December 1998 (Volume 39, Number 4)

Influence of Nasal Fontanel Receptors on the Regulation of Tracheobronchal Vagal Tone

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Aim. To test the hypothesis according that the receptors located in the nasal fontanels influence the regulation of the tracheobronchial tree vagus tone.
Methods. Changes in respiratory parameters (forced expiratory volume in the first second- FEV1 and total resistance- Rt) occurring consequentially to light mechanical nasal stimulation were determined in healthy volunteer, non-smokers using spirometric and body plethysmographic measurements. The parameters were measured before and at 15 and 60 min after mechanical stimulation with cotton pledge.
Results. In subjects in whom the middle nasal meatus was stimulated by a cotton pledge soaked in saline, FEV1 decreased (p=0.01) and Rt increased (p=0.03). In subjects in whom the middle nasal meatus was stimulated by a cotton pledge soaked in 5% cocaine solution, no change was observed. In the control group of subjects, in whom the inferior nasal concha was stimulated by a cotton pledge soaked in saline, only a statistically significant decrease for FEV1 (p=0.04) was found.
Conclusion. There is a reflex communication between the nasal fontanel receptors and lungs, which is regulating the tracheobronchial vagal tone and resistance in lung airways. Further studies of this important physiologic relation are needed.

Key words: bronchoconstriction; lung volume measurements; nasal cavity; nasal mucosa; lung comliance; pulmonary ventilation; respiratory function tests; trachea; vagus nerve

The key role of the nose is to adjust the air flow and nasal resistance (1). Nasal resistance is the crucial element in achieving optimal alveolar ventilation for the respiratory work performed. Studies on the air flow have shown a nearly constant volume flow in particular segments and almost exclusive presence of laminar movement (regardless of the air flow rate) along the surface of nasal mucosa. The flow mostly proceeds through the middle and inferior part of the nose, i.e. the region of middle nasal meatus and inferiorly between inferior nasal concha and septum (2). The nasal cavity lacks flexibility, except in the segment bordering with the maxillary sinuses in the part of middle nasal meatus. There are two spaces covered by mucosa, termed by Zuckerkandel as inferior and posterior nasal fontanel (3). The nonmyelinated cholinergic endings (C-fibers) conduct the stimulus caused by mechanical, chemical and thermal irritants and are the only receptors that have been histologically verified in nasal mucosa. Since they are stimulated by negative pressure, they also function as flow receptors (4,5). Fibers from the nasal mucosa constitute the parts of the first (ophthalmic) and second (maxillary) branches of the trigeminal nerve. They are somatotopically organized and grouped in the Gasserian ganglion and the principal sensory nucleus and spinal trigeminal nucleus (6). A relationship between the trigeminal nerve stimulation and vagal ambiguus nucleus suggests that trigeminal stimulation modifies the neuronal firing pattern and consequently causes changes in the vagal outflow (7). Results of a number of animal experiments have demonstrated that changes in the pulmonary resistance occurring during nasal mucosa stimulation, are eliminated by resection of the ethmoidal nerve or vagal nerve (8). This clearly points to the existence of nerve reflex, but its characteristics, afferent part origin, nature of physiologic stimulation, time of reflex exhaustion, compensatory mechanisms, and pattern of efferent function have not yet been clarified. According to our hypothesis, the region of the afferent part of the reflex in the nose is the one which meets the following conditions: (a) flow of air at a certain rate through a segment of the nose, whereby the amount and rate are constant for certain states of the body (rest, exercise), whereas the rate of air flow through this segment should substantially differ from the flow rate through other segments of the nose; and (b) the structures stimulated on inspiration (negative pressure, Bernoulli's effect) and expiration (positive pressure) should be elastic and free in space to allow the highest possible amplitude, i.e., a free range of possible amplitudes.

The only part of the nose which meets both these criteria is the region in the middle nasal meatus known as the inferior and posterior nasal fontanels. They are made of a network of fibers continuing to the periosteum. Above this network there is a tissue rich in cavernous spaces abundant in nonmyelinated nervous endings on both sides. These structures are bilaterally superimposed by a layer of respiratory epithelium. The average infero-superior length of the anterior fontanel is approximately 11 mm and the anterior-posterior one approximatly 18 mm. Regarding the posterior fontanel, inferio-superior length is approximately 11 mm and antero-posterior one approximately 17 mm (9).

The "father" of modern nasal endoscopy, Professor Messerklinger, noticed movements in the nasal fontanels: I have seen slight inward and outward movements of healthy fontanels with forced nasal breathing (3).

In this study, we tried to cause maximal receptor stimulation by light mechanical tactile stimulation of ethmoidal nerves which are connected with second-order low threshold mechanoreceptive neurons (10) and to compare stimulation and anesthesia of the two regions of the nose. Induced stimulation was assumed to result in the maximal response of the vagus tone, i.e., smooth muscle of the tracheobronchial tree, with resulting changes in spirometric and body plethysmographic parameters. We wanted to confirm the trigeminus-mediated effect on the vagus parasympathetic tone of tracheal and bronchial smooth muscle, and to try and proof the nerve endings – receptors in the nasal cavity mucosa of the nasal fontanels.

Subjects and Methods

Thirty healthy volunteers, non-smokers, 15 women and 15 men, aged 14-61 years, with no chronic diseases in their rhinologic and pulmologic history and no data on acute rhinologic or pulmologic disease during the month preceding the study, were randomly divided into three groups. Group 1 included ten subjects, five women and five men, aged 18-56 years, mean age 31.8 years. Group 2 consisted of ten subjects, five women and five men, aged 18-58 years, mean age 31.3 years. Control group included ten subjects, five women and five men aged 18-61 years, mean age 32.1 years. There was no significant difference in age, body height and weight between the three groups

In the group 1, a cotton pledge soaked in saline was inserted in the middle nasal meatus on both sides. In the group 2, a cotton pledge soaked in 0.5 ml of 5% cocaine solution was inserted in the middle nasal meatus on both sides. In the control group a saline-soaked cotton pledge was bilaterally inserted between inferior nasal concha and septum, up to the upper level of the concha. The air flow through this part is equal to that through the middle nasal meatus (11), but is characterized by the presence of the reflex origin influencing cardiac action via the vagus nerve (12).

The cotton pledge inserted was large enough to adhere to the mucosa, producing light mechanical stimulation without dropping out spontaneously, and without producing discomfort. The pledge was well squeezed out before insertion, to avoid undesirable stimulation or anesthesia of other parts of the nasal mucosa. The first measurement after 15 minute-delay offered the elimination of any pain-caused changes due to insertion of the pledge.

The parameters of lung ventilation were assessed by body plethysmography on a Bodyscreen II (Dräger GmbH, Lübeck, Germany). All parameters were measured three times: one minute before, and 15 and 60 minutes after the insertion of cotton pledges. Mean values were used for statistical evaluation. The parameters measured were: forced expiratory flow in the first second (FEV1), peek expiratory flow (PEF) and total resistance (Rt). These parameters are commonly used in the evaluation of the obstructive character of the tracheobronchial tree pathology.

The study was approved by the hospital ethics committee, and an informed consent was obtained from all subjects.

Data analysis was done using SPSS PC 3.0 software (SPSS inc., Chicago, Ill, USA). Normal distribution was tested by Kolmogorov-Smirnov nonparametric test. As all results showed normal distribution, they were tested by two-tailed paired Student's t test.

Results

Mean values of measured parameters before, and 15 and 60 minutes after the insertion of cotton pledges are shown in Table 1.

Table 1: Respiratory parameters (mean±SD) in the normal subjects in whom a cotton pledge soaked in saline was inserted in the middle nasal meatus on both sides (group 1); those in whom a cotton pledge soaked in 0.5 mL of 5% cocaine solution was inserted in the middle nasal meatus on both sides (group 2); and control group with a saline-soaked cotton pledge bilaterally inserted between inferior nasal concha and septum, up to the upper level of the concha [view this table]

Group 1

A statistically significant decrease between the breathing parameters measured before and 15 min after the saline-soaked pledge insertion was observed for FEV1 ($p=0.01$) and statistically significant increase for Rt ($p=0.03$). After 60 min, a statistically significant decrease from the initial value was found for PEF ($p=0.01$) and an increase for Rt ($p=0.048$).

Group 2

There was no statistically significant difference between the values of the breathing parameter measured before and 15 or 60 min after the insertion of cotton pledge soaked in 5% cocaine.

Control group

With the insertion of a saline-soaked cotton pledge between inferior nasal concha and septum, a statistically significant decrease was observed between the FEV1 values measured before and 15 min after the pledge insertion ($p=0.04$), but not 60 min after the insertion of the pledge.

Discussion

The starting hypothesis of the study was the existence of a reflex arc between the nasal mucosa and smooth muscles of the tracheobronchial tree. There is a reflex, named nasopulmonary reflex, which causes bronchoconstriction in humans after the stimulation of the nasal mucosa by cold air (13,14). This bronchoconstriction in animals can be prevented by the resection of the ethmoidal or vagal nerve (8).

It is well known that the area innervated by the trigeminal nerve is a potent reflexogenic area (diving reflex, corneal reflex, sneezing). The physiology of these reflexes is based on the more or less painful stimuli (mechanical or chemical irritants and low temperature). The most potent of them regarding the influence upon the vagal tone is the diving reflex. It is a protective reflex against drowning and is induced by immersion of the face in ice water or by cooling of the face or forehead (15). Bilateral application of cold stimulus to the individual divisions of the trigeminal nerve showed that the ophthalmic division was the most sensitive pathway for this reflex (16). The nasal cavity is mostly innervated by maxillary division of trigeminal nerve and therefore diving reflex is not engaged in normal reflex physiology connected with the nose. It is also known that the stimulation to the trigeminal branches may cause cardiac arrhythmia, arrest, and changes in the blood pressure (12,17). These reflexes may potentially be more harmful than beneficial to the man, therefore the body must have some regulatory mechanisms to control the reflex duration. This, however, makes research aimed at their exact description quite difficult.

The model of light mechanical (permanent tactile) stimulation of the region was chosen in order to achieve the strongest possible reflex response from the presumed ethmoidal nerve fibers connected with low threshold mechanoreceptive second-order neurons in the trigeminal nuclei. These neurons receive only light tactile input and are not responding to noxious chemical or mechanical stimuli applied to the nasal cavity. These neurons were found in animal studies (10), and it can be presumed that they also exist in humans.

Light mechanical stimulation used in our study closely resembles the physiologic stimulation from air stream and could be considered a modified physiologic stimulation best stimulating nerves within the nasal cavity occurring during air flow in physiologic conditions. In the control group, the same postulates were employed, and the target for the stimulation was the mucosal region between inferior nasal concha and septum which, unlike the middle nasal meatus, has the characteristics of the nasocardial reflex arc structure and origin (12).

Tracheal and bronchial smooth muscles are innervated by parasympathetic innervation via the vagus nerve, which can change their tone and airway diameter (18). The changes occurring in the tracheaobronchial tree and lungs due to the increased parasympathetic, i.e., vagus tone, must therefore entail changes in the spirometric and plethysmographic parameters measuring the airway flow and resistance (FEV1, Rt).

Saline-soaked cotton pledge inserted in the region of the middle nasal meatus, elicited significant changes of respiration parameters 15 minutes after stimulation, pointing to alterations in the width of the major and medium intrapulmonary airways, i.e., increased Rt with decreased FEV1. At 1 hour, a statistically significant difference was found in the values of the parameters of PEF and Rt, which are characteristic of alterations in major and medium intrapulmonary airways (19) but may also suggest a gradual reflex exhaustion.

In the subjects in whom the region of the middle nasal meatus was obstructed by a cotton pledge soaked in 5% cocaine solution, no statistically significant changes in the respiratory parameters were recorded either at 15 or at 60 minutes. This was the caused by the exclusion of regular nerve firing from the region of the middle nasal meatus, and anterior and posterior nasal fontanel caused by nerve ending anesthesia by 5% cocaine solution.

With the cocaine anesthesia of the region, the afferent part of the arc maintained the parasympathetic (vagus) nerve tone at the basal values, despite the middle nasal meatus mechanical stimulation. Recanalization of the complete air flow through the region of the middle nasal meatus, caused by the obstruction of the part of the nose between inferior nasal concha and septum, in the second group, produced a mild increase of trigeminal nerve stimulation. That changed the parasympathetic (vagal) tone as well as the airway diameter trough its action on the smooth muscles of the lungs and tracheobronchial tree.

This indicates that a continuous physiologic stimulus maintains the vagal function at a certain, constant level already known as resting vagal tone (20,21). Changes in the stimulus intensity entail changes in the function of tracheobronchial smooth muscle tone and airway diameter trough the increased vagal tone.

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Recieved: March 23, 1998
Accepted: June 16, 1998

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