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Desflurane, Isoflurane, and...Ragweed

To the Editor:

Recent discoveries in the mechanism of action of ragweed sensitivity may have a bearing on the choice of anesthetic agent. We review some pathways that affect bronchial motor tone and how they may influence the choice of anesthetic agent. Bronchial motor tone is regulated by the parasympathetic nervous system, which exerts a contractile action through activation of M_3 receptors, and by the nonadrenergic noncholinergic pathways having both inhibitory and excitatory effects. The bronchial response to stimulation is in part due to C-fibers in the bronchial wall that are responsible for a local axon reflex, with irritant stimulation of nerve endings leading to the release of bronchoconstricting tachykinins such as substance P, neurokinin A, and calcitonin gene-related peptide.^{1,2} While sevoflurane does not induce increased airway resistance, desflurane-elicited airway constriction appears to be mediated by the release of these tachykinins.³

The transient receptor potential (TRP) family of cation channels is highly expressed by a subset of C-fiber nociceptors, including those in the lung.^{4,5} TRPA1 is expressed in sensory neurons, and colocalizes with TRPV1, calcitonin

gene-related peptide, substance P, and bradykinin receptors.⁶ TRPA1 is activated by the pungent ingredients in mustard and garlic extracts, allyl isothiocyanate⁷ and alliin.⁸ Sensory neurons from TRPA1-deficient mice show greatly diminished responses to each of these compounds, demonstrating that the TRPA1 channel is the primary molecular site by which they activate the irritant and pain pathway,^{9,10} as well as initiate the asthmatic airway inflammation.¹¹ TRPA1 receptors are activated by desflurane and isoflurane,^{3,7,12} similar to the effects of several air pollutants and chemicals that cause airway constriction, such as $\alpha\beta$ -unsaturated aldehydes and acrolein that activate the axon reflex release of tachykinins.^{8,13}

It has been recently reported that the TRPA1 receptor is also activated by the sesquiterpenoids present in the pollen from common ragweed (*Ambrosia artemisiifolia*), and activation of this receptor may contribute to the various respiratory symptoms caused by inhalation of this pollen.¹⁴ The sensitivity of a patient to ragweed suggests enhanced response of the TRPA1-activated tachykinin pathway. This sensitivity may have implications for anesthetic choice in patients with allergy to ragweed and possibly other pollens. Activation of TRPA1 by desflurane and isoflurane may be more likely in this setting of heightened sensitivity, leading to increased airway resistance and decreased lung compliance¹⁵ as well as causing bronchospasm and cough.^{16,17} These effects may in part be counteracted by volatile anesthetics' ability to directly relax airway smooth muscle¹⁸ and by desensitization of the TRPA1 receptor during sustained exposure.¹⁹ Nevertheless, the activation of TRPA1 receptors in the upper airway has been suggested to be in part responsible for the clinical observation of cough and laryngospasm due to desflurane.^{3,4,13}

The role of TRPA1 receptor in irritant-induced cough and increased airway resistance and their stimulation by desflurane and isoflurane could account for some of the clinical side effects of these drugs. Clinicians may want to take these findings into consideration when choosing an anesthetic for their patients. The lack of stimulation of TRPA1 receptors by sevoflurane^{3,12} may explain its relative lack of irritation^{16,17} and make it a less irritating choice in patients who have demonstrated heightened airway sensitivity to ragweed pollen or other chemical irritants.

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