

Asthma, hypersensitivity pneumonitis and cough

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The inflammatory molecule sphingosine-1-phosphate is not effective to evoke or sensitize cough in naïve guinea pigs

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Introduction Sphingosine-1-phosphate (S1P) is an inflammatory mediator that is increased in the tissue in a number of inflammatory conditions. Preliminary data indicate that the vagal afferent neurons express several S1P receptors including S1PR 2-3. Activation of S1P receptors can lead to sensory nerve activation and/or sensitization depending on nerve type and receptor subtype. We therefore evaluated the hypothesis that S1P induces cough and/or enhances the cough evoked by other tussive stimuli in naïve guinea pigs tussive challenge model.

Methods We used a standard TRPV1 receptor activator citric acid in the threshold concentration of 0.2 M and the TRPA1 agonist AITC (3 mM) to evoke cough. Cough reflex sensitivity was determined by the inhalation of aerosols S1P for 5min followed by inhalation of citric acid aerosol or AITC aerosol for 5 min in the continuous presence of S1P. In control experiments the vehicle was used instead of S1P.

Results Inhalation of S1P in the concentrations of 0.1mM and 1mM did not evoke cough (in paired experiments the vehicle and S1P in 1mM concentration evoked 0.8 ± 0.2 and 1.2 ± 0.3 , respectively, $P=0.3$, $n=24$). Preinhalation and continuous inhalation of S1P 1mM during citric acid (0.2M) challenge did not enhance citric acid-induced cough (2.7 ± 0.3 vs. 1.2 ± 0.3 , $P=0.3$, $n=11$). Preinhalation and continuous inhalation during AITC (3mM) challenge also did not enhance AITC -induced cough (the AITC-induced cough was even reduced from 4.4 ± 0.6 to 2.0 ± 0.5 , $n=12$, $P<0.01$).

Conclusion We conclude that S1P was not efficient to evoke cough in awake naïve guinea pigs. S1P was also not effective to sensitize the cough evoked by stimulation of TRPV1 and TRPA1 receptors. Nonetheless it cannot be excluded that S1P influences cough in the context of inflamed airways when the cough-mediating nerves undergo sensory neuroplasticity.

Acknowledgements: *The study was supported by BioMed Martin (ITMS: 26220220187) and VEGA 1/0070/15*