Adherence to asthma controller medication regimens

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\textbf{Summary}

\textbf{Background:} Improved adherence to inhaled corticosteroids (ICS) is recognized as an important factor in reduced morbidity, mortality and consumption of health care resources. The present study was designed to replicate previous reports of patient adherence with fluticasone/salmeterol in a single inhaler (FSC), fluticasone and salmeterol in separate inhalers (FP+SAL), fluticasone and montelukast (FP+MON), fluticasone alone (FP) and montelukast alone (MON).

\textbf{Methods:} A 24-month observational retrospective study was conducted using administrative claims data. Subjects were \textgreater;12 years old with 24 months of continuous enrollment; had \textgreater;1 asthma claim (ICD-9: 493), \textgreater;1 short-acting beta\textsubscript{2}-agonist claim, and \textgreater;1 FSC, FP, SAL, or MON claim. Outcomes included asthma medication refill rates and persistence measured by treatment days. This study was designed with a unique population of patients with asthma from different health plans to validate previous findings.

\textbf{Results:} A total of 3503 subjects were identified based on their index medication: FSC (996), FP+SAL (259), FP+MON (101), FP (1254) and MON (893). Mean number of prescription refills for FSC (3.98) was significantly higher than FP (2.29) and the FP component of FP+SAL (2.36), and FP+MON (2.15), \textit{P}<0.05. No significant differences were observed between FSC and MON fill rates (4.33). Mean number of treatment days was greater for FSC compared to FP, FP+SAL, and FP+MON (\textit{P}<0.0001).

\textbf{Conclusion:} This study confirms a previous report that adherence profiles of fluticasone and salmeterol in a single inhaler are significantly better when compared...
to the controller regimens of fluticasone and salmeterol in separate inhalers, fluticasone and montelukast, or fluticasone alone and similar to montelukast alone. © 2005 Elsevier Ltd. All rights reserved.

Introduction

Inhaled corticosteroids (ICS) have been identified by both the National Asthma Education Prevention Program and the Global Initiative for Asthma (GINA) as the preferred component of controller therapy for patients of all ages and all severity levels of persistent asthma.1,2 In addition these guidelines recommend the addition of a long-acting bronchodilator for patients whose asthma is not controlled with an ICS alone. Increased adherence to therapy with ICS is associated with a reduction in emergency department visits, hospitalizations and mortality.3–6 Studies show that significant reduction in asthma-related morbidity and mortality are achieved with modest refill persistence of 4–6 canisters of ICS dispensed per year.5,6 However, low patient adherence with ICS is common. Refill data indicate that patients treated with ICS have, on average, only 2–4 units of the medication dispensed per year.7,8 Poor adherence to ICS is recognized as a contributor to asthma treatment failure resulting in increased morbidity, mortality and increased consumption of health care resources.9 Furthermore, adherence to pharmaceutical agents in clinical practice may be lower than demonstrated in controlled clinical trials.10

This study was designed to confirm previous findings that demonstrated increased patient adherence with fluticasone and salmeterol in a single inhaler when compared to the inhaled corticosteroid component of fluticasone and salmeterol in separate inhalers, fluticasone and montelukast combination and with fluticasone monotherapy using administrative claims data.8 This study employed a unique population of patients with asthma, in different health plans, different regions of the country and included Medicaid patients not previously studied.

Methods

Data source and timeframe

An observational retrospective cohort study was conducted using administrative claims data from three commercial health plans and one Medicaid plan. The commercial health plans with 8 million members and a Medicaid plan that included both Medicaid-managed care and discounted fee-for-service covering more than 1.6 million recipients. The study period included data from April 1, 2000 to September 30, 2002, which allowed for a 24-month study period (12 months pre-index and 12 months post-index), with the index period occurring between April 1 and September 30, 2001.

Cohort definitions

The study participants were divided into the following five cohorts based on the asthma controller medication(s) filled during the index period: (1) fluticasone propionate and salmeterol in a single dry powder inhaler (FSC), (2) fluticasone propionate and salmeterol in separate inhalers dispensed within 60 days of each other (FP+SAL), (3) fluticasone propionate alone (FP), (4) fluticasone propionate and montelukast dispensed within 60 days of each other (FP+MON), (5) montelukast alone (MON). The first identified controller regimen was defined as the index medication(s). The study period for each patient started 12 months prior to the patient’s index medication and continued for 12 months post-index.

Study population

Subjects in this analysis were required to have one principal or secondary medical diagnosis claim for asthma (International Classification of Diseases, Ninth Revision [ICD-9]: 493.XX) and at least one short-acting beta2-agonist (SABA) prescription claim in the pre-index period. Subjects had one or more pharmacy claim(s) for the medications of interest (FSC, FP, SAL, or MON) during the index period, were 12 years old or older on the index date, and were continuously enrolled during the 24-month study period. Subjects with chronic obstructive lung disease (ICD-9: 491.XX, 492.XX, 494.XX, and 496.XX) or cystic fibrosis (ICD-9: 277.0X) claims during the 24-month study period or claims for any ICS, long-acting beta2-agonist (LABA), or leukotriene modifier (LTM) prescriptions during the 12-month pre-index period were excluded. In order to attain comparable cohorts, patients using the highest strengths of FSC (500/50 mcg) and FP (220 mcg) were excluded from the analyses. During the 60 days after the index event,
subjects could not be dispensed any alternative controller therapy.

Outcomes

The outcomes of interest in the post-index period were (1) asthma medication refill rates and (2) treatment days used as a measure of persistence. Asthma medication refill rates were defined as the number of 1-month (30-day) supply of the medication of interest during the 12-month post-index period. Treatment days for the monotherapy (FSC, FP, and MON) cohorts constituted the total days supply of the medication in the post-index period. Treatment days were calculated for the combination cohorts (FP+SAL and FP+MON) as the total number of days when the FP component of the regimen was supplied. The index prescription for the medication of interest was included in the analyses of refill rates and treatment days. Prescriptions for a 3-month supply were adjusted for this method of dispensing. SABA refill rates in the post-index period were also analyzed for the five cohorts.

Analysis

Descriptive statistics were calculated for each study cohort. Mean and standard deviation or percentage were calculated for continuous and count variables including age, gender, SABA utilization, comorbidities, and percent with a pulmonary function test in the 12-month pre-index period. Chi-square tests were applied for each categorical variable (gender and pulmonary function test) and Wilcoxon rank tests were performed to test the difference between the cohorts for continuous variables (mean age, mean SABA utilization, and mean number of comorbidities).

ANOVA models were used to assess the differences in refill rates and treatment days. For the subjects in the FP+SAL and the FP+MON cohorts, the amount of FP refills and days supply were compared. The models were adjusted for baseline measures, some of which are proxies for severity, including baseline comorbidities, medication use, and hospitalization. All analyses controlled for demographics, health plan, comorbidities, pre-index medication use, pre-index asthma ED/hospitalization, and pre-index asthma-related procedures such as nebulizer, injection of asthma-related drugs, pulmonary function test, and allergy skin test. Differences between the cohorts were defined as statistically significant at $P < 0.05$. SAS Proprietary Software, Release 8.2 was used for all statistical analyses (SAS Institute Inc., Cary, NC).

Results

Subjects

A total of 3503 subjects were identified in the administrative claims data. On the basis of the index medication(s) the patients were classified in one of the following cohorts: FSC ($n = 996$), FP ($n = 1254$), FP+SAL ($n = 259$), FP+MON ($n = 101$) and MON ($n = 893$). Baseline demographics are presented in Table 1. Subjects dispensed FSC were older than those dispensed MON and FP+MON. Mean pre-index SABA use for FSC cohort was significantly higher than for the FP subjects and lower than for MON patients. The FSC cohort had a greater number of comorbidities than those in the MON,

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>FSC</th>
<th>FP+SAL</th>
<th>FP</th>
<th>FP+MON</th>
<th>MON*</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>996</td>
<td>259</td>
<td>1254</td>
<td>101</td>
<td>893</td>
</tr>
<tr>
<td>Male (%)</td>
<td>353 (35.4%)</td>
<td>86 (33.2%)</td>
<td>466 (37.2%)</td>
<td>41 (40.6%)</td>
<td>317 (35.5%)</td>
</tr>
<tr>
<td>Mean age (sd)</td>
<td>39.5 (17.2)</td>
<td>41.2 (16.3)</td>
<td>38.8 (18.0)</td>
<td>34.7 (18.0)</td>
<td>34.8 (18.3)</td>
</tr>
<tr>
<td>Mean SABA use (so)</td>
<td>3.00 (3.46)</td>
<td>2.72 (3.37)</td>
<td>2.45 (2.89)</td>
<td>3.09 (4.38)</td>
<td>3.10 (3.48)</td>
</tr>
<tr>
<td>Mean no. of comorbidities (so)</td>
<td>1.39 (1.33)</td>
<td>1.34 (1.32)</td>
<td>1.22 (1.42)</td>
<td>1.08 (1.30)</td>
<td>1.16 (1.31)</td>
</tr>
<tr>
<td>Pulmonary function test†</td>
<td>36.9%</td>
<td>28.2%</td>
<td>20.7%</td>
<td>22.8%</td>
<td>26.3%</td>
</tr>
</tbody>
</table>

*Significant difference between FSC and MON cohorts $P < 0.05$.  
†Significant difference between FSC and FP+SAL cohorts $P < 0.05$.  
‡Significant difference between FSC and FP cohorts $P < 0.05$.  
§Significant difference between FS and FP+MON cohorts $P < 0.05$.  
MON = montelukast (5 and 10 mg).  
†Percent with at least one test.
FP, and FP+MON cohorts. A significantly higher percentage of the FSC cohort had claims for pulmonary function testing pre-index event when compared to the other groups.

Refill rates

The distribution of the mean number of ICS medication fills dispensed in the five cohorts in the post-index period is shown in Fig. 1. The mean number of medication fills obtained by FSC cohort (3.98; 95% CI 3.78–4.18) was nearly twice that of FP cohort (2.29; 95% CI 2.11–2.47), and of the corticosteroid components of FP+SAL (2.36; 95% CI 1.97–2.75), and FP+MON (2.15; 95% CI 1.52–2.78) cohorts (P < 0.05). There were no significant differences in the mean number of fills between FSC and MON (4.33; 95% CI 4.11–4.54).

Treatment days

The mean number of treatment days for FSC (84.76; 95% CI 79.82–89.69) was statistically greater (P < 0.0001) than for FP+SAL (26.76; 95% CI 17.11–36.40), FP+MON cohort (25.44; 95% CI 10.03–40.84), and FP (29.24; 95% CI 24.84–33.65). There were no significant differences (P = 0.10) between the mean number of treatment days for FSC and MON (78.10; 95% CI 72.89–83.31).

Post-index SABA use

The mean number of SABA prescriptions in the 12-month post-index period for FSC cohort (2.34; 95% CI 2.14–2.55) was significantly lower (P < 0.0001) than the number of SABA prescriptions for MON cohort (2.79; 95% CI 2.57–3.01). There were no significant differences in the mean number of SABA prescriptions dispensed post-index between FSC and FP+SAL (2.59; 95% CI 2.18–2.99); FP (2.62; 95% CI 2.43–2.80); or FP+MON (2.55; 95% CI 1.91–3.20).

Discussion

This study demonstrates that FSC provides the highest level of adherence to the ICS component of controller therapy and equivalent adherence to montelukast alone. The annual refill rate for FSC was 69–85% higher than the rates for FP, as well as the FP component in FP+SAL, and FP+MON cohorts. In addition, there was no difference in adherence between FSC and montelukast monotherapy. This study in a unique population (different health plans, different regions of the country and inclusion of Medicaid claims) confirms a previous report demonstrating that therapy with fluticasone propionate and salmeterol in a single inhalation device is an effective means of achieving adherence to inhaled corticosteroid therapy for asthma.8 The consistent findings from the two studies increase the generalizability of the results.

The study has several limitations. It is an observational investigation of administrative medical and pharmacy claims data that were collected for the primary purpose of reimbursement. These data sets do not include information on the clinical status of these patients. In addition, the days’ supply of controller medication dispensed is a proxy for medication adherence and does not record actual patient adherence behavior with regards to the medication. There may also be other factors influencing these results such as samples and “borrowed” medications not included in this analysis that may alter adherence measures. These limitations may overestimate or underestimate the actual use of the medications, but this bias should be expected to occur in each of the cohorts similarly.

Despite advances in therapy, asthma continues to have significant impact on morbidity, mortality and consumption of health care resources. Proper management of asthma and increased adherence to treatment regimen may result in improved long-term asthma control. The literature suggests that simplification of the treatment regimen with fewer medications should achieve better adherence.11,12 Perceived improvement and simpler medical regimens may motivate and improve patient adherence. This study confirms the findings of a previous paper9 with claims data of unique patients with asthma from different regions and different payer

Figure 1 Mean number of FP prescription claims dispensed in the 12-month post-index period. *P < 0.05 for FSC compared to FP+SAL, FP, FP+MON, P = 0.06 for FSC compared to MON.
types. The findings of these two studies combined with the data from clinical trials demonstrating the superiority of FSC when compared to other controllers adds to the evidence supporting the recommendations of GINA and the NAEP for controller therapy with ICS+LABA.

References