Executive Summary

Outcomes research for complications of inhaled bronchodilators/corticosteroids

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☐ Introduction

Inhaled respiratory medications are a cornerstone treatment for chronic airway diseases. Inhaled corticosteroids (ICS), short- and long-acting inhaled beta-agonists (SABA and LABA), and short- and long-acting inhaled muscarinic antagonists (SAMA and LAMA) are most frequently used for patients with chronic airway diseases, including asthma, chronic obstructive pulmonary disease (COPD) and bronchiectasis.

In this study, we tried to elucidate the association between the use of inhaled bronchodilators/corticosteroids and complications such as hemoptysis, pregnancy -induced hypertension, and cardiovascular disease (acute myocardial infarction and tachyarrhythmia) and to compare the risk of hospital admission or emergency room visit for pneumonia according to inhaler device.

☐ Methods

We used the database of the Health Insurance Review and Assessment Service (HIRA; Seoul, South Korea). The source population consisted of all individuals who were dispensed at least one of the inhaled respiratory medications such as ICS, SABA, LABA,

SAMA, LAMA, ICS/LABA, SABA/SAMA between 1 January 2009 and 31 December 2011.

A retrospective cohort study was conducted and Cox proportional hazard model was applied to compare the risk of hospital admission or emergency room visit for pneumonia between metered dose inhaler (MDI) and dry powder inhaler (DPI). A nested case-control study was conducted using individual matching method and conditional logistic regression was applied to identify the association between the use of inhaler and the risk of hemoptysis, pregnancy-induced hypertension, and cardiovascular disease.

□ Results

In ICS user, the risk of pneumonia was higher in MDI compared with DPI, after adjustment for age, gender, respiratory disease, comorbidities, health care utilization, concomitant medications (HR 1.6; 95% CI 1.2 to 2). Additionally, In ICS/LABA user, the risk of pneumonia was higher in MDI compared with DPI, after adjustment for age, gender, respiratory disease, comorbidities, health care utilization, concomitant medications (HR 1.6; 95% CI 1.3 to 1.9).

SABA was associated with a higher risk of hemoptysis (OR 1.2; 95% CI 1.2 to 1.4), after adjustment for other inhaler medication and age, Charlson comorbidity index (CCI), comorbidities, health care utilization, concomitant medications. This association was observed in LAMA (OR 1.2; 95% CI 1.1 to 1.4) and SAMA (OR 1.6; 95% CI 1.1 to 2.4).

After adjusting for concomitant medications, baselines characteristics, health care utilization, medication history, the risk of PIH was lower in 0~15,000mg of ICS cumulative dose compared with non-user (OR 0.8; 95% CI 0.64 to 0.99). In contrast, the risk of PIH was higher in more than 15,000mg group compared with non-user(OR 1.3; 95% CI 1.01 to 1.79).

SABA was associated with a higher risk of acute myocardial infarction (OR 1.2; 95% CI 1.1 to 1.3), after adjustment for other inhaler medication and age, CCI, comorbidities, health care utilization, concomitant medications. This association was observed in LABA (OR 1.3; 95% CI 1.1 to 1.6).

After adjusting for other inhaler medication and age, CCI, comorbidities, health care utilization, concomitant medications, risk of tachyarrhythmia was higher in ICS with LABA user compared with non-user(OR 1.2; 95% CI 1.0 to 1.3). This association was observed in

LABA (OR 1.3; 95% CI 1.1 to 1.5).

□ Conclusions

We suggest that the use of MDI device may increase the risk of hospital admission or emergency room visit for pneumonia than DPI device when ICS or ICS/LABA use. SABA, LAMA, SAMA may increase the risk of hemoptysis in bronchiectasis patients. As MPR or cumulative dose of ICS is higher, the risk of the PIH in pregnant women is higher.

SABA, LABA or LABA alone may increase the risk of AMI and ICS/LABA or LAMA is associated with a increased risk of tachyarrhythmia.

Inhaled bronchodilators, Inhaled corticosteroids, Pneumonia, Hemoptysis, Pregnancy induced hypertension, Cardiovascular disease