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PROSPECTIVE RANDOMIZED CONTROL STUDY COMPARING GLYCOPYRRONIUM VERSUS TIOTROPIUM ANALYZING TROUGH FEV1, BREATHLESSNESS AND HEALTH STATUS

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ABSTRACT

Background: Presently two long acting muscarinic antagonists (LAMAs) glycopyrornium and tiotropium are widely used for treatment of chronic obstructive pulmonary disease (COPD). This study is plan to compare therapeutic efficacy of these currently available drugs **Methods :** This study include COPD patients subjected to either 50 µg glycopyrronium or 18 µg tiotropium once daily, having an objective to compare patient compliance and health indices between these two groups over a period of 12 week treatment. **Results**: 57 patients were randomized (glycopyrronium: 27; tiotropium: 30) completed the study. Glycopyrronium demonstrated rapid bronchodilation following first dose on Day 1as well as after 12 weels treatment, with significantly higher FEV_1.Glycopyrronium shows comparable improvement in Transition Dyspnea Index (TDI) and the frequency as well as rate of COPD exacerbations. Patients shows markedly low symptom compare to the patients on tiotropium after 12 weeks Adverse events were somewhat similar in incidence with both the drugs glycopyrronium (40.4%) and tiotropium (40.6%).**Conclusion:** glycopyrronium having a faster onset of action as well as shows statistically significant difference in FEV1, breathlessness and patient compliance After 12 weeks of treatment in comparison with tiotropium.

Keywords: acting muscarinic antagonists , Transition Dyspnea Index, chronic obstructive pulmonary disease (COPD).

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is characterized by progressiveconstraintof airflowthat can be presents as breathlessness, reduced exercise capacity, chronic cough and sputum production.**(1)**

Until recently, tiotropium was the drug available for patients with COPD.Tiotropium is a well-known Long Acting MuscaranicAntagonist, is widely prescribed worldwide, and has been shown to recoverlung function, dyspnea, exercise tolerance, and health status, while reducing acute

exacerbations and death, compared with placebo. **(2)** Two LAMAs, twice-daily aclidinium bromide and single dose glycopyrronium have been recently approved for the management of COPD **(3,4)** given in dry powder form. **(5)**

The present study compares glycopyrronium 50 µg OD. with tiotropium 18 µg in southern Rajasthan and the objective was comparative analysis of efficacy and safety of glycopyrronium versus tiotropium in patients with moderate-to-severe COPD

MATERIAL AND METHODS

We include patients with moderate-to-severe stable COPD having age of ≥40 years (Global Initiative for Chronic Obstructive Lung Disease [GOLD] Stage II or III according to the 2010 GOLD guidelines.**(6)**

Exclusion Criteria for exclusion of cases was they should not have history of respiratory tract infection within 4 weeks prior; Patients on antibiotics and/or oral corticosteroids for controlling COPD complications; they were not hospitalized 6 weeks prior to screening; Any other pulmonary diseases other than COPD; contraindications for tiotropium or ipratropium, or history of adverse reactions to inhaled anticholinergics and /or cardiovascular risk (patients with unstable ischemic heart disease, left ventricular failure,

All patients gave written, informed consent to participate in the study and appropriate statistical analysis were done. The study protocol evaluated and approved by Institutional Review Boards and ethics committees.

Pulmonary function evaluation was done by spirometry. Breathlessness measured using Transition Dyspnea Index (TDI) focal score,

RESULTS

A total of 57 patients were included (glycopyrronium: 27; tiotropium: 30) in the study. Same number of patients were discontinued the study in both groups. The reasons for discontinuing treatment were mostly withdrawal of consent and Adverse Effects.

Baseline characteristics were similar between the treatment groups (Table 1). Mean age in both group was near 55 years, more than 60 % of the patients were male and approximately one-half were ex-smokers. Most patients had moderate 54-55% or severe 45-46 %COPD; one patient had mild COPD. The mean duration of COPD was 7.0 years. Approximately 25 % of the patients had a documented history of exacerbations in the previous year. Patients on glycopyrronium/tiotropium shows there was statistically significant difference in FEV1 both day 1 as well as results observe after 12 weeks of therapy. Transient dysnoea index (TDI) shows comparable improvement in COPD patient on glycopyronium.

Table 1- **Baseline demographics and spirometry**

	Glycopyrronium 50 µgo.d. (N = 27)	Tiotropium 18 µgo.d. (N = 30)
Mean (SD) age, years	56	58.2
Male, n (%)	62	68
Severity of COPD (GOLD 2010), n (%)		
Mild	0	1 (0.3)
Moderate	(54.4)	55
Severe	(45.6)	44
Mean (SD) duration of COPD, years	7.1	7.2
Baseline COPD exacerbation history*,(n)		
0 exacerbations	20	22
1 exacerbation	3.0	4
≥2 exacerbations	4	6
Smoking history, (n)		
Ex-smoker	14	16
Current smoker	02	03
Mean (SD) duration of smoking, pack-years	20	21.5

Pack-years = total years of smoking multiplied by cigarette packs smoked per day; *In the year prior to screening; FEV_1 = forced expiratory volume in 1 second;

Table 2- Differences between treatment for primary and secondary efficacy outcomes

Variable	LSM (95%CI) treatment difference glycopyrronium versus tiotropium	p-value
Day 1 **FEV_1 (L)**	0.051 (0.036, 0.066)	<0.001
After 12 Week **FEV_1 (L)**	0 (−0.032, 0.031)	<0.001*

Table 3 comparative analysis of improvement in TDI score

	Glycopyrronium 50 µgo.d. (N = 27	Tiotropium 18 µgo.d. (N = 30
TDI score	+2	+1

DISCUSSION

Glycopyrronium in once-daily dose, is relatively safe, also improves lung function, breathlessness, exercise tolerance, and reduces the risk of exacerbations **(7-9)**

Tiotropium is a new bronchodilators in the treatment of severe to moderate COPD, however there are some challenges in using tiotropium as a control.**(10)** Since tiotropium cannot be easily blinded, a number of studies have used OLtiotropium as a control.**(11-14)** The GLOW2 study also assess glycopyrronium versus OLtiotropium.**(9)**Although there is no any statistical superiority of glycopyrronium compare to tiotropium in GLOW2 study In GLOW -2 study it was observed that both glycopyrronium and tiotropium had acceptable safety and tolerability profiles, similar incidence of AEs between both treatment groups.**(9)**

Similarly in GLOW5 study also, there was a blinded comparison for the effectiveness and safety of glycopyrronium to tiotropium with moderate-to-severe COPD patients.

Occurrence of Adverse effects with equal frequency in the glycopyrronium (3.8%) and tiotropium (4.1%) treatment groups. Infections was the most frequent adverse effect. COPD symptom deterioration occurred more frequently in the tiotropium group (1.7%) than in the glycopyrronium group (0.7%). Incidence of cardio- and cerebro-vascular SAEs was some what similar between the two treatment groups (0.5%). There was no any death reported in our study.

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