COMPARISON OF DIFFERENT TREATMENT CHOICE IN ASTHMATIC SMOKERS

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ABSTRACT

Objective: The primary objective of this study was to determine the treatment choice in asthmatic smokers and whether the drug of choice improved the lung function and quality of life. Study design: The present study was an open labeled study, conducted for a period of two years with mild to severe asthmatic smokers. The study was carried out in a tertiary care hospital and Private clinics in North Malabar region of Kerala. Participants were 99 regular smokers with breathlessness: 45 were diagnosed asthma and received different treatment choice.

Results: All 45 patients received different treatment choice, 24% montelukast, 42% theophylne, 34%Tiotropium were included in asthma therapy. Montelukast added asthma therapy in asthmatic smokers, baseline FEV1 (1.52±0.30) and 90th day follow-up FEV1 (2.2±0.30) therapy had showed 0.68 units clinical improvement in pulmonary function test and QoL improvement had showed -24.2 units, when compared to Tiotropium and theophylne. Conclusion: In this study, patients with asthma who smoke, adjuvant therapy should be add-on therapy to attain asthma control. Montelukast combined therapy achieved better lung function and quality of life compared to Tiotropium and Theophylne in asthmatic smokers.

Keywords: asthma, Tiotropium and theophylne.

INTRODUCTION

Asthma is an inflammatory airway disease that involves both airway inflammation and impaired airflow, and it affects 22 million Americans. Airway inflammation in asthma involves a very complex interaction of cells, mediators, cytokines, and chemokines. Immune and non immunologic environmental factors are important triggers of asthma, including
cigarette smoking and secondhand smoke (SHS)\(^1\). Approximately 25% to 35% of individuals with asthma are current smokers\(^2\). It is well-documented that smoking or exposure to SHS among asthmatics increase asthma-related morbidity and disease severity\(^1\). Prolonged exposure to tobacco smoke in patients with asthma contributes to a decline in lung function: approximately 18% in forced expiratory volume in 1 second (FEV\(_1\)) over 10 years\(^3\). Asthmatic patients who smoke share features similar to those found in the early stages of emphysema\(^4\). Cigarette smoking and asthma are associated with poor symptom control and impaired therapeutic responses to corticosteroids.

**Literature Review**

Poor Control of Asthma Because of Primary Smoking. Several investigators have found that asthmatic patients who smoke are more likely to have poorer disease control compared with asthmatic nonsmokers\(^5,6,7,8\). A survey of 2269 asthmatic patients enrolled in a health maintenance organization showed that smoking was significantly and inversely related to long-term control of asthma (OR, 2.6; 95% CI, 2.0–3.4)\(^5\). McCoy et al\(^6\) showed that asthmatic smokers older than age 10 were more likely to experience an episode of poor asthma control versus asthmatic nonsmokers (OR, 1.785; 95% CI, 1.119–2.847). In 2007, a telephone survey of 11,962 asthmatic adults in the United States revealed that those who currently smoked reported more asthma attacks (OR, 1.2; 95% CI, 1.0–1.4) and more nocturnal asthma symptoms (OR, 2.0; 95% CI, 1.4–2.7) during the past 30 days than those who did not smoke\(^7\). Chaudhuri et al\(^8\) reported that asthmatic smokers had significantly higher scores overall (OR, 2.8; 95% CI, 1.7–3.4) and for each individual asthma symptom on the Juniper Asthma Control Questionnaire, indicating poorer disease control compared with asthmatic nonsmokers. The association between smoking and poor asthma control has also been reported in studies conducted in Canada, France, and Switzerland.

Lazarus et al\(^9\) also reported corticosteroid resistance in 39 asthmatic smokers who received 8 weeks of therapy with inhaled hydrofluoroalkane beclomethasone (160 µg twice daily) compared with 44 nonsmokers. Compared with the nonsmokers, the smokers only experienced significant improvements in daily morning PEF (mean difference 8.30; 95% CI, 0.80–15.81) and sputum eosinophil counts (mean difference −3.44; 95% CI, −6.56 to −0.32). A 23-year observational study of 122 asthmatic patients in The Netherlands revealed that men with >5 pack years of smoking failed to show improvement in the yearly decline of FEV\(_1\) after therapy with ICS was initiated (27.8 ml/year before treatment [range, 14.3–41.3
ml/year); 16.1 ml/year after treatment [range, 3.3–28.9 ml/year])\(^{10}\). In contrast, a 10-year observational study of 234 asthmatic patients reported that smokers experienced significant improvement in FEV\(_1\) after treatment with ICS (57.9 ml/year vs 30.8 ml/year; \(P = .035\))\(^{11}\).

An important environmental factor is active cigarette smoking. It is well known that smoking increase theophylline metabolism, but more importantly, smokers with chronic asthma are less sensitive to the beneficial effects of both inhaled and oral corticosteroids compared with nonsmokers with asthma\(^{12,13}\). Therapeutic studies in asthma often exclude current smokers because of concerns about recruiting participants with chronic obstructive pulmonary disease (COPD) and so information is lacking on which drugs are most appropriate to treat smokers with asthma. Knowing how best to manage this group of patients is of considerable importance because smoking is common among patients with asthma. For example, in developed countries, one-fifth to one-third of adults with asthma are smokers\(^{14}\). Smokers with asthma often have poorer symptom control compared with nonsmokers with asthma\(^{14}\).

Should leukotriene receptor antagonists be recommended as first-line treatment of smokers with asthma? Lazarus and colleagues\(^{15}\) report for the first time that the leukotriene receptor agonist montelukast shows efficacy in smokers with mild asthma, an important finding in view of the data showing corticosteroid insensitivity in this group. However, the beneficial effect on morning peak flow of montelukast in the smokers with asthma was not large nor did the study include supportive data on urinary or sputum leukotriene in smokers versus nonsmokers. The generalizability of the finding is uncertain and, in particular, it is not known whether a similar beneficial effect would be found in smokers with more severe asthma. Lazarus and colleagues\(^{15}\) recommend that a larger prospective study of leukotriene receptor antagonists in smokers be performed and at least one such study is reported to be underway, with a projected enrollment of 1,200 participants\(^{16}\).

**Method**

This was an open labeled study conducted for a period of two years in asthmatic smoker, patients in a tertiary care hospital and Private clinics in North Malabar region of Kerala. Total 45 asthmatic smokers, age between 45-60 years were included in this study. Pulmonary function tests(PFT) and quality of life (QoL) were assessed in the beginning of the study for baseline and on every 15\(^{th}\), 30\(^{th}\),45\(^{th}\), 60\(^{th}\) and 90\(^{th}\) day, PFT, HRQoL and prescribed various asthma medications was documented. Different treatment choice like montelukast, Ipratropium bromide and theophyline received patients were included in this study, treatment
choice for asthmatic smokers were assessed with the help of PFT and HRQoL at end of the follow-up and documented.

RESULTS
Among 99 patients 45 were diagnosed asthma with smokers, all 45 patients were received different treatment choice, 24% montelukast, 42% theophyline and 34% Tiotropium with asthma therapy, represented in fig: 1. Montelukast add on asthma therapy baseline PFT (1.49±0.22and1.52±0.30) and 90th day follow-up PFT (2.2±0.26 and2.2±0.30) had showed 0.71 and 0.68 units clinical improvement in pulmonary function test and QoL improvement had showed -36.4 units and -24.2 units, when compared to montelukast, Tiotropium and theophyline with asthma therapy were represented in Table:1 and 2.

![Fig.1. Adjuvant Therapy in Asthmatic Smokers](image)

Table: 1. Change in FEV1 in Asthmatic Smokers:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline</th>
<th>15th day</th>
<th>30th day</th>
<th>45th day</th>
<th>60th day</th>
<th>90th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>SALB +BUD+MON</td>
<td>1.41±0.26</td>
<td>1.51±0.32</td>
<td>1.68±0.3</td>
<td>1.76±0.32</td>
<td>1.86±0.31</td>
<td>2.1±0.34</td>
</tr>
<tr>
<td>SAL+FLU+MON</td>
<td>1.52±0.30</td>
<td>1.79±0.30</td>
<td>1.87±0.3</td>
<td>1.9±0.3</td>
<td>1.98±0.20</td>
<td>2.2±0.30</td>
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<tr>
<td>SAL +BUD+THEO</td>
<td>1.4±0.25</td>
<td>1.6±0.26</td>
<td>1.7±0.29</td>
<td>1.8±0.29</td>
<td>1.9±0.29</td>
<td>1.98±0.32</td>
</tr>
<tr>
<td>SAL+FLU+TIO</td>
<td>1.44±0.28</td>
<td>1.75±0.33</td>
<td>1.81±0.3</td>
<td>1.83±0.37</td>
<td>1.86±0.38</td>
<td>1.90±0.44</td>
</tr>
<tr>
<td>FOR+BUD+MON</td>
<td>1.49±0.25</td>
<td>1.60±0.23</td>
<td>1.75±0.2</td>
<td>1.82±0.25</td>
<td>2.1±0.25</td>
<td>2.2±0.26</td>
</tr>
<tr>
<td>FOR+BUD+THEO</td>
<td>1.40±0.25</td>
<td>1.60±0.23</td>
<td>1.65±0.2</td>
<td>1.75±0.25</td>
<td>1.84±0.25</td>
<td>1.92±0.26</td>
</tr>
<tr>
<td>FOR+BUD+TIO</td>
<td>1.51±0.2</td>
<td>1.60±0.28</td>
<td>1.72±0.2</td>
<td>1.84±0.27</td>
<td>1.95±0.28</td>
<td>2.1±0.28</td>
</tr>
</tbody>
</table>
Table: 2. Change in SGRQ in Asthmatic Smokers

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Baseline</th>
<th>15th day</th>
<th>30th day</th>
<th>45th day</th>
<th>60th day</th>
<th>90th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>SALB + BUD + MON</td>
<td>47.1 ± 0.3</td>
<td>40.2 ± 0.3</td>
<td>31.5 ± 0.3</td>
<td>28.0 ± 0.3</td>
<td>22.3 ± 0.3</td>
<td>15.3 ± 0.3</td>
</tr>
<tr>
<td>SAL + FLU + MON</td>
<td>54.6 ± 0.2</td>
<td>51.3 ± 0.3</td>
<td>47.7 ± 0.3</td>
<td>45.0 ± 0.3</td>
<td>40.0 ± 0.3</td>
<td>30.4 ± 0.3</td>
</tr>
<tr>
<td>SAL + BUD + THEO</td>
<td>52.5 ± 0.3</td>
<td>42.6 ± 0.4</td>
<td>38.6 ± 0.3</td>
<td>32.8 ± 0.3</td>
<td>24.2 ± 0.3</td>
<td>15.4 ± 0.3</td>
</tr>
<tr>
<td>SAL + FLU + TIO</td>
<td>46.9 ± 0.3</td>
<td>45.0 ± 0.3</td>
<td>41.5 ± 0.3</td>
<td>39.1 ± 0.3</td>
<td>32.6 ± 0.3</td>
<td>22.5 ± 0.3</td>
</tr>
<tr>
<td>FOR + BUD + MON</td>
<td>58.9 ± 0.2</td>
<td>45.0 ± 0.3</td>
<td>41.5 ± 0.3</td>
<td>39.1 ± 0.3</td>
<td>32.6 ± 0.3</td>
<td>22.5 ± 0.3</td>
</tr>
<tr>
<td>FOR + BUD + THEO</td>
<td>56.9 ± 0.4</td>
<td>43.8 ± 0.3</td>
<td>39.2 ± 0.3</td>
<td>33.0 ± 0.4</td>
<td>30.6 ± 0.3</td>
<td>18.4 ± 0.3</td>
</tr>
<tr>
<td>FOR + BUD + TIO</td>
<td>63.1 ± 0.3</td>
<td>60.1 ± 0.5</td>
<td>57.7 ± 0.3</td>
<td>54.1 ± 0.3</td>
<td>48.7 ± 0.3</td>
<td>42.7 ± 0.4</td>
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</table>

CONCLUSIONS

In this study, patients who are asthmatic smokers, adjuvant therapy were required to attain asthma control. The clinical improvements were seen in some outcomes in asthmatic smokers.
treated with adjuvant therapy. Montelukast combined in asthma therapy, achieved better lung function and quality of life compared to Tiotropium and Theophyline in asthmatic smokers.

ABBREVIATION
Pulmonary Function Test (PFT), Forced expiratory volume in one seconds (FEV1) Saint George Respiratory questionnaire (SGRQ), BUD: Budesonide, FLU: Fluticasone, MON: Montelukast, TIO: Tiotropium, SALB: Salbutamol Theo: Theophyline, SAL: Salmeterol, FOR: Formeterol, T: Theophyline

REFERENCE


