic spirometers the patient may leak a small volume of air into the mouthpiece while sealing the lips which will register as the blow.
- Repeat the procedure at least twice until three acceptable and repeatable blows are obtained.
- Maximum of 8 efforts.
- There should be three readings, of which the best two are within 150 mL or 5% of each other and best.
- The best readings of FEV_1 and FVC are usually recorded.

C. Equipment Maintenance and Calibration:

- In order to provide accurate and repeatable results, spirometers must be regularly cleaned and maintained as directed in the manufacturer's instructions.
- The correct functioning must be frequently checked with some form of calibration.
- Ideally, calibration should be performed with a 3- liter syringe which will allow validation of spirometer accuracy.
- Some electronic spirometers can be recalibrated by the user but others only by returning them to the manufacturer.
- Most modern electronic spirometers, however, drift very little from the set calibration levels so use of the 3-liter syringe helps to check that levels are unchanged.
- An alternative is to assess overall performance of the spirometer by regularly testing of a healthy individual every week-a "biological control".
- Generally a variation of more than 5% in FEV_1 or FVC should alert you to a problem which may necessitate further testing and possible return to the manufacturer.

D. Infection Control:

Precautions must be taken to minimize any cross infection via the spirometer. The use of low resistance barrier filters and disposable mouthpieces significantly reduces the risk of infection and also helps to protect the equipment from exhaled secretions. A new filter must be used for each patient.

ST.GEORGE RESPIRATORY QUESTIONNAIRE:[48]

The SGRQ is a self-administered questionnaire designed to measure health impairment in patients with airways disease such as asthma and COPD. A total score incorporates scores from each component of the SGRQ which ranges from 1 to 100, where 0 indicates best health and 100 indicates worst health. This study used the SGRQ in both the Malayalam and English languages. Patients were required to complete the SGRQ before they performed the simple spirometry and 6 minutes' walk test.

PARTS OF SGRQ:

The SGRQ comprises three subsections:

- The symptoms component covers the effects, frequency and severity of respiratory symptoms.
- The activity component covers daily activities that cause or are impaired by breathlessness.
- The impact component covers social functioning and the psychosocial disturbances associated with their respiratory disease.

ADMINISTRATION:

- The questionnaire should be completed in a quiet area, free from distraction and the patient should ideally be sitting at a desk or table.
- Explain to the patient why they are completing it, and how important it is for clinicians and researchers to understand how their illness affects them and their daily life.
- It is designed to elicit the patient's opinion of his / her health, not someone else's opinion of it, so family, friends or members of staff should not influence the patient's responses.
- If the spouse or partner has accompanied the patient they should be asked to wait in a separate area.
- Once the patient has finished, it is very important that you check the questionnaire to make sure a response has been given to every question.
- If they have missed an item return it to the patient for completion, before they leave.

ITEM WEIGHTS:

Each questionnaire response has a unique 'weight'. The lowest possible weight is zero and the highest is 100.

SCORING ALGORITHM:

A total and three component scores are calculated: symptoms, activity and impacts. Each component of the questionnaire is scored separately.

- **Symptoms component:**

This consists of all the questions in part 1. The weights for questions 1 - 7 are summed. A single response is required to each item.

- **Activity component:**

This is calculated from the summed weights for the positive responses to items in questions 9 and 12 in part 2 of the questionnaire.

- **Impacts component:**

This is calculated from questions 8, 10, 11, 13, 14 in part 2 of the questionnaire. The weights for all positive responses to items in questions 10, 11, 13 are summed together with the responses to the single item that should have been checked (ticked) in questions 8 and 14.

In the case of multiple responses to either of these items, the average weight for the item should be calculated.

CALCULATE THE SCORE:

The score for each component is calculated separately by dividing the summed weights by the maximum possible weight for that component and expressing the result as a percentage.

The total score is calculated using the following formula:

$$\text{Score} = \frac{100 \times \text{summed weights from all positive items in the questionnaire}}{\text{Sum of maximum possible weights for all items in the questionnaire}}$$

Sum of maximum possible weights for each component and total

Symptoms = 566.2

Activity = 982.9

Impacts = 1652.8

Total (sum of maximum for all three components) = 3201.

OBSERVATIONS AND RESULTS

The proposed study entitled, **"A Prospective Observational Study on the Efficacy of Formoterol / Budesonide Versus Formoterol / Glycopyrronium & to Assess the Quality Of Life in Patients with COPD"** was carried out in a multispecialty tertiary care hospital. In this study, the data were collected from 50 patients diagnosed with COPD and was analysed. Among the 50 patients selected, 25 were taking Formoterol/Budesonide and 25 were taking Formoterol/Glycopyrronium. The study aimed to compare the efficacy of Formoterol/Budesonide and Formoterol/ Glycopyrronium using Spirometry and to assess the quality of life in patients with COPD using SGRQ-C questionnaire.

DEMOGRAPHIC DETAIL OF THE PATIENTS

The data related to demographic details of patients were collected and recorded

PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON AGE

The percentage distribution of patients based on age is shown in the following table

TABLE 2: PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON AGE

Age distribution (in years)	Number of patient (n)	Percentage (%)
40-50	8	16%
51-60	19	38%
61-70	17	24%
71-80	16	12%
Total	50	100%

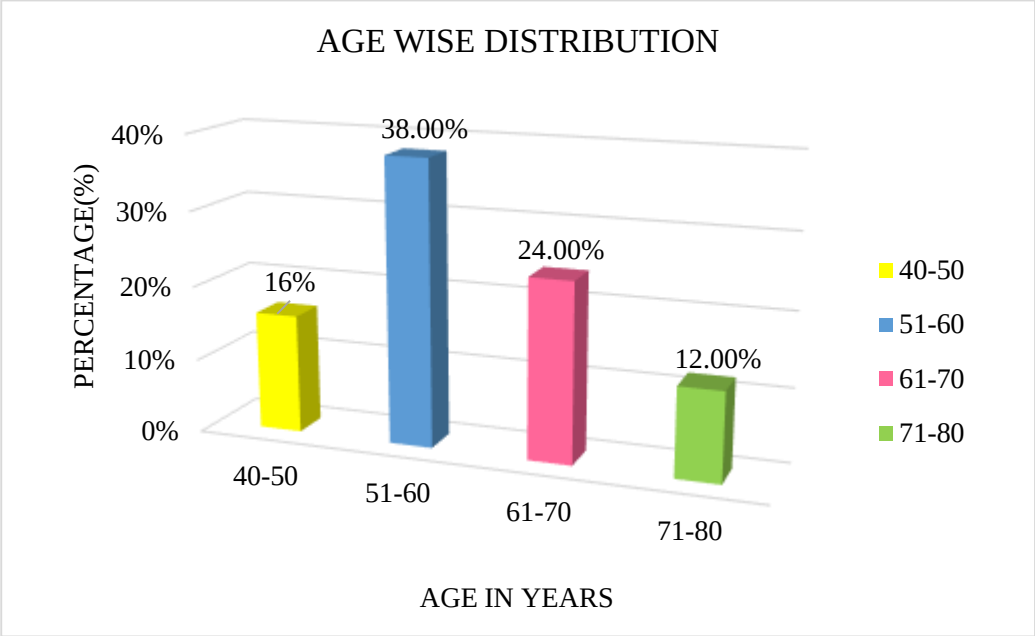


FIGURE 11: DIAGRAMMATIC REPRESENTATION OF PATIENTS BASED ON AGE

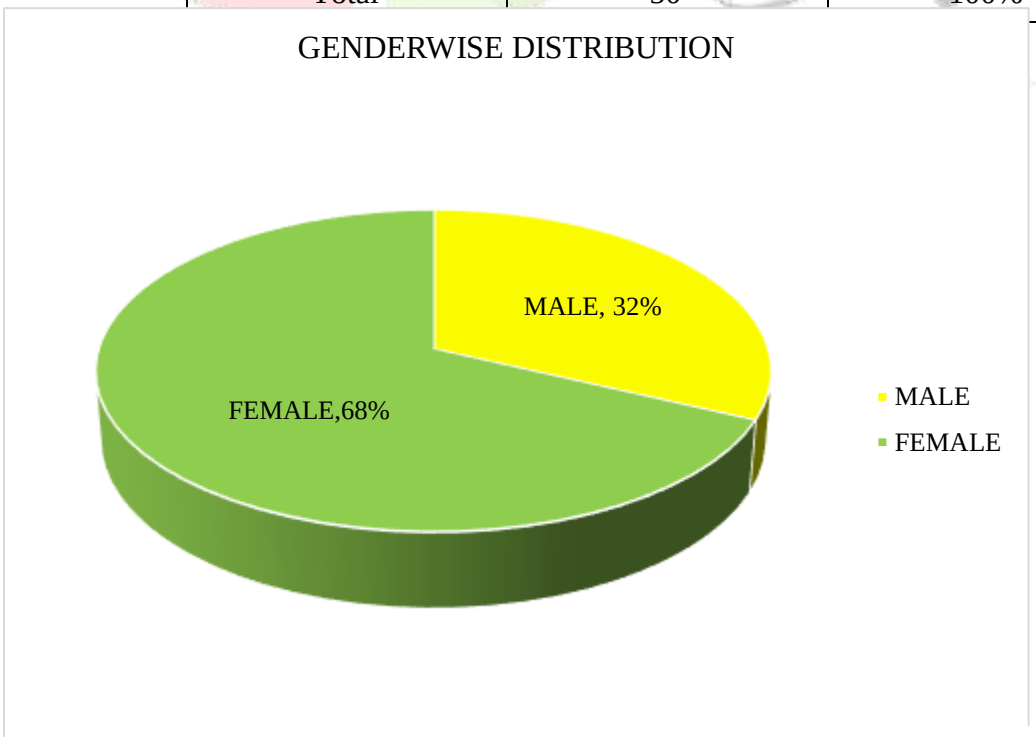
In this study, patients from the age group of 40-90 were included. It was observed that majority of the patient presenting with COPD were from the age group of 51-60 followed by the patient in the age group of 61-70.

PERCENTAGE DISTRIBUTION OF PATIENT BASED ON GENDER

The percentage distribution of patients based on gender is shown in the following table

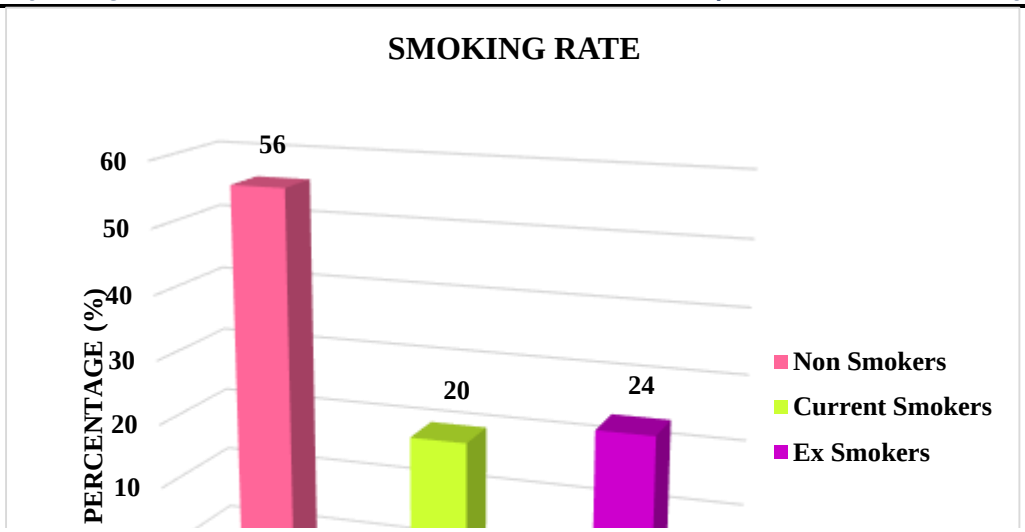
TABLE 3: PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON GENDER

	(n)	
Male	16	32%
Female	34	68%
Total	50	100%



Among a total of 50 patients included in this study, a preponderance of female patients were observed. In this study 34 patients were female (68%) while 16 patients were male (32%).

FIGURE: 12 DIAGRAMMATIC REPRESENTATION OF PATIENTS BASED ON GENDER



PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON THE SMOKING RATE:

The percentage distribution of patients based on smoking rate is shown in the following table

TABLE: 4 PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON THE SMOKING RATE

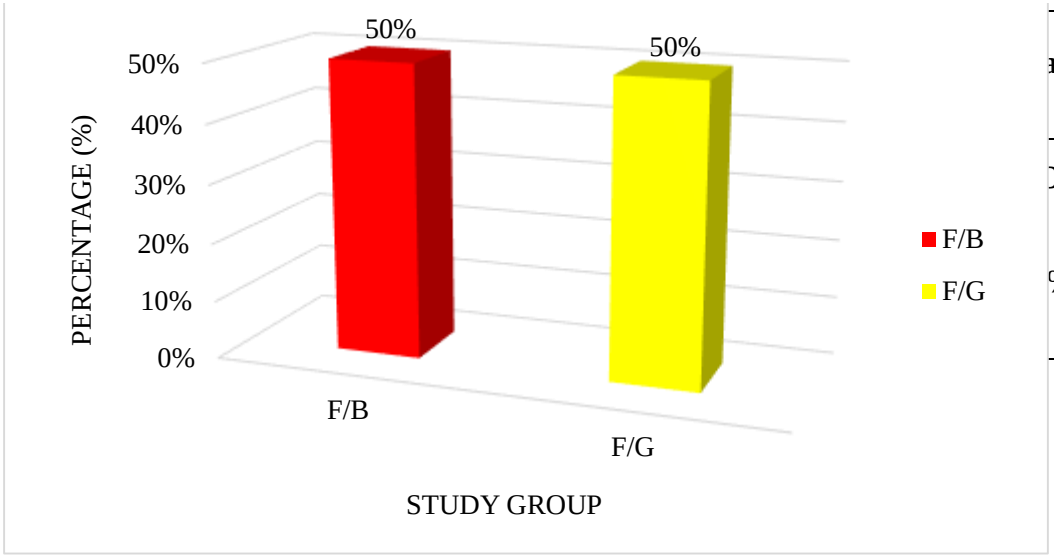
SMOKING GROUP		(%)
Non Smokers	28	56%
Current Smokers	10	20%
Ex Smokers	12	24%
Total	50	100%

Among a total of 50 patients included in this study, a preponderance of non-smokers were observed. In this study 28 patients were non-smokers (56%), 10 patients were current smokers (20%) & 12 patients were ex-smokers (24%) respectively.

PERCENTAGE DISTRIBUTION OF PATIENTS BASED ON TAKING FORMOTEROL/BUDESONIDE VERSUS FORMOTEROL/ GLYCOPYRRONIUM

The percentage distribution of patients based on taking Formoterol/Budesonide VS Formoterol/Glycopyrronium is shown in the following table

TABLE: 5 PERCENTAGE DISTRIBUTION OF PATIENTS TAKING FORMOTEROL/BUDESONIDE VERSUS FORMOTEROL/GLYCOPYRRONIUM



Amongst a total of 50 patients included in this study,

TAKING FORMOTEROL/BUDESONIDE VS FORMOTEROL/ GLYCOPYRRONIUM

25 were taking Formoterol/Budesonide (50%) and 25 were taking Formoterol/Glycopyrronium (50%).

ASSESSMENT OF EFFICACY USING SPIROMETRY:

PERCENTAGE COMPARISON OF EFFICACY IN TWO GROUPS BEFORE TREATMENT

The percentage comparison of efficacy in patients taking Formoterol/Budesonide VS Formoterol/Glycopyrronium before therapy is shown in the following table

TABLE: 6 PERCENTAGE COMPARISON OF EFFICACY IN TWO GROUPS BEFORE TREATMENT

Formoterol/Budesonide	0.66±0.09
Formoterol/Glycopyrronium	0.65±0.09

From the above table, the mean difference in the efficacy before treatment in patients taking Formoterol/ Budesonide is 0.66 & Formoterol/ Glycopyrronium is 0.65.

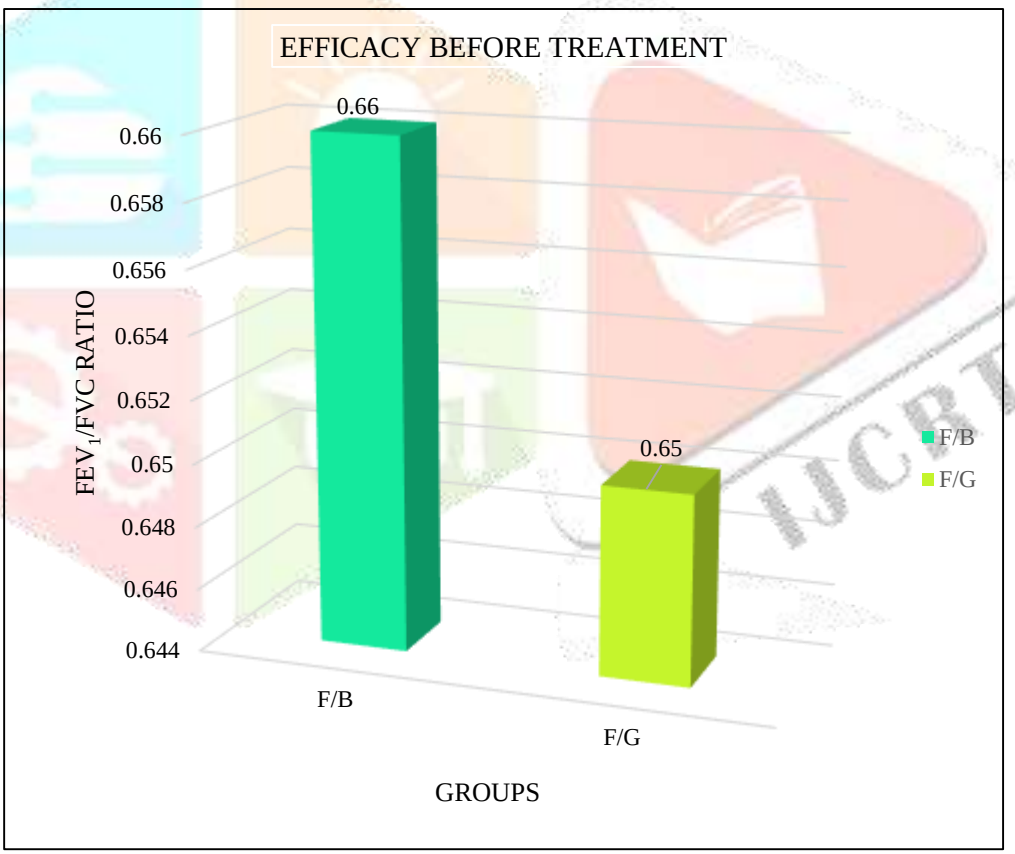


FIGURE 15: DIAGRAMMATIC REPRESENTATION OF PERCENTAGE COMPARISON OF EFFICACY BEFORE THERAPY BETWEEN TWO GROUPS

PERCENTAGE COMPARISON OF EFFICACY IN TWO GROUPS AFTER TREATMENT

The percentage comparison of efficacy in patients taking Formoterol/Budesonide VS Formoterol/Glycopyrronium after therapy is shown in the following table

TABLE: 7 PERCENTAGE COMPARISON OF EFFICACY IN TWO GROUPS AFTER TREATMENT

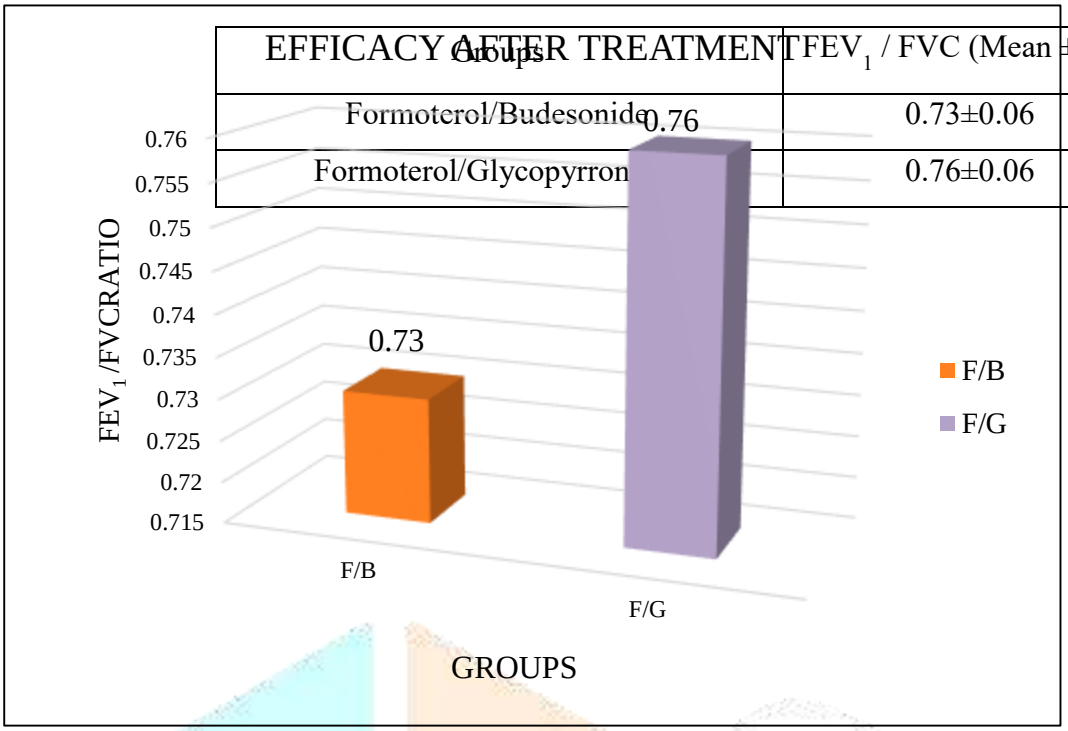


FIGURE 16: DIAGRAMMATIC REPRESENTATION OF PERCENTAGE COMPARISON OF EFFICACY IN AFTER THERAPY BETWEEN TWO

From the above table, the mean difference in the efficacy after therapy in patients taking Formoterol/ Budesonide is 0.73 & Formoterol/ Glycopyrronium is 0.76.

PERCENTAGE COMPARISON OF EFFICACY IN BEFORE AND AFTER THERAPY IN PATIENTS TAKING FORMOTEROL/ BUDESONIDE

The percentage comparison of efficacy in before & after therapy in patients taking Formoterol/Budesonide is shown in the following table

TABLE: 8 PERCENTAGE COMPARISON OF EFFICACY IN BEFORE AND AFTER THERAPY IN PATIENTS TAKING FORMOTEROL/ BUDESONIDE

EFFICACY	FORMOTEROL/BUDESONIDE	p-value
	Mean ± SD	
Before Therapy	0.66±0.09	0.001
After Therapy	0.73±0.06**	
***p-value <0.005 is considered as significant, p-value= 0.001*		

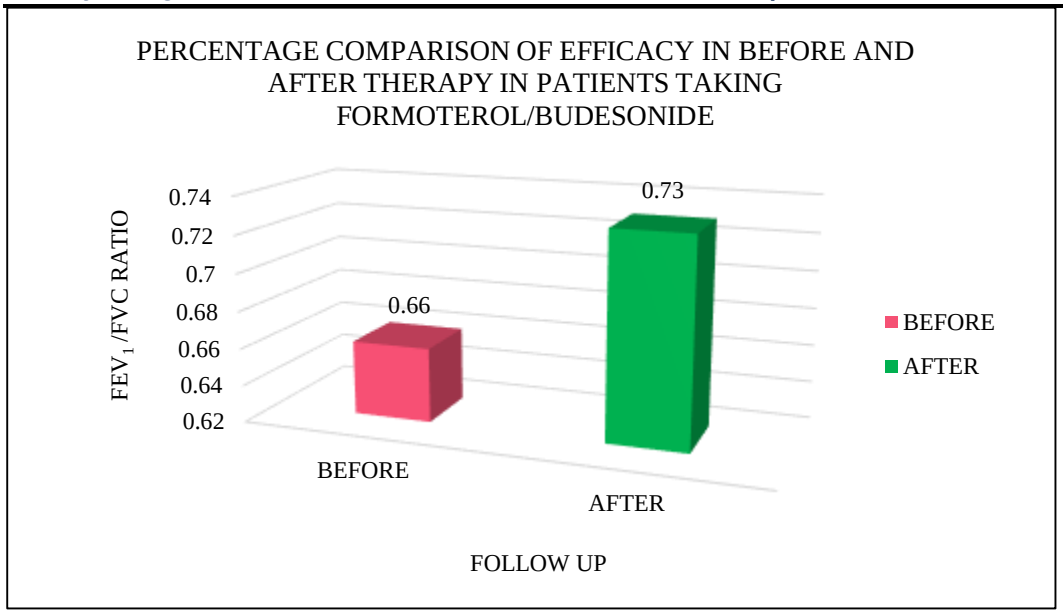


FIGURE 17: DIAGRAMMATIC REPRESENTATION OF COMPARISON OF EFFICACY IN BEFORE & AFTER THERAPY IN PATIENTS TAKING FORMOTEROL/BUDESONIDE

The efficacy of Formoterol/Budesonide before and after therapy is compared with a paired t-test and found that the paired mean difference is drastically increased and this is found to be statistically significant. P-value = 0.001*

PERCENTAGE COMPARISON OF EFFICACY IN BEFORE AND AFTER TREATMENT IN PATIENTS TAKING FORMOTEROL/ GLYCOPYRRONIUM

The percentage comparison of efficacy in before and after therapy in patients taking Formoterol/Glycopyrronium is shown in the following table

TABLE 9: PERCENTAGE COMPARISON OF EFFICACY IN BEFORE AND AFTER TREATMENT IN PATIENTS TAKING FORMOTEROL/

Efficacy	FORMOTEROL/BUDESONIDE	p-value
	Mean ± SD	
Before Therapy	0.65±0.09	0.001
After Therapy	0.76±0.01**	
***p-value <0.005 is considered as significant, p-value= 0.001*		

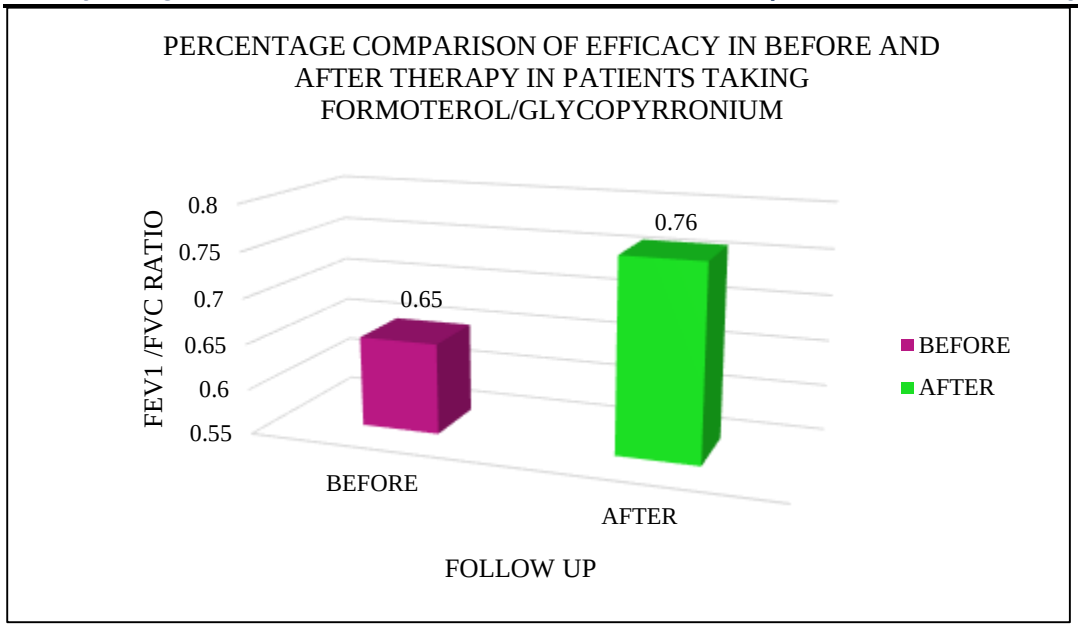


FIGURE 18: DIAGRAMMATIC REPRESENTATION OF COMPARISON OF EFFICACY IN BEFORE & AFTER THERAPY IN PATIENTS TAKING FORMOTEROL/GLYCOPYRRONIUM

The efficacy of Formoterol/Glycopyrronium before and after therapy is compared with a paired t-test and found that the paired mean difference is drastically increased and this is found to be statistically significant. P-value = 0.001*

OVERALL COMPARISON OF EFFICACY OF FORMOTEROL/ BUDESONIDE VERSUS FORMOTEROL/ GLYCOPYRRONIUM

The overall comparison of efficacy of Formoterol/Budesonide versus Formoterol/Glycopyrronium is shown in the following table

TABLE: 10 OVERALL COMPARISON OF EFFICACY OF FORMOTEROL/ BUDESONIDE VERSUS FORMOTEROL/ GLYCOPYRRONIUM

		FEV_1 / FVC	
Formoterol/Budesonide	Before Therapy	0.66±0.09	0.001
	AFTER THERAPY	0.73±0.06**	
Formoterol/Glycopyrronium	Before Therapy	0.65±0.09	
	AFTER THERAPY	0.76±0.01**	

***p-value <0.005 is considered as significant, p-value= 0.001*

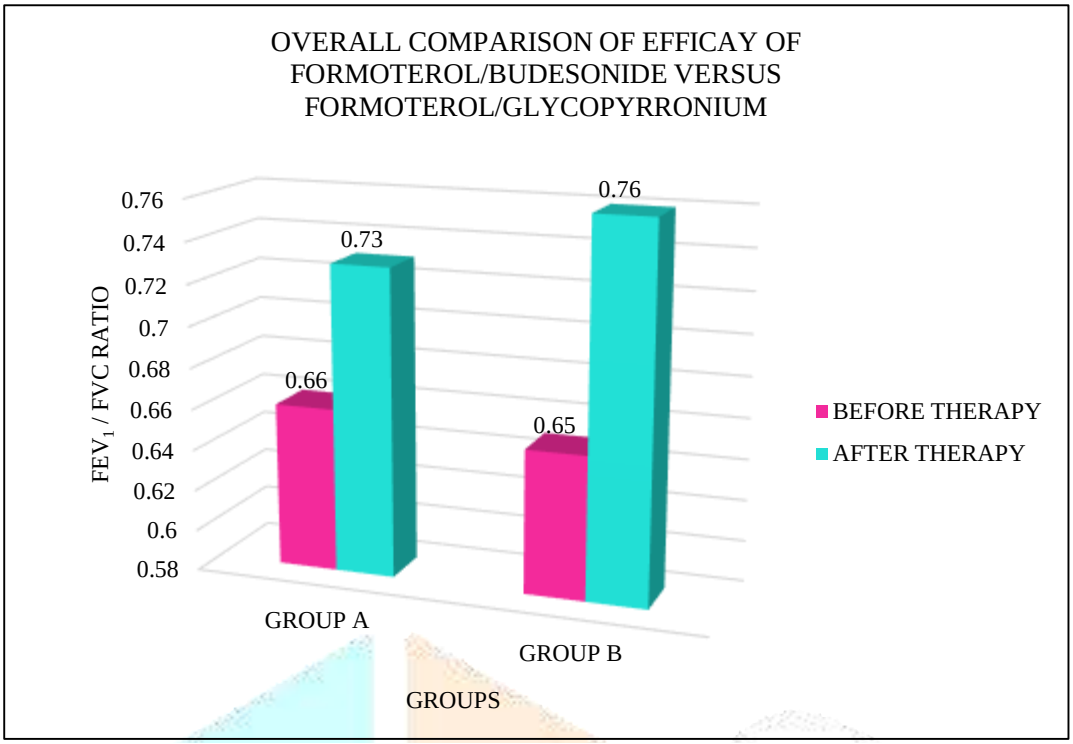


FIGURE 19: DIAGRAMMATIC REPRESENTATION OF OVERALL COMPARISON OF EFFICACY OF FORMOTEROL/BUDESONIDE VERSUS FORMOTEROL/GLYCOPYRRONIUM

On comparing the mean after therapy in the Formoterol/Glycopyrronium group it is found that the mean difference is statistically increased, as compared to Formoterol/Budesonide. The p-value = 0.001*.

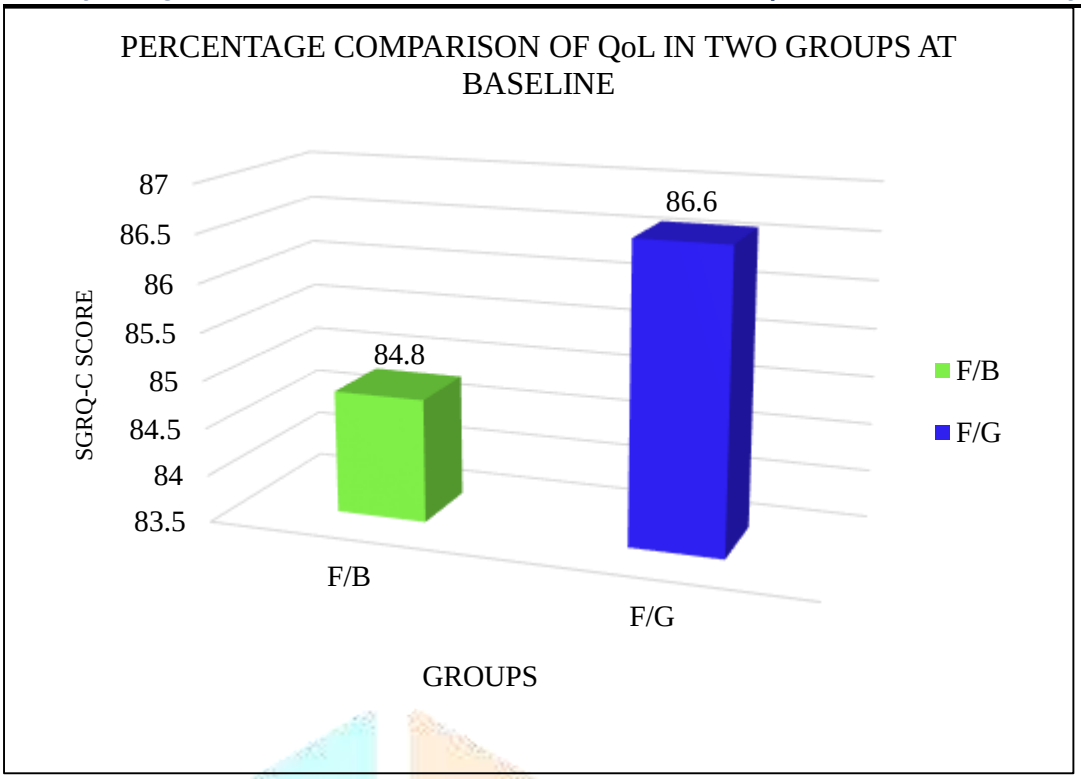
ASSESSMENT OF QUALITY OF LIFE USING ST.GEORGE RESPIRATORY QUESTIONNAIRE – COPD

PERCENTAGE COMPARISON OF QoL IN TWO GROUPS AT BASELINE

The percentage comparison of QoL in patients taking Formoterol/Budesonide VS Formoterol/Glycopyrronium at baseline is shown in the following table

TABLE: 11 PERCENTAGE COMPARISON OF QoL IN TWO GROUPS AT BASELINE

Groups	SGRQ-C Score (Mean ± SD)
Formoterol/Budesonide	84.8±8.8
Formoterol/Glycopyrronium	86.6±11.4



From the above table, the mean difference in the QoL at baseline in patients taking

FIGURE 20: DIAGRAMMATIC REPRESENTATION OF PERCENTAGE COMPARISON OF QoL AT BASELINE BETWEEN TWO GROUPS

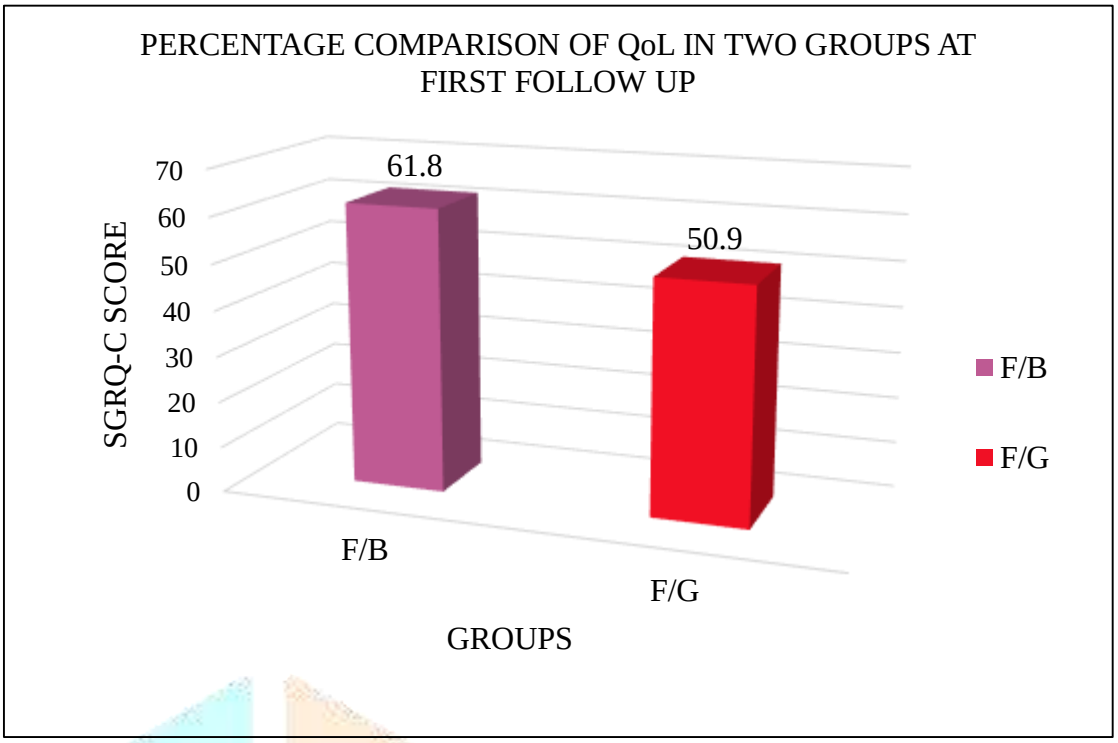
Formoterol/Budesonide is 84.8 & Formoterol/ Glycopyrronium is 86.6.

PERCENTAGE COMPARISON OF QoL IN TWO GROUPS AT FIRST FOLLOW UP

The percentage comparison of QoL in patients taking Formoterol/Budesonide VS Formoterol/Glycopyrronium at first follow up is shown in the following table

TABLE: 12 PERCENTAGE COMPARISON OF QoL IN TWO GROUPS AT FIRST FOLLOW UP

Groups	SGRQ-C Score (Mean ± SD)
Formoterol/Budesonide	61.8±9.3
Formoterol/Glycopyrronium	50.9±9.05



From the above table, the mean difference in the QoL at baseline in patients taking Formoterol/Budesonide is 61.8 & Formoterol/ Glycopyrronium is 50.9.

PERCENTAGE COMPARISON OF QoL IN TWO GROUPS AT SECOND FOLLOW UP

The percentage comparison of QoL in patients taking Formoterol/Budesonide VS Formoterol/Glycopyrronium at second follow up is shown in the following table

TABLE: 13 PERCENTAGE COMPARISON OF QoL IN TWO GROUPS AT SECOND FOLLOW UP

Groups	SGRQ-C Score (Mean ± SD)
Formoterol/Budesonide	37.4±9.8

From the above table, the mean difference in the QoL at second follow up in patients taking

FIGURE 21: DIAGRAMMATIC REPRESENTATION OF PERCENTAGE COMPARISON OF QoL AT FIRST FOLLOW UP BETWEEN TWO

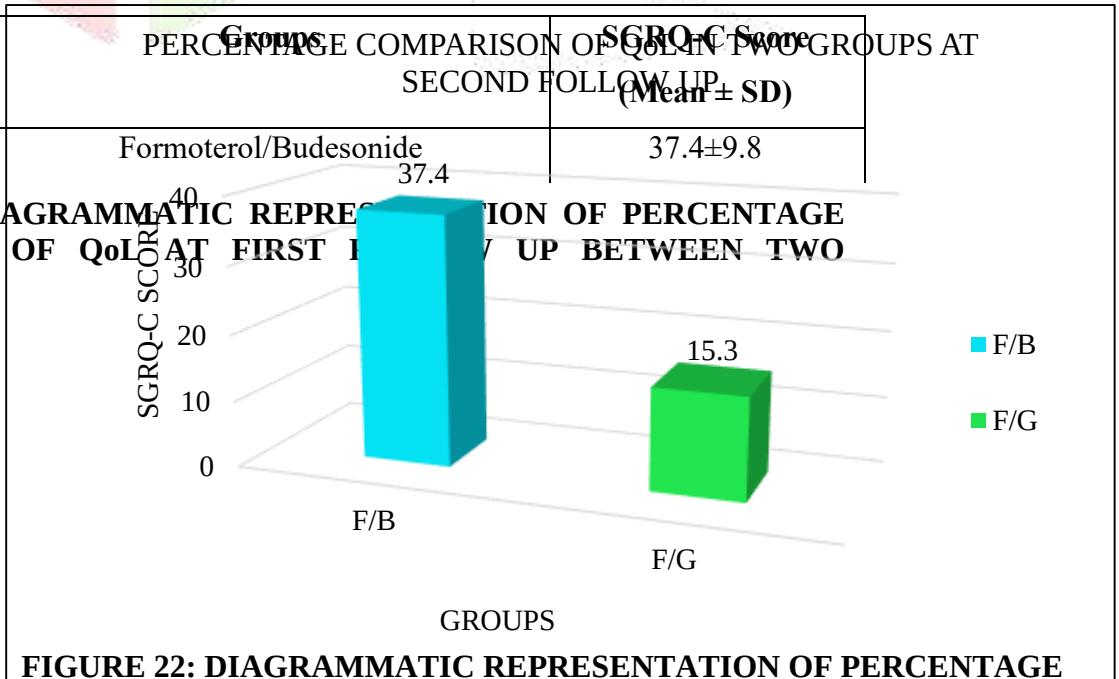


FIGURE 22: DIAGRAMMATIC REPRESENTATION OF PERCENTAGE COMPARISON OF QoL AT SECOND FOLLOW UP BETWEEN TWO GROUPS

Formoterol/Budesonide is 37.4 & Formoterol/ Glycopyrronium is 15.3.

PERCENTAGE COMPARISON OF QoL IN PATIENTS TAKING FORMOTEROL/BUDESONIDE

The percentage comparison of QoL in different follow up in patients taking Formoterol/Budesonide is shown in the following table

TABLE: 14 PERCENTAGE COMPARISON OF QoL IN PATIENTS TAKING FORMOTEROL/BUDESONIDE

In

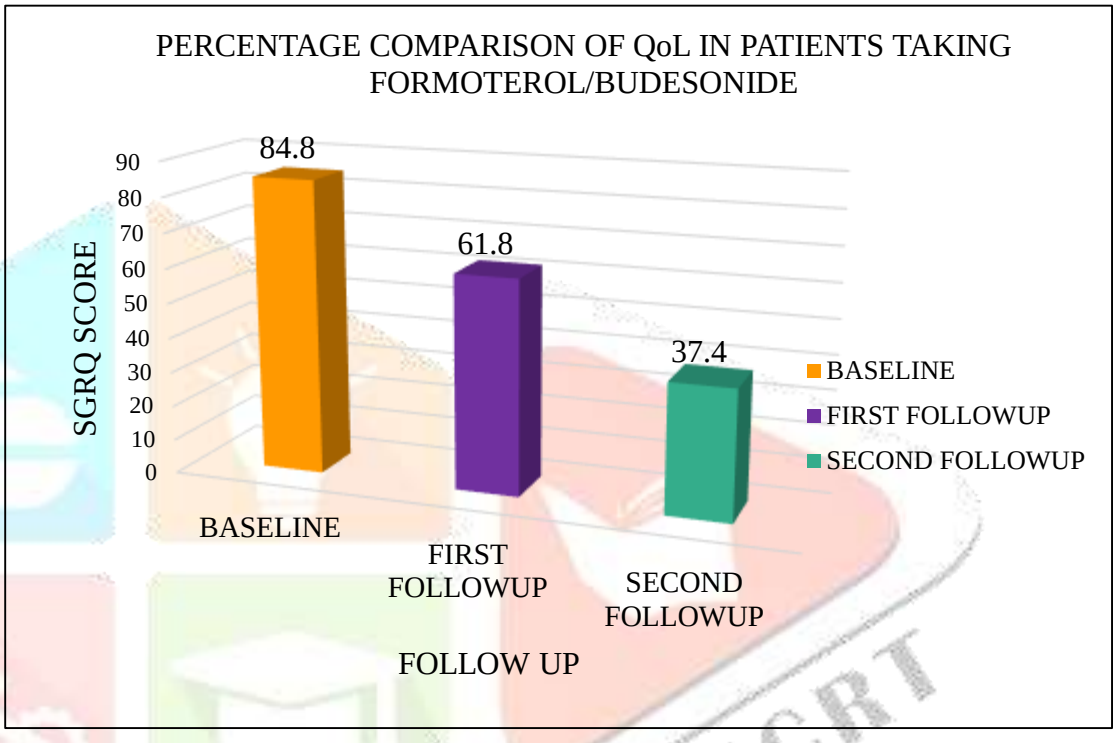


FIGURE 23: DIAGRAMMATIC REPRESENTATION OF COMPARISON OF QoL BETWEEN DIFFERENT FOLLOW UP OF PATIENTS TAKING FORMOTEROL/BUDESONIDE

Formoterol/Budesonide group as the duration increases the mean has been significantly reduced and the maximum reduction is at 12 weeks.

PERCENTAGE COMPARISON OF QoL IN PATIENTS TAKING FORMOTEROL/GLYCOPYRRONIUM

QoL (Formoterol/Budesonide)	SGRQ-C Score	P-Value
	Mean ± SD	
Baseline	84.8 ± 8.8	0.001
First Follow Up	61.8 ± 9.3	
Second Follow Up	37.4 ± 9.8**	

The percentage comparison of QoL in different follow up in patients taking Formoterol/Glycopyrronium is shown in the following table

TABLE: 15 PERCENTAGE COMPARISON OF QoL IN PATIENTS TAKING FORMOTEROL/GLYCOPYRRONIUM

QoL (Formoterol/Glycopyrronium)	SGRQ-C Score Mean ± SD	P-Value
Baseline	86.6±11.4	
First follow up	50.9±9.05	0.001
Second follow up	15.3±9.2**	0.001

**p-value <0.005 is considered as significant, p-value= 0.001*

In

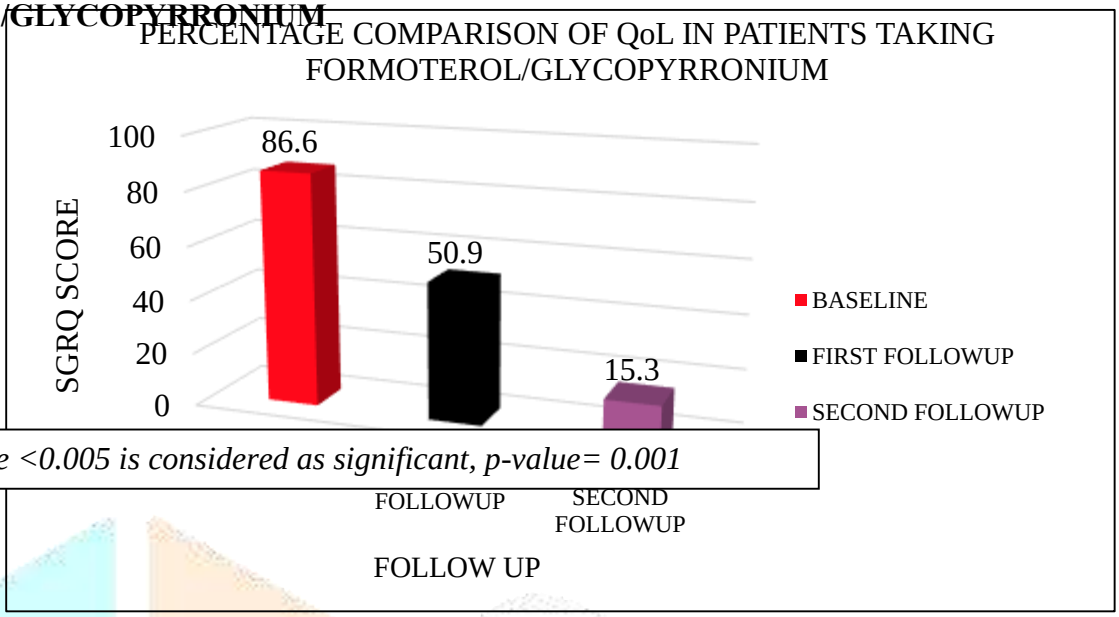


FIGURE 24: DIAGRAMMATIC REPRESENTATION OF COMPARISON OF QoL IN PATIENTS TAKING FORMOTEROL/GLYCOPYRRONIUM

Formoterol/Glycopyrronium group as the duration increases the mean has been significantly reduced and the maximum reduction is also at 12 weeks.

OVERALL COMPARISON OF QoL IN PATIENTS TAKING FORMOTEROL/ BUDESONIDE VERSUS FORMOTEROL/GLYCOPYRRONIUM

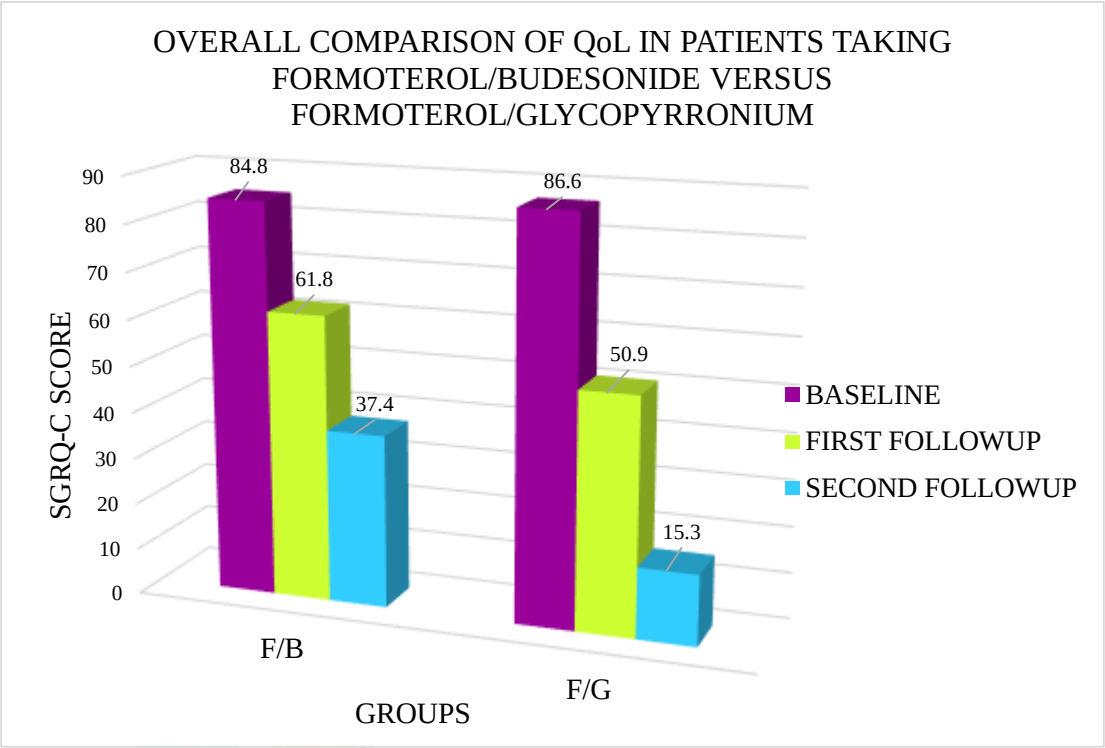
The overall comparison of QoL in patients taking Formoterol/Budesonide versus Formoterol/Glycopyrronium is shown in the following table

TABLE: 16 OVERALL COMPARISON OF QoL IN PATIENTS TAKING FORMOTEROL/BUDESONIDE VERSUS FORMOTEROL/GLYCOPYRRONIUM

Groups	QoL	SGRQ-C Score Mean ± SD	P-value
Formoterol/Budesonide	Baseline	84.8 ± 8.8	0.001
	First Follow Up	61.8 ± 9.3	
	Second Follow Up	37.4 ± 9.8**	
Formoterol/Glycopyrronium	Baseline	86.6±11.4	0.001
	First Follow Up	50.9±9.05	
	Second Follow Up	15.3±9.2**	

**p-value <0.005 is considered as significant, p-value= 0.001*

On



comparing

FIGURE 25: DIAGRAMMATIC REPRESENTATION OF OVERALL COMPARISON OF QoL IN PATIENTS TAKING FORMOTEROL/BUDESONIDE VS FORMOTEROL/ GLYCOPYRRONIUM

Formoterol/Budesonide and Formoterol/Glycopyrronium, it is found that at 6 weeks the reduction in mean value is significant. P-value=0.001

On comparing Formoterol/Budesonide and Formoterol/Glycopyrronium, it is found that at 12 weeks the reduction in mean value is significant. P-value=0.001*

DISCUSSION

Chronic Obstructive Pulmonary Disease (COPD) is a common lung disease causing restricted airflow and breathing problems. In people with COPD, the lungs can get damaged or clogged with phlegm. Symptoms include cough, sometimes with phlegm, difficulty in breathing, wheezing and tiredness. Smoking and air pollution are the most common causes of COPD. Inhalational bronchodilators namely, Long Acting β-agonists (LABAs), Long Acting Muscarinic Antagonists (LAMAs), Inhaled Corticosteroids (ICS) are prescribed either alone or as a combination in moderate-severe COPD management. Spirometry is the essential test to assess how well your lungs work. St. George Respiratory Questionnaire-COPD (SGRQ-C) is designed to measure the impact on overall health in patients with obstructive airways disease.

This study aims to compare the efficacy of Formoterol/Budesonide and Formoterol/Glycopyrronium & to assess the Health-related Quality of life using the SGRQ-C questionnaire in patients with COPD. The two combination drugs considered in this study are Formoterol/Budesonide and Formoterol/Glycopyrronium.

Formoterol is a long-acting beta agonists (LABAs) that works locally in the lungs as a bronchodilator, relaxing smooth muscle and opening up the airways.

Budesonide is an inhaled corticosteroid (ICS) that works to make breathing easier by reducing the irritation and swelling of the airways.

Glycopyrronium acts as a highly potent, competitive muscarinic receptor antagonist that binds to muscarinic receptors in bronchial smooth muscle and inhibits acetylcholine-mediated bronchoconstriction.

In this study, 50 patients with COPD were taken. Among these, 25 patients taking Formoterol/Budesonide and 25 patients taking Formoterol/Glycopyrronium were selected. Statistical analysis was performed using paired t-test and a detailed analysis was performed.

DEMOGRAPHIC FEATURES:

AGE: The age of the study population was categorized into 40-50(16%), 51-60(38%), 61-70(24%) and 71-80(12%) in our study. The patients belonging to 61-70 years were more prone to develop COPD. This study was similar to the study conducted by ***Jingyu Chen et.al***, on the topic **"Chronic Obstructive Pulmonary Disease Prevalence and Associated Risk Factors in Adults aged 40 years and older in Southeast China: A Cross-sectional Study During 2019-2020"**, which shows that the patients belonging to the age group above 40 years had more chance of occurrence of COPD.

GENDER: In this study gender-wise distribution was categorized into males 16 (32%) and females 34 (68%), were women have more chance of occurrence of COPD. This study correlated with the study conducted by ***Maeva Zysman et.al,*** on the topic **"Women's COPD",** which shows that comparing men and women, were women had more common incidence of COPD.

SMOKING: In this study smokers were categorized into non-smokers 28 (56%), current smokers 10 (20%), ex-smokers 12 (24%), were non-smokers have more chance of occurrence of COPD. This study correlated with the study conducted by ***Anne G Wheaton et.al,*** on the topic **"Chronic Obstructive Pulmonary**

Disease and Smoking Status-United States, 2017", which shows that comparing the smokers, were non-smokers had more common incidence if COPD.

EFFICACY: In this study, the mean score of baseline and after treatment score is compared and the improvement in the efficacy of patients is seen with the patients taking Formoterol/Glycopyrronium. This study was similar to the study conducted by ***Nalini Jayanthi et.al,*** on the topic, **"Comparative Study on the Effectiveness of Glycopyrrolate/Formoterol Versus Tiotropium/Formoterol in Patients with Chronic Obstructive Pulmonary Disease",** which states that efficacy scoring is improving in patients taking Formoterol/Glycopyrronium.

QUALITY OF LIFE: In this study, the mean score during the baseline, 1st follow-up and 2nd follow-up was done respectively. From the 2nd follow-up there is an improvement in the quality of life in patients who were taking Formoterol/Glycopyrronium and the p-value was statistically significant. This study was similar to the study conducted by ***Mohammed A et.al,*** on the **"Quality of life in COPD patients",** which concluded that quality of life improved in patients taking Formoterol/Glycopyrronium.

CONCLUSION

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable chronic lung disease which affects men and women worldwide. Higher exacerbation state is reported among women as compare to men.

In the present study, Formoterol/Budesonide and Formoterol/Glycopyrronium were given to the respective group of patients, and improvement in quality of life was assessed using the SGRQ-C questionnaire and the efficacy was assessed using the Spirometry. It concluded that a higher chance of occurrence of COPD was found to be between the age group of 60-80 years.

From this study, it was concluded that Formoterol/Budesonide and Formoterol/Glycopyrronium have almost similar effects on the efficacy in patients with COPD. However, in patients taking Formoterol/Glycopyrronium there is a significant improvement in the quality of life when compared to that of Formoterol/ Budesonide. Much improvement is shown in patients with COPD after taking Formoterol/Glycopyrronium.

After comparing the change in efficacy of drugs before treatment and after treatment, it was concluded that the efficacy of drugs in patients had improved with the treatment.

The major limitation of this study was the lack of cooperation of some patients which made it difficult to gather the information required for completing the study. Another one was the inadequate time period for completing the study, which affected the accuracy of the result to some extent. Another limitation of the study was that some patients failed to follow up after particular weeks which affected the procedure of data collection for the study.

Pharmacists are in an ideal position to provide patient education and optimize patient care. Understanding the aspects of COPD, the effect of Formoterol/Budesonide and Formoterol/Glycopyrronium on health-related quality of life, and the efficacy of the drug, yields better therapeutic outcomes. Hence the well-being of the patients is ensured. In the future, this study could help to ensure the most effective treatment for COPD.

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