Irritated Noses

We all suffer from an occasional sneeze, or a runny nose when bicycling or skiing. However, when these symptoms occur continuously in our patients something is wrong and we call it hyperreactivity [1]. An obvious reason for hyperreactivity is allergy. However, about half of the patients visiting our clinics with symptoms of persistent rhinitis do not have allergy [2, 3]. Also in these non-allergic rhinitis patients hyperreactivity plays an important role. The pathophysiology of non-allergic rhinitis seems to be heterogeneous ranging from inflammatory reactions like local allergy and NARES on one side and non-inflammatory forms of the disease like idiopathic rhinitis and gustatory rhinitis on the other [3-5]. In this issue of the journal, a comprehensive review of the literature about non-allergic rhinitis is given by van Gerven and colleagues [6]. Especially the clear explanatory figures are very helpful. Also in this journal, Ottaviano and colleagues show nasal dysfunction induced by chlorinated water in competitive swimmers [7]. They show that nasal mucociliary transport time and olfaction is impaired by daily contact with chlorinated water. The great success of the Olympic games will surely bring more patients with these problems to our offices. It would be helpful when further studies also give suggestions how to treat these patients.

When looking at irritated noses the trigeminal nerve seems to play an important role. Scheibe et al. in this issue describe that there are consistent topographical differences in the arrangement of trigeminal receptors of the human nasal cavity; highest somatosensory sensitivity seems to be located in the anterior part [8].

Today specific receptors of the trigeminal system have been identified, like the TRP receptors. These receptors lead to potential new treatment options in respiratory disease like non-allergic rhinitis [9,10].

Transient receptor potential ion channels (TRPs) are a large protein family that allow for the flux of cations and anions across membranes. The first member of this family described in 1997 was the transient receptor protein vanilloid 1 (TRPV1). Six thermo TRPs have now been characterized responding to high (TRPV1-TRPV4) or low (TRMPM8 and TRPA1) temperatures [11]. TRPV1, TRPM8 and TRPA1 are expressed by sensory nerves, which innervate the human nasal mucosa [12]. In the nose, the local TRPV1 expressing sensory C-fibers play a critical role in the development of nasal hyper-responsiveness in non-allergic rhinitis. It has been proposed that blocking the nasal sensory nerve stimulation may control nasal hyper-responsiveness and therefore prevent the induction of rhinitis symptoms. Desensitization of sensory nerves by repeated application of high concentrations of capsaicin suppresses nasal hyper-reactivity to cold dry air or hypertonic saline in NAR and allergic rhinitis subjects [13] and has been shown to achieve control of symptoms in non-allergic rhinitis patients [14]. The application of capsaicin in the nose is painful and TRPV1 antagonists are now developed to treat hyperreactivity of the airways without this side-effect.

The exact relationship between (allergic) inflammation and hyperreactivity is complex. However, until now capsaicin has not been shown to be able to control hyperreactivity in allergic rhinitis [15], as was a TRPV1 inhibitor not able to reduce allergic symptoms [9]. This would mean that hyperreactivity as seen in idiopaic non-allergic rhinitis has another base that hyperreactivity in allergic rhinitis. Further studies are needed to further understand these differences. It is unknown whether capsaicin or treatment with TRP inhibitors is effective in other inflammatory forms of non-allergic rhinitis like local allergy. The concept of local allergy has been introduced by Powe, a decade ago [16, 17] and rejuvenated recently by the group of Rondon [5]. It has been shown by this group that part of the non-allergic rhinitis patients present with a localized nasal allergic response in the absence of systemic atopy characterized by local production of specific IgE (sIgE) antibodies, a T(h)2 pattern of mucosal cell infiltration during natural exposure to aeroallergens, and a positive nasal allergen provocation test response with release of inflammatory mediators (tryptase and eosinophil cationic protein).

A very interesting concept is the efficacy of azalastine, a histamine receptor-1 antagonist in non-allergic rhinitis [18]. It could be that the patients in these trials were patients with local allergy reacting favourably to the anti-inflammatory effects of azelastine, but on the other hand azelastine has been shown to reduce parasympathetic function and reduce methacholine-induced contraction of tracheal smooth muscle in an animal model (19). It might in that way also be effective in patients with non-allergic rhinitis. Patients with irritated noses, especially when caused by non-allergic disease comprise an important and difficult to treat population in our practices. The research in this area is exiting and gives us numerous new clues how we might treat this disease. If all medical treatment fails vidian neurectomy seems to be a viable treatment option that with new endoscopic techniques ensuring that the nerve is indeed severed has been shown to have long lasting positive effects [20,21].

This issue of the journal teaches us a lot of new things on irritated noses: a part of rhinology underexposed and in need of new insight that can be reported.

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