Original article:

Assessment of Efficacy of Indecaterol Among COPD Patients at District Hospital

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is one of the major disease involving lungs and has got higher mortality and morbidity. Indacaterol is a novel, once-daily, inhaled ultra- LABA17 currently in development for the treatment of COPD. This study was conducted to assess the efficacy of indacaterol among COPD patients.

Materials & Methods: This study was conducted on 150 patients and 75 found positive of COPD. It included single-dose treatment periods of single doses of indacaterol (150, 300, or 600 µg) or placebo via a single-dose dry-powder inhaler. Efficacy (primary endpoint: standardised FEV1AUC22-24h) and safety were assessed for 24 h post-dose in each treatment period.

Results: off 75 patients, males were 75 and females were 30. The difference was non- significant. Standardised FEV1AUC22-24h was significantly higher for all indacaterol doses as compared with placebo, with clinically relevant differences of 130, 160, and 170 mL for 150 and 300 respectively ($P < 0.001$). The improvement in FEV1 was seen as early as 5 min post-dose with indacaterol and sustained for 24 h.

Conclusion: Single doses of indacaterol (150, 300, and 600 µg) provided sustained 24-h bronchodilation, with onset of action within 5 min post-dose. All doses were well tolerated.

Key words: Chronic Obstructive Pulmonary Disease, Dyspnoe, Indacaterol.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive obstructive airways disease with incomplete improvement in lung function in response to therapy. COPD is estimated to affect 10% of the world's population aged 40 years and its prevalence is expected to continue to increase over the next decade or more.[1] An accelerated decline in forced expiratory volume in 1 second (FEV1) occurs alongside a decline in ability to undertake physical activities and social functioning, reflected in the measurement of clinical outcomes including dyspnea and health status. Regular pharmacotherapy using long-acting inhaled bronchodilators has been shown to provide not only rapid improvement in lung function, but clinically important decreases in dyspnea and exacerbation rate with a corresponding improvement in health status.[2] Bronchodilators have therefore become the cornerstone of treatment for COPD of all severity stages.

Chronic obstructive pulmonary disease (COPD) was previously known as chronic bronchitis and emphysema. Chronic bronchitis has been defined by (BMRC) as "daily productive cough for at least three consecutive months for more than two successive years.Emphysema has been defined as an "anatomic alteration of the lung characterized

by an abnormal enlargement of the air spaces distal to the terminal, non-respiratory bronchiole, accompanied by destructive changes of the alveolar walls."[3]

Recent studies have reported 2.7% females and 5% males prevalence of COPD. Among various causative factors for COPD, smoking, consumption of biomass and environmental exposures play important role. Biomass combustion results in high levels of pollutants such as benzo(a)pyrene, carbon monoxide, formaldehyde, oxides of nitrogen and sulphur, and benzene that are a major source of respiratory irritants leading to COPD.[4]

Chronic obstructive pulmonary disease (COPD) has high mortality and morbidity and is the main reason for death. It is responsible for a huge social and economic burden for the health care infrastructure. The prevalence of COPD is approximately9% in men and 7% in women. There have been a few reports on COPD epidemiology in India in the past. But most of those reports were based on studies on limited population groups.[5]

Indacaterol is a novel, once-daily, inhaled ultra- LABA17 currently in development for the treatment of COPD. The efficacy and safety of once-daily dosing of indacaterol in COPD patients have already been demonstrated in several studies that involved mostly the Caucasian population. This is the first study evaluating the effect of indacaterol in Japanese patients with COPD, and given its similarity to a study conducted in a Caucasian population it helps to evaluate the ethnic sensitivity of the efficacy and safety of indacaterol.[6] This study was conducted to assess the efficacy of indacaterol among COPD patients.

MATERIALS & METHODS

The present study was conducted in the department of Chest and TB of M.G. Hospital, Bhilwara, Rajasthan. This study was conducted on150 patients and 75 found positive of COPD. All were informed regarding the study and written consent was obtained. Information such as name, age, sex etc. was recorded.

It included single-dose treatment periods of single doses of indacaterol (150, 300) or placebo via a single-dose dry-powder inhaler. Efficacy (primary endpoint: standardised FEV1AUC22-24h) and safety were assessed for 24 h post-dose in each treatment period. Results thus obtained were tabulated and subjected to statistical analysis using chi square test. P value less than 0.05 was considered significant.

RESULTS

Table I shows that adverse events was GIT disorders seen in 1 cases each with indacaterol (150, 300) and placebo. Infections & Infestations was seen with 300 indacaterol and placebo, cardiac disorder was seen only with placebo and vascular disorder 1 case each with indacaterol (150, 300) and placebo. The difference was non- significant (P> 0.05).

Graph I shows that off 75 patients, males were 45 and females were 30. The difference was non- significant.Graph II shows that Standardised FEV1AUC22-24h was significantly higher for all indacaterol doses as compared with placebo, with clinically relevant differences of 130, 160, and 170 mL for 150 and 300 respectively ($P < 0.001$). The improvement in FEV1 was seen as early as 5 min post-dose with indacaterol and sustained for 24 h.

DISCUSSION

COPD affects twice as many males as females, this difference will diminish, given the fact thatmore and more females throughout the world have taken up smoking in the past few years in developed countries, and non-smoking

females are exposed to biomass combustion products in developing countries.We found that out of 75 patients, males were 75 and females were 30. The difference was non- significant. This is in agreement with Cook.[7]

Until recently, the only available LABAs were salmeterol and formoterol, both of which have an approximate 12-hour duration of bronchodilator action, and hence are used twicedaily for maintenance therapy in COPD. Indacaterol is the first once-daily long-acting β2-selective agent, sometimes referred to as an ultra-LABA, indicated for maintenance treatment in patients with moderate to severe COPD, has been approved in more than 40 countries (including throughout the European Union) at a recommended dose of 150 μg once daily and a maximum dose of 300 μg once daily,8 and has been shown to be effective and well tolerated by subjects with COPD during 12 weeks of treatment.9 With any new treatment intended for long-term use, it is important to evaluate safety and to determine if efficacy remains unblunted with regular use. A thorough characterization of safety is particularly relevant for a long-acting bronchodilator, given the recent interest in the safety of these agents in the treatment of COPD.[8]

Long-acting bronchodilators have been shown to improve multiple clinical outcomes in chronic obstructive pulmonary disease (COPD) including lung function, symptoms, dyspnea, quality of life, and exacerbations. Indacaterol is a novel, inhaled, long-acting β2-agonist providing 24-hour bronchodilation with once-daily dosing. It is currently approved for the maintenance treatment of COPD to be administered as 150 or 300 μg once-daily doses as licensed in many countries and 75 μg as licensed in the US by means of a single-dose dry powder inhaler. The data from clinical development support a favorable safety and tolerability profile within the β2-agonist drug class, with no relevant issues identified. Current evidence indicates that indacaterol is suitable for use as first-line monotherapy in COPD patients with moderate disease (Global Initiative for Chronic Obstructive Lung Disease [GOLD] stage II) and beyond that do not require an inhaled corticosteroid (ICS) as per GOLD guidelines, or in combination with an ICS in severe or very severe patients with repeated exacerbations.This is similar to Aggarwal.[9]

COPD is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, most commonly cigarette smoke. Patients with COPD have been reported to have increased numbers of neutrophils in sputum, lung tissue and bronchoalveolar lavage (BAL)and neutrophils are important cells in the pathogenesis of COPD.[10]

Hashimoto S et al evaluated safety and efficacy of indacaterol (IND)/glycopyrronium (GLY) 110/50 μg once daily (od) compared with GLY 50 μg od, IND 150 μg od, open-label tiotropium (TIO) 18 μg od, and placebo. The primary end point was trough forced expiratory volume in 1 second (FEV1) at Week 26. Other key end points included peak FEV1, area under the curve for FEV1 from 5 minutes to 4 hours (FEV1 AUC5 min–4 h), Transition Dyspnea Index focal score, St George's Respiratory Questionnaire total score, and safety. Here, we present efficacy and safety of IND/GLY in the Japanese subgroup. Of 2,144 patients from the SHINE study, 182 (8.5%) were Japanese and randomized to IND/GLY (n=42), IND (n=41), GLY (n=40), TIO (n=40), or placebo (n=19). Improvement in trough FEV1 from baseline was 190 mL with IND/GLY and treatment differences versus IND (90 mL), GLY (100 mL), TIO (90 mL), and placebo (280 mL) along with a rapid onset of action at Week 26. IND/GLY showed an improvement in FEV1 AUC5 min–4 h versus all comparators (all $P<0.05$). All the treatments were well tolerated and showed comparable effect on Transition Dyspnea Index focal score and St George's Respiratory Questionnaire total score. The effect of IND/GLY in the Japanese subgroup was consistent to overall SHINE study

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population. IND/GLY demonstrated superior efficacy and comparable safety compared with its monocomponents, open-label TIO, and placebo and may be used as a treatment option for the management of moderate-to-severe COPD in Japanese patients.[11]

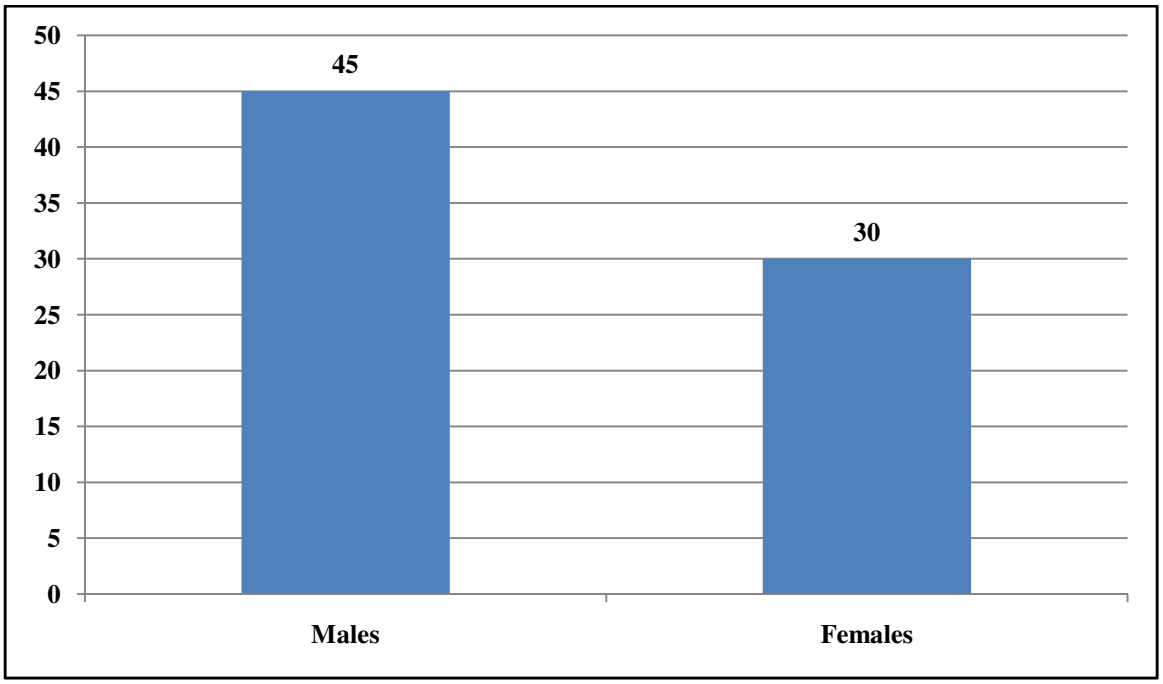
CONCLUSION

Single doses of indacaterol (150, 300) provided sustained 24-h bronchodilation, with onset of action within 5 min post-dose. All doses were well tolerated.

Table I: Adverse events with indacaterol

Adverse events	150 indacaterol	300 indacaterol	Placebo
GIT disorders	1	1	1
Infections & Infestations	0	1	1
Cardiac disorder	0	0	1
Vascular disorder	1	1	1

Graph I: Distribution of patients



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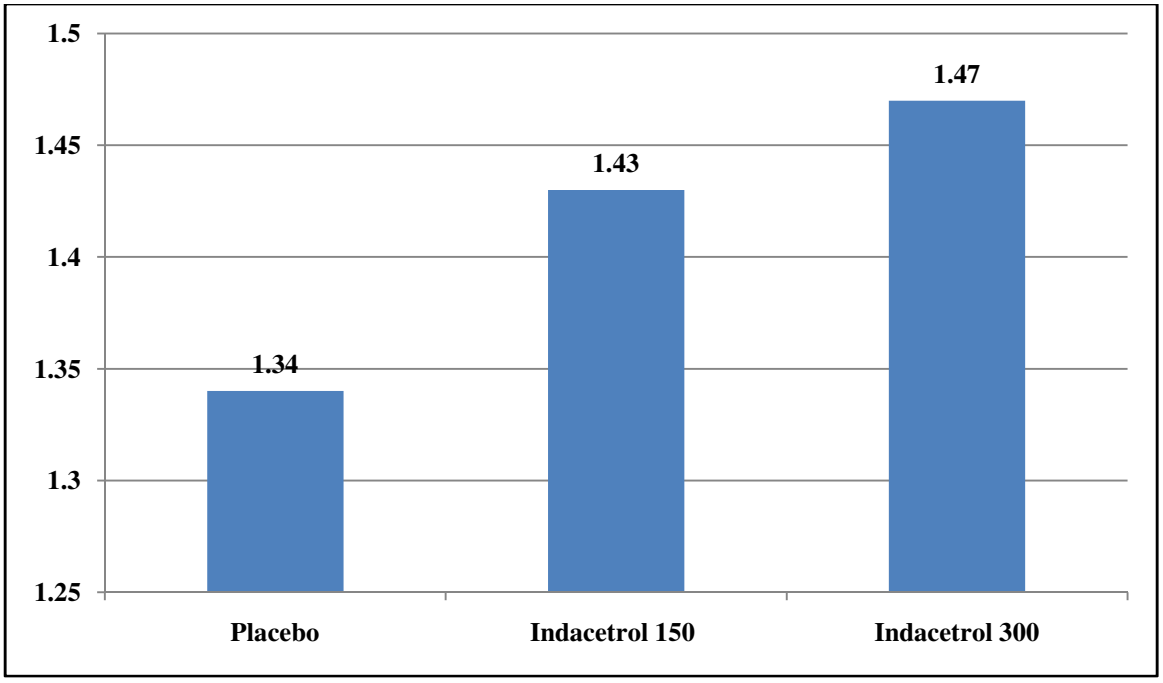
Graph II: Standardized FEV1AUC (22-24h)



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