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Inhaled Steroids May Increase Risk of Nontuberculous Mycobacteria Lung Disease

ATS 2016, SAN FRANCISCO – Patients with obstructive lung disease who take inhaled corticosteroids (ICS) may be at greater risk for nontuberculous mycobacteria pulmonary disease (NTM PD), according to new research presented at the ATS 2016 International Conference.

The researchers analyzed the medical records of 417,494 older adults living in Ontario, Canada, who were treated for COPD, asthma or both diseases between 2001 and 2013 and identified 2,964 cases of NTM PD.

Nontuberculous mycobacteria are widely dispersed and increasingly found in the environment. In most cases, they are harmless. However, some people can develop serious lung infections as a result of inhaling NTM that must be treated with multiple antibiotics, typically over 18 months.

“We know that COPD and asthma are risk factors for NTM PD. We also know that inhaled steroids can increase the risk of pneumonia in COPD patients,” said lead investigator Sarah K. Brode, MD, assistant professor of medicine at the University of Toronto, noting that only a small Danish study had previously looked at ICS and NTM PD.

Among current ICS users, researchers in the current study found a statistically significant increase in NTM of:

- 84 percent among all obstructive lung disease patients
- 210 percent among those with COPD only
- 55 percent among those who had both COPD and asthma

The researchers adjusted all results for potential confounders, including comorbidities, age, rurality of their residence and medications associated with NTM, such as anti-rheumatism drugs. They did not find a statistically significant link between current ICS use and asthma. Nor did they find an association between previous ICS use and NTM in obstructive lung disease patients.

Study results included five inhaled steroids then in use in Ontario. Fluticasone was the most widely prescribed of the five, and researchers found a statistically significant association between the drug and NTM PD. Researchers did not find a statistically significant association between budesonide, the second most commonly prescribed drug.

Dr. Brode speculates the difference between the two drugs may be explained by their potency. "Often people using fluticasone are using the highest dose, and the highest dose of fluticasone is a lot more potent than the highest dose of budesonide," she said. "Although one cannot be certain, I don't think it's something innate in the molecules themselves."

In support of her hypothesis, Dr. Brode also noted the study's finding of a strong dose-response relationship between incident NTM and cumulative ICS dose over one year. Those receiving a high dose were two to nearly three times as likely to have NTM PD, while those receiving a low dose were only slightly more likely to develop NTM than those not taking an ICS.

Dr. Brode said the take home message for physicians should be to minimize the dose of ICS they prescribe to their patients with COPD and asthma patients. "Patients with mild to moderate COPD with infrequent flare-ups may not need an ICS at all," she said. "On the other hand, the benefits of ICS outweigh the risks for asthma patients, except for those with the mildest symptoms." In all patients using ICS, Dr. Brode added, doctors should be alert to the symptoms of NTM PD.

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Abstract 6187

The Risk of Pulmonary Nontuberculous Mycobacterial Disease Associated with Inhaled Corticosteroid Use

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Rationale: Inhaled corticosteroids (ICS) are widely used to treat asthma and chronic obstructive pulmonary disease (COPD). However, corticosteroids inhibit immune function, and ICS use is associated with pneumonia. Our objective was to determine if ICS use is associated with an increased risk of nontuberculous mycobacterial pulmonary disease (NTM PD) in persons with obstructive lung disease (OLD).

Methods: We conducted a population-based nested case-control study using linked laboratory and health administrative databases in Ontario, Canada. The study cohort included Ontario adults aged ≥66 years with OLD (asthma, COPD, or asthma-COPD overlap syndrome [ACOS]) who were prescribed at least one medication for OLD between 2001 and 2013. We identified NTM PD amongst cohort members microbiologically, and identified drug exposures using outpatient prescription medication claims. Cases of NTM PD were defined using microbiologic criteria, and each case was matched to up to 4 controls. We estimated odds ratios comparing ICS current and prior use with non-use among NTM cases and controls using conditional logistic regression, adjusting for age, sex, income, rurality, and comorbidities and medications associated with NTM. We also adjusted for markers of severity of OLD, including use of OLD medications, hospitalization for OLD, use of spirometry, and use of home oxygen.

Results: Among 417,494 older adults with treated OLD, we identified 2964 cases of NTM PD. Current ICS use was associated with significantly increased risk of NTM compared with non-use (adjusted OR [aOR] 1.84; 95%CI, 1.59-2.13). Prior ICS use was not significantly associated with NTM. The association between NTM and current ICS use was greatest for patients with COPD only (aOR=2.10; 95%CI, 1.73-2.54), intermediate for patients with ACOS (aOR=1.55; 95%CI, 1.17-2.04), and not statistically significant for patients with asthma only (aOR=1.42; 95%CI, 0.85-2.36). The association was statistically significant for fluticasone use (aOR=2.08; 95%CI, 1.79-2.42), but not for budesonide use (aOR=1.17; 95%CI, 0.96-1.43). There was a strong dose-response relationship between incident NTM and cumulative ICS dose over 1 year (figure). The association between current ICS use and NTM remained significant when including only cases of NTM PD who received antimicrobial treatment (aOR=1.89; 95%CI, 1.32-2.71).

Conclusions: ICS use is associated with an increased risk of NTM PD. Physicians should consider this risk when prescribing ICS, particularly for patients with COPD, who appear most vulnerable.