Original Article

Reliability and Validity of Clinical COPD Questionnaire and Chronic Respiratory Questionnaire in Patients with COPD using Tiotropium Over a Period of 26 Weeks

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Abstract

Objectives. Patient-centred outcomes, such as health-related quality-of-life (HRQoL) are as important as improvement in the lung function for the optimal management of the patients with chronic obstructive pulmonary disease (COPD). Questionnaires used to assess HRQoL of the patients with COPD should have good reliability, validity and responsiveness. The aim of this study was to investigate and compare the reliability, validity and responsiveness of the Clinical COPD Questionnaire (CCQ) and Chronic Respiratory Questionnaire (CRQ) in patients with mild-to-moderate COPD taking tiotropium.

Methods. Seventy-one newly diagnosed patients with mild-to-moderate COPD according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria were included in the study and started on tiotropium (18mcg Transcaps/9mcg metered-dose inhaler), as tiotropium improves the quality-of-life in patients with COPD. Lung function tests were done with a spirometer. The CCQ and CRQ were completed for these patients along with a proforma. Patients were then followed up to 26 weeks with repeat questionnaires and spirometry.

Results. Sixty-six patients were analysed as five patients were lost to follow-up. The CCQ was found to be more reliable as compared to CRQ with a Crohnbach's alpha of 0.88. The total score of CCQ and CRQ at baseline were able to discriminate between the GOLD stages making both CCQ and CRQ valid. The CCQ and CRQ were responsive at 8 weeks, 16 weeks and 26 weeks in all domains after the administration of tiotropium as compared to baseline.

Conclusions. The CCQ was observed to be more reliable than CRQ. Moreover, the CCQ is easier to administer and interpret compared to CRQ. Therefore, CCQ is better than CRQ for the optimal management of COPD; however, both the questionnaires can be used for future studies involving patients with mild-to-moderate COPD. **[Indian J Chest Dis Allied Sci 2020;62:197-201]**

Key words: COPD, Clinical COPD Questionnaire, Chronic Respiratory Questionnaire, Quality-of-life

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality in the industrialised and developing countries. It is estimated that the total deaths due to COPD are projected to increase by more than 30% in the next 10 years, making it the third leading cause of death by 2030.[1] The prevalence of COPD in India is about 3.7% with an estimated burden of about 1.5 crore cases.[2]

According to Global Initiative for Chronic Obstructive Lung Disease (GOLD) management guidelines[3], primary aim of the treatment of COPD patients is to reduce the symptoms and the future risk of exacerbations; while improving the health-related quality-of-life (HRQoL). The HRQoL assessment is as important as lung function measurement in patients with COPD to evaluate the effectiveness of therapeutic interventions. It is important to appreciate that a relatively small change in the lung functions may not always reflect the impact of the disease or intervention on patients' physical and psychological well-being. There was an urgent need for the development of simple tools that will help the clinicians, not only to focus on the clinical status of the airways, but also activity limitation and emotional dysfunction. The clinical COPD questionnaire (CCQ) and clinical respiratory questionnaire (CRQ) are health status instruments that give sensitive and specific information about the frequency and severity of the symptoms and physical and emotional well-being of the patient.

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Although there are a number of questionnaires, the CCQ and CRQ are simple, short and available in many translations. These can be filled by the patients themselves, thereby allowing the physicians to assess the health quality accurately and optimise the disease management. The CCQ and the CRQ-SR ('self-reported' used in this study) are both reliable and valid.[4,5]

Tiotropium is a once daily, inhaled, long-acting anticholinergic drug that provides 24-hour improvement in the airflow and hyperinflation in patients with COPD. Tiotropium has shown an improvement in patients with COPD, which can consistently translate into improvement in lung function, exercise tolerance, and HRQoL.[6] Hence, it was used to assess the reliability and validity of the CRQ and CCQ.[6] Therefore, the present study was undertaken to assess the reliability and validity of the CCQ and CRQ-SR in patients with COPD taking tiotropium over a period of 26 weeks.

Material and Methods

The present study was a prospective study done over a period of one year in a tertiary care hospital. The data was collected from the patients who were diagnosed to have COPD, as per GOLD guidelines in the out-patient department of Pulmonary Medicine at KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi. Universal sampling technique was used and the sample was collected by including consecutive COPD patients according to the inclusion criteria in 1:2 proportion. The sample size was calculated by using the formula: N = Distribution of 50%/ (Margin of error %/confidence level score).[2]

Patients of more than 40 years of age having mild, moderate and severe COPD according to GOLD criteria (GOLD stage 1-3) and started on tiotropium (18mcg Transcaps/9mcg metered-dose inhaler) for ≤2 months from the outpatient clinic were enrolled in the study. Details about the age, gender, height, weight, body mass index (BMI), presenting symptoms, past history and duration of COPD, history of smoking, presence of co-morbidities, such as diabetes, hypertension; and previous history of hospitalisation were obtained through a questionnaire.

Patients with very severe COPD (GOLD 4: forced expiratory volume in one second (FEV_1) <30%), psychiatric disease, history of asthma, allergic rhinitis or atopy, patients on oral corticosteroids for COPD and significant psychiatric ailments were excluded from the study. The study was approved by the Institutional Ethical and Research Committee. The selected patients were briefed about the study and written informed consent was obtained.

Lung function tests were done at baseline, such as post-bronchodilator FEV_1, forced vital capacity (FVC) and FEV_1/FVC ratio were recorded. The CCQ and CRQ were completed for these patients at baseline. The total scores and the individual domain scores in each of the questionnaire were calculated and recorded. Patients were then followed-up at the end of 8th week, 16th week and 26th week with repeat questionnaires and spirometry in the outpatient department.

Statistical Analysis

The reliability of the questionnaires was assessed by calculating the Crohnbach's alpha for each item in the questionnaire. A Cronbach's alpha of more than 0.70 was considered good consistency. The discriminant and convergent validity of the questionnaires were assessed using Spearman's rho. The other variables were analysed using student t-test; while the categorical variables, such as sex, smoking status and status of co-morbidities were compared with the scores using Chi-square test. The total and domain scores of the CCQ and CRQ-SR were recorded at different points of time during the course of the study and were analysed with the baseline scores using student unpaired t-tests. A P-value of <0.05 was considered to be statistically significant.

Results

A total of 71 patients with COPD were included in the study; out of which five were lost to follow-up. Therefore, a total of 66 patients were analysed at the end of 26 weeks. There were 41 male and 25 female patients with 8 patients in 45-54 years age group. 36 patients in 55-64 years age group and 22 patients in >65 years age group. About 42.2% of the patients (all males) were smokers; out of which 31.8% patients were current smokers and 10.6% were reformed-smokers.

In our study, the Cronbach's alpha for CCQ was 0.88 and for CRQ was 0.30 making CCQ more reliable than CRQ. The Crohnbach's alpha for the individual domains in CCQ (symptom, functional and mental state) ranged from 0.85 to 0.89; whereas in CRQ (dyspnoea, fatigue, emotional, mastery domain) ranged from 0.22 to 0.23.

In the present study, there were 39 patients from COPD stage 3 (59.1%), 19 patients from stage 2 (28.8%) and 8 patients from stage 1 (12.1%). It was observed that the baseline total scores of CCQ and CRQ could discriminate between the COPD stages with higher score of CCQ and lower score of CRQ indicating a poor quality-of-life (QoL) and more advanced COPD. A statistically significant (P<0.05) correlation between the baseline scores of the CCQ and CRQ was observed showing

its ability to measure HRQoL of patient with COPD. Hence, the CCQ and CRQ had good convergent validity.

There was a significant correlation between the pack years of smoking and the symptom, mental and total scores of CCQ, a higher number of pack years having higher scores in these domains and impaired QoL. After comparing the baseline domain scores and total score with the baseline FEV_1, it was found that only symptom domain of CCQ and the dyspnoea domain of CRQ significantly correlated with FEV_1. This finding also confirms that lung function measurement by FEV_1 values alone is a poor indicator of the effectiveness of therapeutic interventions as well as QoL in patients with COPD.

There is no significant correlation between an increase in FEV_1 and improvement in the total scores of CCQ and CRQ with the treatment, indicating that spirometry is a poor indicator for the assessment of QoL in patients with COPD. Although only the baseline symptom score of CCQ and the dyspnoea score of CRQ had a correlation with FEV_1, it was observed that all the CCQ domains and total score had a significant correlation with the modified Medical Research Council (mMRC) dyspnoea grades, with higher scores in patients with higher grades of dyspnoea and impaired QoL.

After analysing the different domains of CCQ, it was observed that the symptom scores showed statistically significant improvement at 8 weeks, 16 weeks and 26 weeks as compared to baseline (P<0.001). The functional domain scores also showed significant response at 8 weeks, 16 weeks and 26 weeks when compared to baseline. The CCQ also showed good response in the mental domain scores and total scores at 8 weeks, 16 weeks and 26 weeks as compared to the baseline. Similarly, among different domains of CRQ, there was significant response in the scores at 8 weeks, 16 weeks and 26 weeks as compared to baseline (P<0.001).

Discussion

The prevalence of COPD is highly under-estimated in India and still remains the 'tip of the iceberg' phenomenon due to lack of real time nationwide data and appropriate validated studies. The main aim of treatment of COPD is to relieve the symptoms and improve the exercise tolerance; while preventing the disease progression and future exacerbations, thereby improving the QoL. Today, QoL assessment has become a major criterion to evaluate the effectiveness of therapeutic intervention in patients with COPD. This was due to the fact that lung function measurement, that remained the "holy grail" of COPD management was inappropriate to optimise the patient management strategies.

The use of QoL questionnaires in the assessment and management of patients with COPD was first addressed in the 2011 revision of GOLD guidelines. It recommended the use of COPD assessment test (CAT) to risk the stratify patients into four groups to guide the management of COPD patients. However, CAT has certain disadvantages. Although the scores can predict exacerbations, day-to-day variations may not be picked up by the CAT.[7] COPD specific questionnaires, like CCQ, can detect day-to-day variation with its daily version. Moreover, CCQ can also pick up treatment failure during an exacerbation by its daily version, which can not be achieved by CAT. In addition, CAT scores cannot predict mortality; which can be done using CCQ.[8]

There are very few studies assessing the reliability and validity of CCQ and CRQ. Furthermore, there is a paucity of studies comparing these questionnaires with each other and assessment of its reliability and validity after the administration of a drug, like tiotropium which improves the QoL in patients with COPD. *To the best of our knowledge*, this is the first study evaluating the reliability, validity and responsiveness of CCQ and CRQ after the administration of tiotropium. We also compared the two questionnaires to evaluate for a better questionnaire for use in daily clinical practice. We analysed a total of 66 patients with mild-to-moderate and severe COPD after the administration of CCQ and CRQ, and followed them for 8 weeks, 16 weeks and 26 weeks with repeat questionnaires and spirometry after the administration of tiotropium.

In the present study, we observed that CCQ was highly reliable with a Crohnbach's alpha of 0.88 as compared to CRQ with Crohnbach's alpha of 0.30. The Cronbach's alpha for the individuals domains in CCQ (symptom, functional and mental state) ranged from 0.85 to 0.89, whereas in CRQ (dyspnoea, fatigue, emotional, mastery domain) it ranged from 0.22 to 0.23. These findings of a high reliability of CCQ has also been reported in other studies.[5,9] Van der Molen *et al*[5] reported a Cronbach's alpha of 0.91, while Reda *et al*[9] observed it to be around 0.77. Tsiligianni *et al*[10] observed that both CCQ and CAT were highly reliable with a Crohnbach's alpha of 0.89 and 0.86, respectively.

However, reliability of CRQ in the present study was very low as compared to other studies[4,5,10]. Wijkstra *et al*[4] reported the Cronbach's alpha for CRQ to be 0.51 for the dyspnoea domain and 0.71 to 0.88 for fatigue, mastery and emotional domains. Molken *et al*[11] reported Cronbach's alpha of CRQ from 0.84 to 0.87, whereas Reda *et al*[9] showed it to be 0.91 in the fatigue and emotional domains.

In the present study, there was a significant correlation between the total scores of CCQ, CRQ and the GOLD stages with higher scores of CCQ and lower

scores of CRQ pointing towards higher COPD stages. However, it should be noted that there is no single score that distinguishes GOLD stages from each other. The significant correlation between the two questionnaires indicates that both the questionnaires assess the health status of the same clinical condition, *i.e.* COPD. Our findings were similar to the findings of Reda *et al*.[9]

A good correlation of the symptom domain of CCQ and the dyspnoea domain of CRQ with FEV_1 was observed in the present study, in contrast to other studies.[4,9-11] Although this finding was contradictory to many previous studies[4,9-11], it can be postulated that there may be a correlation between the symptom domains, *i.e.* dyspnoea scores of both CCQ and CRQ as compared to other domains.

The CCQ achieved its minimally clinically important difference of 0.44 in all domains within eight weeks of the administration of tiotropium, showing an improvement in the QoL. Similarly, CRQ showed significant improvement in the scores in all the domains and total scores up to 26 weeks. Reda *et al*[9] observed that there was a significant change only in the symptom domain, mastery domain and total score of CRQ-SR. Molken *et al*[11] observed that in CRQ, the emotional domain and total score was most responsive to change. This difference in the results of our study could be due to the usage of tiotropium drug to assess the responsiveness of the questionnaires, which was not done in the previous studies.[10,11] In earlier studies, smoking cessation was the most common intervention to assess the responsiveness of these questionnaires.

Results of the present study also confirms that tiotropium improves the QoL in patients with COPD in all the domains as evident by the excellent responsiveness in the questionnaire scores within eight weeks of the treatment. This is similar to the findings in other studies. Understanding Potential Long-term Impacts on Function with Tiotropium (UPLIFT) trial showed mean absolute improvement in the St. George's respiratory questionnaire (SGRQ) score of 2.3 to 3.3 units at each time point throughout the 4-year period with tiotropium. Vincken *et al*[13] observed an improvement in SGRQ scores and these improvements were maintained over the year in the tiotropium group as compared to the ipratropium group. In our study, both CCQ and CRQ were valid and responsive for use in clinical practice, with CCQ being more reliable than CRQ. Moreover, CCQ becomes more feasible for the use than CRQ as less number of items have to be completed in CCQ. Therefore, the time to completion of CCQ is much lower than CRQ. In view of these facts, it is suggested that CCQ is a better questionnaire than CRQ to assess the QoL in patients with COPD. Recently Singh *et al*[14] compared body-mass index, airflow obstruction, dyspnoea, and exercise (BODE) index with CAT and CCQ in patients with COPD, and observed that BODE index correlated significantly with CAT and CCQ score in stable COPD patients, and the score also correlated statistically with FEV_1%.

We observed that female patients had significantly higher scores in all domains and total scores in CCQ and higher scores in the mastery domain of CRQ, which indicates a poor QoL in them. The PLATINO study conducted in Latin American countries observed that female patients with COPD had worse symptoms in terms of dyspnoea, lower exercise capacity, more anxiety and depression and worse HRQoL.[15] The reasons for these are not well understood, but it has been suggested that the increased perception of breathlessness in females is related to hormonal effects on the airways.[16] After 26 weeks of the treatment with tiotropium, it was observed that there were comparable scores between male and female patients in the symptom and functional domains of CCQ, but higher mental scores among the female patients. This confirms the hypothesis of the PLATINO study that women have higher incidence of anxiety and depression leading to increased perception of breathlessness and worse QoL as compared to males.[15]

In the present study, we observed that higher the pack years of smoking, worse is the health status scores and poor QoL. Spencer *et al*[17] observed that current smokers had higher scores in the symptom domain and total scores in SGRQ. This was similar to the results of the present study which showed comparable scores in current smokers and reformed smokers at 26 weeks of the treatment. In the present study, it was also observed that the presence of co-morbidities had no effects on the total score or any of the domains in CCQ or CRQ in COPD patients. Anja *et al*[18] observed that five co-morbidities, *i.e.* depression, anxiety, peripheral artery disease, cerebrovascular disease, coronary heart disease and/or heart failure had the largest impact on patient reported health status as measured by a new index with acronym COMCOLD index (Co-morbidities in Chronic Obstructive Lung Disease). Burgel *et al*[19] reported higher SGRQ scores in patients with depression; but not in patients with cardiovascular comorbidities or diabetes. In a recent study by Wacker *et al*,[20] the SGRQ showed the best discrimination between the COPD stages and less influenced by the comorbidities

Conclusions

The present prospective study not only assessed the reliability and validity of COPD specific questionnaires;

but also studied the impact of various variables on the quality-of-life in patients with mild-to-moderate COPD. This study has the strength of being the first study of its kind to assess the reliability and validity of COPD specific HRQoL questionnaires after the administration of tiotropium. The CCQ and CRQ were both valid and responsive for the use in the clinical practice, with CCQ being more reliable than CRQ. It is also important to appreciate that CCQ becomes more feasible for day-to-day use as compared to CRQ due to the lower number of questions and the lesser time required for completing the questionnaire.

This study has some limitations. It is a single centre study and sample size is small. Also, there was no control group to compare the variation in scores in patients without COPD.

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