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Original Article

# Lung Function and Health Status in Patients of Chronic Obstructive Pulmonary Disease on Treatment with Tiotropium

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## Abstract

**Introduction:** Chronic obstructive pulmonary disease (COPD) is a group of chronic and slowly progressive respiratory disorder characterized by reduced maximum expiratory flow during forced exhalation. Tiotropium, a long-acting antimuscarinic agent, has well-known documented effect on improving lung function and quality of life (QOL). There are many studies globally on tiotropium and its effect on lung function, but limited studies available in our Indian set up. Hence, we planned this study.

**Materials and Methods:** Patients were recruited from chest clinic and outpatient department from the Department of Medicine of University College of Medical Sciences and GTB Hospital. It was a prospective observational cohort study conducted from November 2017 to April 2019. Tiotropium was given as meter dose inhaler in dose of 18 µg per dose, in schedule as prescribed by the Global Initiative for Chronic Obstructive Lung Disease-2017 guidelines. Patients were followed up for 3 months with periodic assessment of lung functions, Saint George's Respiratory Questionnaire (SGRQ) score, and symptoms assessment.

**Results:** A total of 65 patients were recruited for study which included 57 (87.7%) males and 8 (12.3%) females. Among the pulmonary function tests measured, there is a significant change in mean forced expiratory volume ($FEV_1$) at the end of follow-up period compared to $FEV_1$ at baseline. There is a significant change in mean forced vital capacity at the end of follow-up study compared to start of the study. There was no significant change in mean SGRQ score after 1 month of start of drug, but significant statistical change observed at end of the 3rd month of the study compared to the 1st month that implies SGRQ score decreased and patients health status and QOL improved. There is a significant change in mean SGRQ score at the end of follow-up study compared to baseline. In our study, 16 patients (24.6%) complained of dry mouth, 7 (10.7%) complained of pharyngitis or throat irritation, and 3 (4.6%) patients complained of constipation.

**Conclusion:** There was a statistically significant change in lung functions and improvement in QOL scores as assessed by SGRQ at the end of the study compared to baseline by use of inhaled tiotropium in COPD patients.

**Key words:** Chronic obstructive pulmonary disease, Long-acting antimuscarinic agents, Quality of life, Saint George's Respiratory Questionnaire, Tiotropium

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an underdiagnosed, progressive, incurable lung disease. Its prevalence is on rise globally as well as in India. COPD is currently the fourth leading cause of death in the world,[1] but its projected to be third leading cause by 2020.[2] The national burden was thus estimated to be 14.84 million. In the past 50 years, COPD has overtaken tuberculosis and pneumonia as the leading cause of death.

Quality of life (QOL) is a much broader multidimensional concept. The World Health Organization defines QOL as the individuals perception of their position in life in the context of culture and value system in which they live and in relation to their goals, expectations, standards, and concerns.

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Health status is defined as perceived heath in descriptive terms of physical and mental symptoms, disability, and social dysfunction related to the health condition.[1] Saint George's Respiratory Questionnaire (SGRQ)[2] and COPD assessment test (CAT) measure health status of COPD patient in recent scenario. Spirometry is required to make diagnosis of COPD, the presence of post-bronchodilator (BD) forced expiratory volume ($FEV_1$)/forced vital capacity (FVC) <0.7 confirms the presence of persistent airflow limitation.[3] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) assigns patients with COPD into four groups based on degree of airflow restriction, symptom score as per CAT test, and number of exacerbation in 1 year. Group A comprises low risk and less symptoms, Group B comprises low risk and more symptoms, Group C comprises high risk and less symptoms, and Group D comprises high risk and more symptoms.

Tiotropium bromide, a long-acting antimuscarinic agent (LAMA) used in our study, has well-known documented effect on improving lung function and QOL. There are many studies globally on tiotropium and its effect on lung function, but limited studies available in our Indian set up. Tiotropium bromide rapidly dissociates autoinhibitory M2 receptors, but slowly dissociates from M1 and M3 receptors which mediate acetylcholine-mediated bronchoconstriction and mucus secretion. This increased duration of binding at M3 receptor result in prolonged bronchodilation allowing once daily dosage compared to 3–4 times daily dosage of ipratropium. Tiotropium has other effects in body as side effects. Hence, we planned this study to see the changes in lung function and health status of patient on tiotropium bromide and its other side effects.

### Aim

This study aims to see changes in lung function and health status in patients of COPD on treatment with tiotropium.

### Objectives

The objectives of the study were as follows:

- To compare the changes in pulmonary function of COPD patients on tiotropium before and after 3 months of follow-up period
- To compare health status of COPD patients before and after 3-month follow-up using SGRQ
- To document the side effects of tiotropium use if any.

## MATERIALS AND METHODS

It was a prospective observational cohort study done in November 2017–April 2019 at chest clinic and medicine outpatient department (OPD) from the Department of Medicine of University College of Medical Sciences (UCMS) and GTB Hospital, Delhi.

A total of 65 patients with diagnosis of COPD presenting in chest clinic and medicine OPD and receiving inhaled tiotropium bromide drug were recruited for the study.

### Inclusion Criteria

The following criteria were included in the study:

- All patients diagnosed with COPD in GOLD-2017 Stages B and C
- Patients between 40 and 70 years of age.

### Exclusion Criteria

The following criteria were excluded from the study:

- Known cases of asthma, allergic rhinitis, and atopy
- Patients in Stage A and D GOLD-2017 guidelines
- Patients in acute exacerbation in the past 1 month
- Patients with symptomatic GERD
- Patients on oral corticosteroids.

### Methodology

Ethical clearance was taken from the Institutional Ethics Committee and informed written consent was taken from each subject. This study was done on patients recruited from chest clinic and medicine OPD from the Department of Medicine, UCMS and GTB Hospital, patients between 40 and 70 years according to the GOLD COPD guidelines were selected for the study. During the study period, the following medications was prescribed: BDs: LAMA (tiotropium) in dose of 18 μg/dose per day, LABA (salmeterol) 50 μg/dose as twice a day, and LAMA (tiotropium) was given either alone or in combination with LABA (salmeterol). This was as per management guidelines by GOLD-17. Patients were also looked for clinical features suggestive of acute exacerbation of COPD (AECOPD), i.e., sustained worsening of symptoms from stable stage triggered by infections, pollutants that result in addition therapy to the regular medications in a COPD patient. AECOPD is classified as mild, moderate, and severe depending on clinical features and medications needed: Mild (treated with short-acting BDs [SABDs] only), moderate (treated with SABDs plus antibiotics and/or oral corticosteroids), and severe (patient requiring hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure. Patients were managed with BDs (short acting), corticosteroids (i.v or oral), and antibiotics.

Simultaneously, patients was assessed for features suggestive of hospitalization such as sudden worsening of resting dyspnea, high respiratory rate, decreased oxygen saturation, acute respiratory failure, onset of new physical signs, cyanosis, peripheral edema, failure to response to initial medical management, and presence of serious comorbidities. After the onset of these events, patient was hospitalized and managed as per standard protocols.

Patients were followed for 3 months duration, and detailed history and clinical examination were done. Pulmonary function test (PFT) and intraocular pressure (IOP) were measured before prescribing tiotropium. Tiotropium was given as meter dose inhaler in dose of 18 μg per dose, through inhaled route which was available free of cost in our hospital supply. Proper standard inhaler technique was demonstrated to every patient.

PFT and IOP were again assessed at the end of the 1st month and 3 months of follow-up periods. SGRQ was used to assess QOL at baseline, 1st month, and end of the study. Data were obtained from all subjects by

- Details history and clinical examination
- PFT
- QOL patients were assessed using SGRQ
- Statistical analysis.

### Detailed History and Clinical Examination

Patients having clinical features suggestive of COPD like history of smoking or smoke exposure, cough and expectoration were evaluated. The diagnosis was confirmed by spirometery.

## RESULTS

### Demographic Profile of the Study Population

#### *Age distribution*

The age of subjects ranged from 40 to 70 years. The mean standard deviation (SD) age of cases was 57.91 (7.89) years.

#### *Age at diagnosis of COPD in the present study*

The mean age of diagnosis of COPD patients in this study was 55.26 ± 7.28. The minimum and maximum age of diagnosis of patients was 39–70 years.

#### *Gender distribution*

There were 57 males and 8 females in the current study.

#### *Body mass index (BMI)*

Out of total 65 patients recruited in our study, BMI ranged from 14.15 to 29.51. Mean BMI of patients was 19.86 ± 3.40 kg/m$^2$.

#### *Smoking status*

Out of 65 COPD patients recruited in our study, 43 were either ever smoker category (current or past), whereas 22 patients belonged to never smoker category.

#### *Clinical profile and history of patients*

Out of total recruited patients in our study, 34 patients complained of dyspnea on exertion along with cough without sputum, 15 patients complained of dyspnea on exertion along with cough and sputum, 8 patients complained of dyspnea on exertion only, 6 patients complained of only dry cough, and 2 patients complained of dyspnea while performing day-to-day activities.

On clinical examination (chest auscultation) of patients, 25 patients had decreased air entry bilaterally, 21 patients had wheeze, 16 patients had rhonchi, and 3 patients had crackles along with wheeze.

### Laboratory Profile of the Study Population

#### *$FEV_1$*

$FEV_1$ was measured at 0, 1, and 3 months of study.

In Table 1, it was observed that there is a significant change in mean $FEV_1$ at the end of 1st month of follow-up period and at the end of the study compared to $FEV_1$ at baseline.

### FVC

FVC was measured at 0, 1, and 3 months of the study.

In Table 2, there was no significant change in FVC after 1 month of start of drug and no significant statistically change observed at the end of 3 months of study compared to the 1st month.

There is a significant change in mean FVC at the end of follow-up study compared to baseline.

### Ratio of $FEV_1$/FVC

FEV1/FVC was calculated at baseline, at the end of 1 month, and end of 3 months of study. In Table 3, there was a significant change in FEV1/FVC after 1 month of start of drug and no significant statistical change observed at the end of 3 months of study compared to the 1st month. There is a significant change in mean FEV1/FVC at the end of follow-up study compared to start of study.

Overall, comparison of lung function changes at baseline, 1 month, and 3 months by repeated measure ANOVA [Table 4].

### SGRQ Score

SGRQ score of patient was calculated at 0, 1, and 3 months of study. In Table 5, there was no significant change in SGRQ score after 1 month of start of drug, but significant statistical change observed at end of 3 months of study compared to the 1st month. There is a significant change in mean SGRQ score at the end of follow-up study compared to start of study [Figure 1 and Table 5].

### Side Effects Observed with Use of Tiotropium

Out of 65 patients, we followed up in our study some patients complained of side effects such as dry mouth, pharyngitis, URTI, and constipation with use of tiotropium.

**Table 1: Comparison of $FEV_1$**

| Group-wise comparisons | | $FEV_1$ (as % of predicted value) Mean±SD | Observed difference between two time points | *P*-value* |
|---|---|---|---|---|
| Baseline value versus 1 month | Baseline value | 32.37±9.95 | 3.45 | <0.05# |
| | Value at 1 month | 35.82±10.69 | | |
| 1 month versus 3 months | Value at 1 month | 35.82±10.69 | 1.55 | >0.05 |
| | Value at 3 month | 37.37±12.53 | | |
| Baseline value versus 3 months | Baseline value | 32.37±9.95 | 5 | <0.05# |
| | Value at 3 month | 37.37±12.53 | | |

*Repeated measures ANOVA followed by *post hoc* Tukey's test. #Statistically significant. $FEV_1$: Forced expiratory volume, SD: Standard deviation

**Table 2: Comparison of FVC**

| Group-wise comparisons | | $FVC_1$ (as % of predicted value) Mean±SD | Observed difference between two time points | *P*-value |
|---|---|---|---|---|
| Baseline value versus 1 month | Baseline value | 56.06±16.60 | 1.89 | >0.05 |
| | Value at 1 month | 57.95±16.35 | | |
| 1 month versus 3 months | Value at 1 month | 57.95±16.35 | 2.56 | >0.05 |
| | Value at 3 month | 60.51±16.83 | | |
| Baseline value versus 3 months | Baseline value | 56.06±16.60 | 4.45 | <0.05# |
| | Value at 3 month | 60.51±16.83 | | |

*Repeated measures ANOVA followed by *post hoc* Tukey's test. #Statistically significant. FVC: Forced vital capacity, SD: Standard deviation

**Table 3: Comparison of $FEV_1$/FVC**

| Group-wise comparison | | $FEV_1$/FVC ratio Mean value±SD | Observed difference between two time points | *P*-value* |
|---|---|---|---|---|
| Baseline value versus 1 month | Baseline value | 58.18±8.09 | 3.68 | <0.05 |
| | Value at 1 month | 61.86±9.46 | | |
| 1 month versus 3 months | Value at 1 month | 61.86±9.46 | 0.03 | >0.05 |
| | Value at 3 month | 61.89±10.95 | | |
| Baseline value versus 3 months | Baseline value | 58.18±8.09 | 3.71 | <0.05# |
| | Value at 3 month | 61.89±10.95 | | |

*Repeated measures ANOVA followed by *post hoc* Tukey's test. #Statistically significant, SD: Standard deviation, FVC: Forced vital capacity, $FEV_1$: Forced expiratory volume

**Table 4: Summary of spirometric findings**

| Pulmonary function | Baseline | 1 month | 3 months | *P*-value |
|---|---|---|---|---|
| $FEV_1$ | 32.37±9.95 | 35.82±10.69 | 37.37±12.53 | <0.001 |
| FVC | 56.06±16.60 | 57.95±16.35 | 60.51±16.86 | <0.001 |
| $FEV_1$/FVC | 58.18±8.09 | 61.86±9.46 | 61.89±10.95 | <0.001 |

FVC: Forced vital capacity, $FEV_1$: Forced expiratory volume

**Table 5: Comparison of SGRQ score**

| Group-wise comparison | SGRQ score Mean±SD | Observed difference between two time points | *P*-value* |
|---|---|---|---|
| Baseline value versus 1 month | 52.95±5.29<br>51.55±3.88 | 1.4 | >0.05 |
| 1 month versus 3 months | 51.55±3.88<br>48.88±4.27 | 2.67 | <0.05# |
| Baseline value versus 3 months | 52.95±5.29<br>48.88±4.27 | 4.07 | <0.05# |

*Repeated measures ANOVA followed by *post hoc* Tukey's test. #Statistically significant, SD: Standard deviation, SGRQ: Saint George's Respiratory Questionnaire

## DISCUSSION

The aim of our study was to see the changes in lung function and health status in patients of COPD on treatment with tiotropium bromide for a period of 3 months. Health status was assessed using SGRQ which was designed to measure impact on overall heath, daily life, and perceived well-being in patients with the disease.

A total of 65 patients were recruited for study which included 57 (87.7%) males and 8 (12.3%) females. The age of subjects ranged from 40 to 70 years. The mean (SD) age of patients recruited was 57.91 (7.89) years. The age at diagnosis of subjects ranged from 39 to 70 years. The mean age at diagnosis of COPD patients in our study was 55.26 ± 7.28 years. BMI of patients ranged from 14.15 to 29.51 kg/ $m^2$. The mean BMI of patients was 19.86 ± 3.40 kg/ $m^2$. Out of 65 COPD patients recruited in our study, 43 (66.2%)

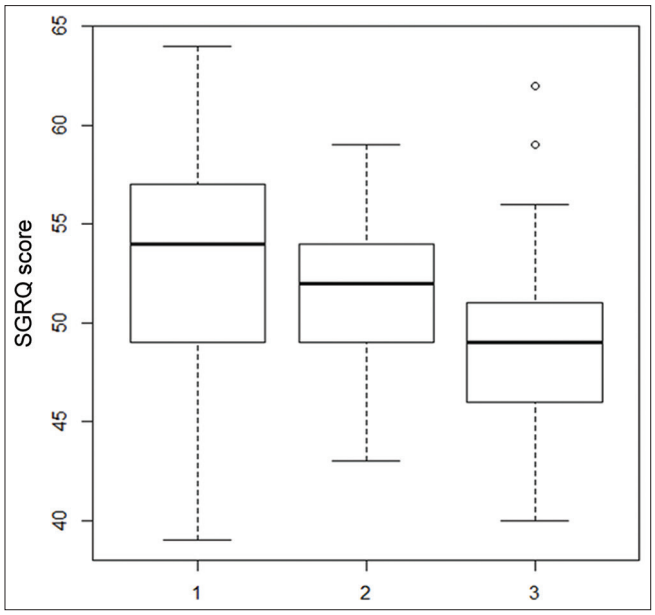


**Figure 1: Boxplot depicting Saint George's Respiratory Questionnaire score at baseline, 1 month, and 3 months of follow-up**

belonged to smoker category, whereas 22 (33.8%) patients belonged to non-smoker category. Among the pulmonary function tests measured, there is a significant change in mean $FEV_1$ at the end of follow-up period compared to $FEV_1$ at baseline (32.37 ± 9.95% of predicted value), but there was no statistically significant change observed in $FEV_1$ at the 3rd month (37.37 ± 12.53% of predicted value) compare to the 1st month (35.82 ± 10.69% of predicted value). There was no significant change in FVC after 1 month (57.95 ± 16.35% of predicted value) of start of drug and no significant statistical change observed at the end of 3 months (60.51 ± 16.83% of predicted value) of the study compared to the 1st month. There is a significant change in mean FVC at the end of follow-up study compared to baseline (56.06 ± 16.60% of predicted value). There is a significant change in mean $FEV_1$/FVC ratio at the end of 1 month (61.86 ± 9.46%) and follow-up period of 3 months (61.89 ± 10.95%) compared to the baseline (58.18 ± 8.09%). However, the change in mean $FEV_1$/FVC ratio of the 1st and 3rd months was not significant statistically. There was no significant change in mean SGRQ score after 1 month (51.55 ± 3.88) of start of drug, but significant statistical change observed at the end of 3rd month (48.88 ± 4.27) of study compared to the 1st month that implies SGRQ score decreased and patients health status and QOL improved. There is a significant change in mean SGRQ score at the end of follow-up study compared to baseline (52.95 ± 5.29). In our study, 16 patients (24.6%) complained of dry mouth, 7 (10.7%) complained of pharyngitis or throat irritation, and 3 (4.6%) patients complained of constipation.

According to the GOLD 2019 guidelines in the past, most studies have reported greater prevalence of COPD among males compared to females, but more recent data from developed countries have reported equal prevalence among males and females. Some studies have also suggested females more susceptible to COPD compared to males. According to the Global Adult Tobacco Survey in India, 19% of males and 2% of females are tobacco smokers so in our Indian setup as smoking is more common in males compared to females; hence, most of the patients were males in our study.[3] COPD is a disease of elderly. Majority of patients are diagnosed after 40 years of age.

Age is often listed as a risk factor for COPD patients. It is unclear if healthy aging as such leads to COPD or if age reflects the sum of cumulative effect of exposure to risk factors throughout life.[4] In a study a 4-year trial of tiotropium in COPD patient by Donald *et al.*, the mean age (years) in tiotropium group was 64.5 ± 8.4 and placebo group was 64.5 ± 8.5, respectively. The percentage of male sex was 75.4% in tiotropium group and 73.9% in placebo group. In another Indian study, the clinicophysiological effect of inhaled tiotropium bromide in severe COPD by Prakash *et al.*[5] mean age (years) was 58.81 ± 9.32, which was very similar to mean age groups of patients recruited in our study.

Nutritional depletion and weight loss are features of COPD patients. There are many studies documented the prognostic value of low body weight in patients of COPD. Patients with low BMI are at increased risk for developing severity of COPD. Low BMI is also an independent negative determinant of survival in patients with COPD. In study on BMI of patients with COPD by Wu *et al*, it was observed that BMI was moderately correlated with pulmonary function positively and exacerbations negatively. BMI might be useful indicator to predict the prognosis of COPD patients and long-term management. In a study of the effect of tiotropium on lung function decline in early stage of COPD patients, Lee *et al.*, mean BMI ($kg/m^2$) of tiotropium group patients was 22.7 ± 3.43 and control group was 23.0 ± 2.96. Hence, in our study, the observed mean BMI was significantly low compared to other studies.[6]

Smoking is the most studied risk factor in COPD patients, but <50% develop COPD during life time. In a 25-year follow-up study of the general population by Løkke *et al.*, the absolute risk of developing COPD among continuous smokers is at least 25%. The 25-year incidence of moderate and severe COPD was 20.7% and 3.6%, respectively, with no apparent difference in men and women.[7] Smoking cessation, especially early in follow-up, decreases the risk of developing COPD substantially compared with continuous smoking. About 92% of the COPD deaths occurred in subjects who were current smokers at the beginning of follow-up period. In another study, the prevalence and incidence of COPD in smokers and non-smokers by

Terzikhan *et al.*, 21.7% of the study participants were current smokers, 41.7% were former smokers, and 34.2% were never smokers.[8] In smokers, 17.8% had COPD, whereas in non-smokers, the prevalence of COPD was 6.4%. In our study, 43 patients were smokers accounting to 66.2% and 22 were non-smokers accounting 33.8% of the patients. Hence, in our study, majority of patients were smokers.

Pulmonary functions of patients were compared after prescribing tiotropium bromide. They were followed up for 3 months. Baseline pulmonary functions were compared with changes at 1 month and follow-up period of 3 months. Various parameters measured were $FEV_1$, FVC, and $FEV_1$/ FVC ratio. A retrospective analysis of the understanding potential long-term impacts on function with tiotropium (UPLIFT) trial data was performed by Halpin *et al.* It graded patients by the 2013 GOLD severity groups.[9] Mean $FEV_1$ was higher with tiotropium than usual care (control) in all GOLD groups at all post-baseline time points during treatment. In a study called the effect of tiotropium on lung function decline in early stage of COPD patients by Lee *et al.*, out of 587 patients enrolled in the study, 257 took tiotropium following propensity score matching, 404 patients were included in the analysis.[6]

The mean annual rate of post-BD $FEV_1$ decline was 23.9 (tiotropium) and 22.5 (control) ml/year ($P = 0.31$), respectively. Mean annual rate of post-BD FVC decline was 55.1 (tiotropium) and 43.5 (control) ml/year ($P = 0.33$), corresponding pre-BD values were 37.1 and 33.3 mL/ year ($P = 0.13$).

Therefore, tiotropium does not reduce the rate lung function decline in COPD patients with $FEV_1$ ≥70%. In our study, there is a significant increase in mean $FEV_1$ at 1 month follow-up and at the end of study period of 3 months compared to baseline with the use of tiotropium, although change in mean $FEV_1$ was not statistically significant between the 1st and 3rd month. In our study also, similar findings were seen as other studies.

In our study, there was statistically significant difference in mean FVC at the end of study period compared to baseline, but there was no significant change observed in FVC at the end of 1st month compared to baseline. Similarly, no significant change was observed in mean FVC of the 1st and 3rd month. In another study Prakash *et al.* compared the effect of tiotropium bromide in severe COPD patients on pulmonary function parameters (PFT), functional exercise capacity (6MWD), exertional and overall dyspnea (visual analogue scale and MRC dyspnea scale), symptom score, drug score, health related QOL (HR QOL) (CRDQ).[5] Thirty-two patients (16 patients each in tiotropium) of severe COPD were followed up for 12 weeks (6 weeks of run in period and 6 weeks of study period). In tiotropium group, there was more improvement in FVC, 6 min walk distance, MRC, CDRQ, symptom score, and drug score. In a study by Adams *et al.*, tiotropium treated patients had significant improvement in $FEV_1$ and FVC.[10] Significant changes in mean ratio of $FEV_1$/FVC were observed in our study at the follow-up period of 1 month compared to baseline, but no significant statistical change observed at the end of 3 months of study compared to the 1st month. Hence, overall, there is a significant change in mean $FEV_1$/ FVC at the end of follow-up study compared to start of study. Health status instruments used in COPD patients are CAT, clinical COPD questionnaire, and SGRQ. In our study, we have used SGRQ score for health status an indicator of QOL. SGRQ has become one of the most widely used instruments for assessing HR QOL in respiratory patients and has been translated into several languages. It is a disease-specific instrument designed to measure impact on overall health, daily life, and perceived well-being in patients with obstructive pulmonary disease. In our study, there was no significant change in SGRQ score after 1 month of start of study, but significant statistical difference observed at the end of 3 months of study compared to 1st month. There is a significant change in mean SGRQ score at the end of follow-up period compared to baseline. In a 4-year trial of tiotropium in COPD by Tashkin *et al.* concluded that the patients in COPD, therapy with tiotropium was associated with improvements in lung function, QOL, and exacerbations during a 4-year period but did not significantly reduce the rate of decline in $FEV_1$.[11] The mean absolute total score on the SGRQ was improved (lower) in the tiotropium group, as compared with the placebo group, at each point throughout the 4-year period (ranging from 2.3 to 3.3 units, $P < 0.001$). At 4 years and 30 days, tiotropium was associated with a reduction in the risks of exacerbations, related hospitalizations, and respiratory failures. In a study by Vincken *et al.*, tiotropium is effective in improving dyspnea, exacerbations, HR QOL, and lung functions in patients of COPD.[12] The data support use of tiotropium once daily as first-line maintenance treatment in patients with COPD.

In a study role of ipratropium bromide and tiotropium bromide in COPD patients by Khan *et al.*, 57 patients were recruited, tiotropium showed significant reduction in exacerbation and improvement in QOL, health status, and dyspnea compared to ipratropium.[13] In another study, role of tiotropium in the treatment of COPD by Rice *et al.*, tiotropium slowed the rate of decline in $FEV_1$, reduces lung hyperinflation with associated improvement in exercise capacity, subjective dyspnea, and HRQL scores.[14] It also reduced exacerbations and hospitalization but did not affect overall mortality. Similar results were also seen in our study. The aim of our study

was to see the changes in lung function and health status in patients of COPD on treatment with tiotropium bromide for a period of 3 months. Health status was assessed using SGRQ which was designed to measure impact on overall heath, daily life, and perceived well-being in patients with the disease. We also measured changes in IOP of patient's pre- and post-observation period using Goldmann applanation tonometer and documented the presence of any side effect associated with the use of drug. The most commonly reported adverse effect observed was dryness of mouth, with a total of 10 studies reporting incidence. The cumulative incidence was 7.4% in tiotropium patients, 3.9% in ipratropium patients, and 1.6% in salmeterol patients. The incidence of dry mouth was significantly increased in eight studies which compared tiotropium with placebo. Studies have consistently reported that tiotropium is safe and well tolerated in clinical trials that ranged from 3 months to 48 months. Other adverse events associated with tiotropium include constipation, tachycardia, urinary retention, raised IOP, and angina rarely. In a large long-term clinical trial in COPD patients, tiotropium added to other standard therapies had no effect on cardiovascular risk.

In our study, 16 patients (24.6%) complained of dry mouth, 7 (10.7%) complained of pharyngitis or throat irritation, and 3 (4.6%) patients complained of constipation. Hence, in our study, the most common side effect observed was dry mouth which was also seen in other studies.

Strength of our study is a prospective observational cohort study so it was better than other study which were cross sectional, so patients were recruited and followed up on a regular basis after being diagnosed with COPD or were diagnosed earlier on the basis of history and PFT. Adding SGRQ as a tool for HRQOL is another strength of our study as it provides descriptive heath status of COPD patient.

Limitations of our study, we could not perform randomized control trials, used in UPLIFT study of COPD patients which would have been a better study design due to limited resources, investigators, and time period. We followed patients for a period of 3 months which is a limited time period to see changes in lung function, as certain studies where changes lung function started to occur where of longer period.

## CONCLUSION

Thus, we conclude that tiotropium bromide improves lung functions, overall health status, and QOL of COPD patients.

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