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Vasomotor rhinitis – pathophysiological aspects

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SUMMARY

Vasomotor rhinitis is commonly defined as an unspecific hyperreactivity of the nasal mucosa. The symptoms might be due to increased parasympathetic activity to the nose with the release of vaso-secretory active substances.

Experimental data from the cat suggest that the postganglionic parasympathetic mediator of nasal secretion is cholinergic, whereas the vascular responses appears to be due to a different mechanism. Apart from a rich sympathetic and parasympathetic innervation of the nasal mucosa there are other nerve fibres containing substance-P (SP) and vasoactive intestinal polypeptide (VIP). The secreto-vasomotor responses can be influenced by activation of these fibres and the atropine resistant vasodilatation seen following Vidian nerve stimulation thus may partly be due to activation and release of SP and VIP. Furthermore, other vasoactive substances released such as e.g. SRS or Kallikrein may participate in these reactions.

Vasomotor rhinitis (VMR) is commonly defined as an unspecific hyperreactivity of the nasal mucosa. No history or demonstrable evidence of allergy supports the diagnosis of allergic rhinitis. In some cases of VMR, the symtoms are assumed to result from increased parasympathetic activity to the nasal mucosa (Malcomson, 1959) and Vidian neurectomy is now a well proven treatment in intractable cases of VMR where watery secretion and sneezing attacks are the dominating symtoms (Golding-Wood, 1970).

In previous experimental studies (Änggård, 1974) it was demonstrated that vascular and secretory responses in the nasal mucosa are activated simultaneously following activation of so called parasympathetic nerve fibres in the Vidian nerve. Atropine blocked the secretory response but had no effect on the vascular responses. These results suggest that the mediator of nasal secretion is cholin-

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ergic, whereas the vasodilatation appears to be due to different mechanisms, not sensitive to atropine.

Recently, a large number of peptides have been located to endocrine cells and neurons. Such peptides include e.g. substance-P (SP) and vasoactive intestinal polypeptide (VIP). These substances, if present in the nasal mucosa, can be responsible for the atropine resistant vasodilatation described above.

The aim of the present experimental studies was to evaluate the occurrence as well as the release of various possible vasoactive substances in the nasal mucosa of the cat following Vidian nerve stimulation.

To investigate whether substance-P or VIP could be found in the nasal mucosa, specimens from cat nasal mucosa were assayed radioimmunochemically. Substance-P like immunoreactivity in amounts ranging from 0.89–2.2 ng/g was found in the nasal mucosa (Änggård et al., to be published) whereas VIP like immunoreactivity occurred in amounts ranging from 17–47.5 pmol/g (Fahrenkrug and Änggård, unpubl. data) Table 1. It is to be observed, however, that in some specimens the supporting cartilage of the turbinates was included as this was difficult to separate from the mucosa and the calculated amounts will thus be too small.

Table 1. Vasoactive substances in nasal mucosa (cat).

Substance	Nasal mucosa	Nasal secretion	Vascular effect threshold dosage
Substance-P	0.89–2.2 ng/g	23–117 pg/ml	5 ng/min.
VIP	17–47,5 pmol/g		
SRS		1000 u/ml	800 u/min.

Were any of these substances responsible for the atropine resistant vasodilation in the nasal mucosa, they would presumably be found in the venous effluent and /or in nasal secretion following stimulation of the Vidian nerve. In cats where a superior cervical ganglionectomy previously had been performed so the Vidian nerve was deprived of sympathetic fibres, venous blood or nasal secretion obtained during stimulation of the Vidian nerve was analysed for substance-P like immunoreactivity (SPLI). In the venous effluent from the pterygopalatine vein no SPLI was found (Burcher et al. 1977) whereas nasal secretion contained SPLI in amounts ranging from 23–117 pg/ml (Änggård et al., to be published). Furthermore, nasal secretion was analysed for slow reacting substance (SRS) which was found in amounts of 1.000 U/ml (Änggård and Strandberg, to be published). To determine whether or not similar amounts of these substances would affect the nasal vascular responses, the effect of SP and SRS on nasal blood flow was tested. SP proved to be a very potent vasodilator in the nasal mucosa and clear-cut increases were observed at close intra-

arterial infusions of 5 ng/min. Threshold responses of SRS were seen at infusion of 800 U/min.

In order to localize substance-P and VIP-like immunoreactivity, specimens of nasal mucosa were studied using immunohistochemical techniques (Änggård et al., to be publ.). The indirect immunofluoresence technique used was according to Coons et al. (1955). Thin slightly varicose fluorescent substance-P positive fibres were seen under the epithelium and single fibres sometimes penetrated into the epithelial layer. Fibres were also seen in connection with thick walled blood vessels.

When similar techniques were used for the localization of VIP immunoreactivity, VIP nerves were observed around the nasal glands forming dense plexa around the acini. The localization of VIP-ergic nerves has been extensively studied by Malm et al. (1978), who demonstrated many large VIP immunoreactive nerve cell bodies in the pterygopalatine ganglion. This would suggest the VIP nerves of the nasal mucosa of the cat originate in that ganglion or higher up.

The present data suggest that apart from the strong influence of sympathetic adrenergic and parasympathetic cholinergic nerve fibres (see Änggård, 1976) other nerve fibres may also participate in the regulation of the secreto – vasomotor activities in the nasal mucosa. There is growing evidence that substance-P, a peptide originally discovered by von Euler and Gaddum (1931), is present in primary sensory neurones and may serve as a neurotransmitters in these neurones (Otsuka, 1975). The subepithelial localization of SP – positive nerves in the nasal mucosa and the projection of fine calibre fibres into the epithelium indicate that these fibres even here may represent sensory fibres (Figure 1). The appearance of SPLI in nasal secretion following stimulation of the Vidian nerve may thus be due to the release of the transmitter following an antidromic stimu-

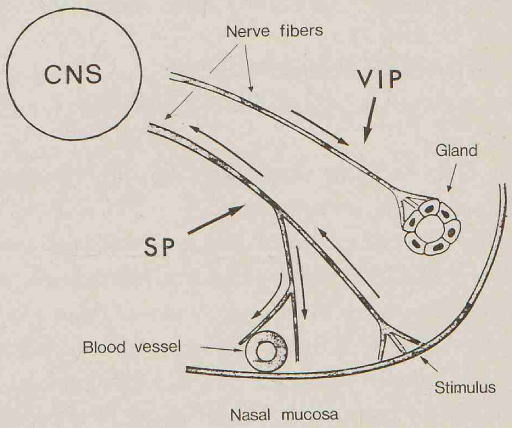

Figure 1. Tentative localization of SPLI- and VIP positive nerve fibres in the cat nasal mucosa.

lation of afferent SP positive nerve fibres in the Vidian nerve. The present findings of a very high vasodilatory activity of SP on the nasal vascular bed indicate that, if SP is released locally e.g. following the irritation of sensory nerve fibres or as a local axon reflex (Jansco et al., 1967) even small amounts of SP can effect the vasomotor activities. The findings of VIP immunoreactive nerve cell bodies in the pterygopalatine ganglion (Malm et al., 1978) suggest that the VIP immunoreactive nerves do not represent only short neurones within the mucosa. It is therefore possible that they are efferent nerve fibres to the nose (Figure 1).

The SRS – like activity found in nasal secretion following Vidian nerve stimulation suggests that other mechanisms than the release of putative neurotransmitters are also activated. Thus, the presence of a kallikrein-like substance has already been demonstrated in nasal secretion following Vidian nerve stimulation (Eccles and Wilson, 1973).

In conclusion, the present experimental data suggest that apart from the rich sympathetic and parasympathetic innervation of the nasal mucosa there are other nerve fibres containing substance-P and VIP. The secreto-vasomotor responses can be influenced by activation of these fibres and the atropine resistant vasodilatation seen following Vidian nerve stimulation thus may partly be due to activation of SP and VIP positive nerves. Furthermore, other vasoactive substances released such as e.g. SRS or kallikrein may participate in these reactions. The physiological significance and the clinical significance of these findings, however, are not yet established and merit further research.

ZUSAMMENFASSUNG

Die vasomotorische Rhinitis wird gewöhnlich als Folge einer unspecifischen Hyperreaktivität in der Nasenschleimhaut definiert. Die klinischen Befunde können von erhöhter parasympatischer Aktivität in der Nasenschleimhaut mit nachfolgender Freisetzung von vasomotorischen, aktiven Substanzen verursacht werden.

Experimentelle Katzenversuche zeigen, dass die Sekretion bei der Aktivierung von postganglionären, kolinergen parasymatischen Nervenfasern ausgelöst wird.

Die Gefässeffekte sind doch atropinresistent und sie werden von anderen Mechanismen verursacht.

Ausser einer reichlichen parasympatischen und sympatischen Innervation der Nasenschleimhaut gibt es andere Nerven die Substanz-P und VIP enthalten.

Die vasomotorischen Reaktionen können also durch Aktivierung von diesen Nervenfäden und durch Freisetzung von Substanz-P und VIP verursacht werden. Möglicherweise ist das die Ursache zu den atropinresistenten Gefässeffekten die man nach Stimulierung des Nervus Vidianus sieht.

Ausserdem können andere vasoaktiven Substanzen als SRS und Kallikrein in dieser Reaktion teilnehmen.

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