Nicotine impairs inflammation-induced airway relaxation in an in vitro murine model of asthma

Body: Cigarette smoke worsens asthmatic symptoms and increases the risk for exacerbation. The present study investigates the effects of nicotine on airway relaxations in isolated murine tracheal segments. Segments were cultured for 24h in presence of vehicle, nicotine (10 µM) and/or dexamethasone (1 µM). Airway relaxations were assessed in myographs after pre-contraction with carbachol. Inflammatory mediator expressions were assessed by qRT-PCR. Organ culture per se selectively increased dilation to bradykinin (selective kinin B2 receptor agonist) and des-Arg9-bradykinin (selective kinin B1 receptor agonist). The relaxations were epithelium- and COX-2-dependent and accompanied with drastically enhanced mRNA levels of kinin B1 and B2 receptors, as well as COX-1, COX-2 and mPGES-1, and inflammatory mediators MCP-1 and iNOS. Nicotine selectively suppressed the organ-culture-enhanced relaxations. MG624 (α7-nicotinic acetylcholine receptor inhibitor) blocked the nicotine effects on the kinin B2 receptors, but not B1. Kinin receptor mRNA expressions were not affected by nicotine, whereas the mPGES-1 expression was reduced along with similar tendency for COX-2. Dexamethasone further attenuated nicotine-impaired airway relaxations along with suppression of inflammatory mediators. Hence, it is tempting to conclude that a local inflammatory process per se could be beneficial to airways by increasing the kinin receptor mediated relaxations and that nicotine added as a result of smoking might impede this safety mechanism. Dexamethasone fails to reverse nicotine’s detrimental effects, but rather further impair the airway relaxations. The latter might contribute to cortisone resistance often seen among smokers.