Rhinology, 27, 263-269, 1989

Nasal provocation with histamine: A comparison of the determination of the threshold of reactivity by three methods of rhinomanometry

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SUMMARY

Three methods of rhinomanometry were compared with each other with respect to their ability to determine the histamine threshold (histamine concentration for a 100% increase of the initial total nasal resistance): the active anterior rhinomanometry (A.A.R.), the active posterior rhinomanometry (A.P.R.) and the passive anterior rhinomanometry (P.A.R.). Nasal challenge and consecutive measurement by the three methods of rhinomanometry were conducted in a group of 11 volunteers. The three methods gave significantly different histamine concentration thresholds ($p=0.002$).

Unilateral histamine thresholds as available from A.A.R. and P.A.R. (at a flow of 250 cm^3/sec) did not differ significantly ($p=0.299$). For A.A.R. and A.P.R., histamine thresholds were assessed at five different pressure values as well as at five different flow values.

The thresholds did not appear to be significantly different at any one of those pressure gradients ($p=0.690$) or flow values ($p=0.357$).

The aim of the present investigation consists in assessing the ability of the active posterior rhinomanometry (A.P.R.) in determining the histamine threshold with respect to both the active anterior rhinomanometry (A.A.R.) and the passive anterior rhinomanometry (P.A.R.). A.P.R. - being generally considered the more physiological (simultaneous measurement of both nasal cavities) but difficult approach - is compared with the better established methods of rhinomanometry

Paper presented at the 12th Congress of the European Rhinologic Society including the VIIth I.S.I.A.N., Amsterdam (The Netherlands), June 1988.

as A.A.R. and P.A.R. While threshold assessment by means of P.A.R. is always performed at a fixed flow, the influence of different flow and pressure gradient values on the threshold determination was investigated for A.A.R. as well as A.P.R.

MATERIAL AND METHODS

Eleven volunteers (six women and five men, aged between 20 and 43 years) were selected at random without regard to the anatomy of their nasal septum or to a possible history of allergic or vasomotor rhinitis: three out of the 11 subjects had a minor septal deviation, four had an obvious deviation, while the remaining four volunteers had straight septa. Only one subject had an allergic rhinitis (house dust mite) while the history of all other volunteers was in favour of a normal nasal sensitivity.

After measurement of the initial nasal airway and application of an aerosol with control solution, the following eight concentrations of histamine (Hall company) were applied to both nasal cavities: 0.25 mg/ml, 0.5 mg/ml, 1 mg/ml, 2 mg/ml, 4 mg/ml, 8 mg/ml, 16 mg/ml, 32 mg/ml (2,25 mmol; 4,50 mmol; 9,00 mmol; 18,00 mmol; 36,00 mmol; 72,00 mmol; 144,00 mmol; 288,00 mmol). This nasal provocation was done with a Heyer nebulizer in the following way (Clement, 1975; 1981): After a full inspiration the volunteer was asked to say "AAA" with open mouth during 10 seconds. Meanwhile the provocation was performed. Immediately afterwards the mouth was closed and the subjects expired through the nose. This procedure was repeated six times (60 sec.).

Since the nebulizer pulverises about 0,3 ml/min, histamine doses can easily be calculated by multiplying the given concentrations by 0,3. Each subject received all the doses. When using aerosols, it is never possible to know the exact dose the patient receives. One does not have any information about the amount lost in the rhinopharynx, swallowed or lost via the contralateral nostril. After each application, the three types of rhinomanometry were performed in the following order: A.A.R., A.P.R. and finally P.A.R. These measurements are not supposed to have any effect on each other, except for the lapse of time between first and last method of measurement. This lapse of time was a short as possible.

Active anterior rhinomanometry (A.A.R.) and active posterior rhinomanometry (A.P.R.) were both carried out with a Rhinotest MP rhinomanometer of Medicomess GmbH, Ludwigshafen. For the passive anterior rhinomanometry a P.A.R. rhinomanometer of the Heyer company was used. For the A.P.R. method, the free end of the tube which samples the nasopharyngeal pressure was connected to a small home-made plastic plate (50 × 28 × 5 mm). This plate rested on the tongue while the subject held the edge, connected to the tube, with his/her lips. This enabled to overcome the so annoying oropharyngeal reflexes caused by the otherwise free-floating end of the tube.

For the A.A.R. method, the unilateral nasal resistances

$$\left(R = \frac{\Delta P}{\dot{V}}\right)$$

where determined for five different pressure gradients (ΔP) as well as five different flow values ($\dot{V}$). These pressure gradients were: 50, 75, 100, 125 and 150 Pa. As flow values, we choose 50, 100, 150, 200 and 250 cm^3/sec. The total nasal resistance was computed as:

$$R_{tot} = \frac{R_{right} \cdot R_{left}}{R_{right} + R_{left}}.$$

As far as the A.P.R. method is concerned, the total nasal resistance was determined for those five pressure and flow values mentioned with the A.A.R. method. All A.A.R. and A.P.R. resistances are related to inspiration.
The P.A.R. method gives pressure gradients at a fixed flow of 250 cm^3/sec. The total nasal resistance was computed from the measured unilateral values with the same formula as that mentioned for A.A.R. The "histamine concentration threshold" was defined as the concentration at which a 100% increase of the initial nasal resistance (= the resistance five minutes after application of the control solution) occurred.

RESULTS

1. *Comparison of the three methods of rhinomanometry*

With regard to the assessment of the histamine concentration threshold, the three methods of rhinomanometry (A.A.R., A.P.R. and P.A.R.) can be compared with each other only as far as the total nasal resistance is concerned and for the sole flow value of 250 cm^3/sec. (The total nasal resistance is computed from the measured unilateral resistances in A.A.R. and P.A.R., and measured as such in A.P.R.). Under these conditions, the three methods of rhinomanometry gave significantly different ($p = 0.002$, 2 way ANOVA on logarithmically transformed data) histamine concentration thresholds. Furthermore, when the 11 responders were ranked from least to most sensitive, the rank orders of the individuals proved to be different according to the method of rhinomanometry.

2. *Comparison of the two methods of rhinomanometry that provide unilateral values*

Since A.P.R. measures the total nasal resistance, A.A.R. and P.A.R. can only be compared as far as unilateral values are concerned. At a flow of 250 cm^3/sec (this is the flow generated by the P.A.R.-rhinomanometer), the unilateral histamine

concentration thresholds as determined with A.A.R. and P.A.R. did not differ significantly ($p = 0.299$, 2 way ANOVA on logarithmically transformed data). These unilateral thresholds refer to the nasal side with the most marked reaction to provocation. Incidentally, the mean histamine concentration threshold for our 11 subjects happened to be on the right side (Table 1). For the opposite ("insensitive") side, histamine thresholds were significantly different ($p = 0.003$).

Table 1. Mean histamine concentration thresholds for the three different methods of rhinomanometry, determined at the respective flow or pressure gradients. Mean histamine concentrations expressed in mg/ml.
For statistical analysis, the arbitrary concentration of "64 mg/ml" was introduced when a 100% increase of the initial nasal resistance was not reached even at 32 mg/ml.

	left		right		total	
	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	s
A.A.R. test subjects ($n = 11$)						
ΔP (Pa)						
50	1.48	1.38	42.45	26.57	26.23	30.06
75	2.20	2.33	39.91	28.91	26.41	29.90
100	2.25	2.29	42.45	26.57	27.86	29.08
125	7.89	18.74	45.64	26.58	27.14	29.50
150	7.89	18.74	44.27	28.56	27.14	29.50
$\dot{V}$ (cm^3/sec)						
50	1.80	2.31	36.77	31.57	27.64	29.29
100	7.39	18.90	22.66	28.18	26.55	30.04
150	1.39	1.07	28.11	29.96	26.57	30.02
200	1.20	1.10	27.27	29.58	19.77	28.53
250	1.29	1.12	32.41	30.73	20.93	28.04
A.P.R. test subjects ($n = 11$)						
ΔP (Pa)						
50					8.32	18.58
75					8.68	18.46
100					9.77	18.25
125					15.50	24.15
150					15.50	24.15
$\dot{V}$ (cm^3/sec)						
50					8.30	18.70
100					7.84	18.78
150					7.73	18.80
200					1.64	1.34
250					1.52	1.04
P.A.R. test subjects ($n = 11$)						
$\dot{V}$ (cm^3/sec)						
250	16.82	24.95	47.45	28.34	31.45	31.23

3. *Influence of the different pressure gradient and flow values*
In contrast to P.A.R., nasal resistances can be determined in A.A.R. as well as A.P.R. for different pressure gradient and flow values (see: Materials and Methods). By means of 3 way ANOVA on logarithmically transformed data it could be concluded that - though there existed a strong dependence of the histamine concentration thresholds as determined with A.A.R. and A.P.R. ($p = 0.000$) - no significant differences appeared for the five pressure gradients ($p = 0.690$) or for the five flow values ($p = 0.357$).

CONCLUSIONS

1. The practical problems inherent in collecting the nasopharyngeal pressure in A.P.R. could be overcome by means of a simple plastic device (see: Materials and Methods). This allowed us to measure the simultaneous reaction of both nasal cavities on provocation with histamine for all of the test subjects.
2. Comparison of the histamine threshold determined with A.A.R., P.A.R. (on the basis of a calculated total nasal resistance) and A.P.R. (measured total nasal resistance), proved nevertheless to be very disappointing.
3. For each of the two methods of rhinomanometry separately (A.A.R. and A.P.R.), histamine thresholds seemed to be comparable, regardless of the flow value or pressure gradient at which the nasal resistances were obtained.
4. All provocations and consecutive measurements were repeated after one week. Especially for the A.P.R. method reproducibility seemed to be rather poor. Therefore, we renounced to a complete statistical analysis of this second set of data. According to previous studies reproducibility seemed good for A.A.R. and slightly less for P.A.R.

DISCUSSION

Many authors used or compared different methods of rhinomanometry with regard to several kinds of nasal provocations (Crifò, 1975; Fanet et al., 1980; Clement et al., 1985; Ghaem et al., 1986; Gleeson et al., 1986; Bachmann, 1987). However, few publications deal with A.P.R. as a possible method of assessment of nasal response to provocation (Ghaem et al., 1986; Gleeson et al., 1986). This is probably due to the high rate of failure (Kumlien et al.: 25%; Kortekangas: 40%; Bachmann, Clement et al.: 30–50%; Gleeson: two out of 12 subjects; Ghaem quotes 50%) caused by oropharyngeal reflexes so frequently encountered with A.P.R.

With the use of the earlier mentioned small plastic plate we were able to collect A.P.R. data for all of our test subjects. In spite of this practical solution, histamine thresholds as determined with the three different methods of rhinomanometry

appeared to the significantly different. The reason for this discrepancy is not obvious. Those disparities are maybe inherent in differences proper to each of the methods of rhinomanometry. For instance, total nasal resistance as measured by A.P.R. is always higher than the resistance computed with A.A.R. (Ghaem: twice as high with A.P.R.; Jones: 16% higher). With respect to this higher total nasal resistance in A.P.R., Ghaem (1985) points out that the presence of the pharyngeal probe could give rise to some form of contraction of the soft palate, thereby leading to a narrowing of the nasopharynx. Whether our plastic plate enhances or reduces this eventual narrowing has yet to be investigated. For Jones (1987), the higher values are due to posterior rhinomanometry measuring the resistance of the nasopharynx as well as the resistance of the nose. Another possible reason for the discrepancy between histamine thresholds could ensue from the fact that measured total nasal resistances (A.P.R.) are compared with computed total resistances (A.A.R. and P.A.R.). Nevertheless, Jones (1987) states that the total nasal resistance as measured with A.P.R. was not significantly different from total nasal resistance derived with the parallel resistance equation from unilateral resistances (also measured with A.P.R., but with one occluded nostril). A last feature probably of importance is the fact that nasal response on bilateral stimulation always leads to an asymmetrical reaction: while the resistance of one of both nasal cavities rises markedly, the resistance of the other nasal cavity is far less affected. Since unilateral histamine thresholds - determined for the nasal side with the most marked reaction - are not significantly different with A.A.R. and P.A.R., one wonders what the influence of the "insensitive" side is on A.P.R. For instance, very often we observed only minor changes in the slope of the A.P.R. curves, while an obvious - but unilateral - response was apparent with A.A.R.

Finally, from a clinical point of view, even though we were able to perform A.P.R. with all of our test subjects, ther is no major advantage in using this bilateral (though "physiological") method. Other authors compared - with respect to nasal provocation - either A.A.R. with P.A.R. (Clement, 1985) or A.A.R. with A.P.R. (Ghaem et al., 1986; Gleeson et al., 1986). In accordance with their findings we can probably state that P.A.R. is the most practical method of rhinomanometry for (unilateral) histamine threshold assessment.

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