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氏名	福光 研介
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学位論文の題名	Tiotropium attenuates refractory cough and capsaicin cough reflex sensitivity in patients with asthma (チオトロピウムは喘息患者における治療抵抗性の咳とカプサイシン咳感受性を緩和させる)  J Allergy Clin Immunol Pract 2018 [Epub].
論文審査担当者	主査： 中西 良一 副査： 大矢 進, 新実 彰男

## **Abstract**

Asthmatic cough is often refractory to standard treatments such as inhaled corticosteroids and long-acting  $\beta_2$  agonists (ICS/LABA). Tiotropium may modulate cough reflex sensitivity of acute viral cough, but its efficacy in asthmatic cough remains unknown. To evaluate whether tiotropium improves cough and cough reflex sensitivity in asthmatic patients refractory to ICS/LABA. Seventeen consecutive asthmatic patients with chronic cough despite the use of ICS/LABA [13 females; 43.4 (19.0) years-old; average ICS dose 651 (189)  $\mu\text{g}/\text{day}$ , fluticasone equivalent] were additionally treated with tiotropium (5  $\mu\text{g}/\text{day}$ ) for 4 to 8 weeks to examine its effects on pulmonary function and capsaicin cough reflex sensitivity (cough thresholds; C2 and C5). Cough severity, cough-specific quality of life, and asthma control were also evaluated using cough visual analog scales (VAS), the Japanese version of Leicester Cough Questionnaire (J-LCQ), and Asthma Control Test (ACT), respectively. Patients with an improved cough VAS of  $\geq 15$  mm were considered responders to tiotropium. Tiotropium significantly improved cough VAS, J-LCQ, and ACT scores, but not forced expiratory volume in 1 second ( $\text{FEV}_1$ ). Changes in cough VAS correlated with those in C2 ( $r=-0.58$ ,  $p=0.03$ ), C5 ( $r=-0.58$ ,  $p=0.03$ ), and ACT scores ( $r=-0.62$ ,  $p=0.02$ ), but not in  $\text{FEV}_1$  in the overall patients. When analyses were confined to the 11 responders, tiotropium significantly improved capsaicin cough reflex sensitivity within the subgroup (C2:  $p=0.01$  and C5:  $p=0.02$ ), and versus the non-responders (C2:  $p=0.004$  and C5:  $p=0.02$ ). Tiotropium may alleviate asthmatic cough refractory to ICS/LABA by modulating cough reflex sensitivity but not thorough bronchodilation.