Rhinology, 25, 167-179, 1987

Relationship between nasal patency and clearance

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SUMMARY

Nasal airway patency and nasal clearance were measured bilaterally on six different test days in ten subjects. Nasal patency was evaluated using anterior rhinomanometry and clearance was measured using a dyed saccharin method. The results showed large intra- and inter-subject variances in the clearance times. Clearance times determined by the saccharin taste method were shorter than those determined by the dye method, but these measures were positively correlated. Also, the mean clearance rate was directly related to the mean nasal conductance. In seven of ten subjects, the clearance rate for a given side of the nasal passage was relatively faster when that side was the more patent. These results suggest that the clearance rate is a function of the patency of the nasal passage and may also exhibit alternating cyclic fluctuations.

INTRODUCTION

In the majority of adults, alternating congestion and decongestion of the nasal mucosa can be documented (Eccles, 1978). Moreover, for the left and right nasal passages these fluctuations are 180 degrees out of phase, such that when one side is relatively patent, the contralateral side is congested. This phenomenon is called the nasal cycle and is commonly studied by measuring, longitudinally, the resistances to airflow afforded by the two nasal passages. Because of the reciprosity in the resistances of the left and right nasal passage, the total resistance remains relatively constant and the large unilateral resistances are not appreciated by most individuals (Eccles, 1978; Haight and Cole, 1984; Hasegawa, 1982).

The physiologic basis for the rhythm of the nasal cycle is not understood completely. The majority of evidence suggests that the nasal cycle represents an autonomically mediated peripheral expression of a central cycle regulated by the hypothalamus (Stoksted, 1952; Eccles and Lee, 1981; Eccles et al., 1979). More controversial is the functional significance of this cycle to nasal physiology. One suggestion is that the cycle represents a spaciotemporal compartmentalization of nasal activity affording one side a rest while the other attends to the various functions of the nose including breathing, conditioning of the inspired air and mucociliary clearance of deposited materials (Williams, 1973). Accordingly, the cyclic reversals in the side dominance of nasal airway patency represent abrupt transitions between periods of rest and activity.

Implicit in this hypothesis is the suggestion that the mucociliary clearance function of the nose also exhibits cyclic fluctuations in side dominance which are synchronized in phase to those of nasal patency. While a number of investigators reported that the production of nasal secretions varied directly with the relative patency of the ipsilateral nasal passage (Heetderks, 1927; Lillie, 1923), to the authors' knowledge no previous study reported data evidencing periodic fluctuations in clearance rate. Consequently, the present study was designed to evaluate nasal patency and clearance concurrently in a group of adult patients with a negative history of nasal disease or pathology. The hypothesis tested was that nasal clearance is more rapid during periods of decreased mucosal congestion.

MATERIALS AND METHODS

Individuals for study were recruited from the student and faculty population of the University of Pittsburgh. Enrolled subjects were non-smokers, had a negative history for allergy, had no history of pulmonary disease, were free of signs and symptoms of upper respiratory infection for the preceding three months and showed no evidence of nasal obstruction or pathology on routine ear, nose, and throat (ENT) examination. Five male and five female subjects, 20–34 years of age, were studied. Institutionally approved informed consent was obtained for all participants.

The experiment was subdivided into six test sessions conducted between the hours of 13:00 and 18:00 on different days. For each session, the subjects reported to the ENT Basic Research Laboratory at the Children's Hospital of Pittsburgh. Room temperature and humidity were controlled centrally; temperature measurements varied between 22 and 24 degrees centigrade. After a 20 minute rest period, left and right nasal airway patencies were evaluated using active anterior rhinomanometry. Fifteen minutes later, these tests were repeated. A comparison of the bilateral nasal resistance values defined the dominant resistive side of the nasal cavity and thus, the subject's relative position within his/her nasal cycle. If this was unchanged for the two measures, the nasal clearance function was evaluated. If the subject's dominant side of nasal resistance was not the same for the two tests, the rhinomanometric tests were repeated before the clearance function was evaluated. After completion of the clearance test, nasal patency was evaluated again. If during the clearance test, a change in the side dominance of the nasal resistance was observed, the entire test protocol was repeated after a two hour rest period.

Nasal airway patency was evaluated for the left and right nasal cavities using a computer based rhinomanometric system developed in our laboratory. All tests were performed using an anterior rhinomanometric technique (Cole, 1982). For these tests, a plastic nozzle serially aligned to a pneumotach was gently applied to the nostril to be tested. Airflow through that nasal cavity was measured by a differential pressure transducer in parallel with the pneumotach. A nasal olive was applied against the contralateral nostril to estimate posterior nasopharyngeal pressure. Transnasal pressure was measured by a differential pressure transducer serially aligned between the nasal olive and the nozzle. Each test consisted of monitoring the transnasal pressure and airflow over a 40 second period of relaxed nasal breathing. Transducer signals were sampled every 20 milliseconds, amplified, digitized by an A-D converter board and channeled to the memory of a microcomputer (IBM PC). On-line monitoring of the subject's performance was available as a video display of the flow versus pressure plots for each breathing cycle. All sampled data for each test were stored on floppy disks. Task specific software allowed for the retrieval, editing and analysis of the collected data. A variety of calculated parameters was available for study including: work/liter, nasal power, and mean, mode or median resistances. The functions relating the values of these parameters to time were similar. Data for the mean inspiratory resistances were transformed to conductance values by taking the reciprocal of these values.

Clearance time was determined using a modification of the methods reported by Duchateau and colleagues (1985). Two and one-half microliters of a test solution was placed bilaterally in the anterior part of the nasal cavity, at the bottom of the inferior meatus on the mucosa just behind the internal ostium. The test solution consisted of 8 mg/ml indigo carmine, 3 mg/ml saccharin and 45 mg/ml sorbitol (pH adjusted to 7.4). The subjects swallowed as required and were asked to report the first occurrence of a sweet taste; then, the pharyngeal cavity was examined for the appearance of the blue dye. Repeat inspections of the pharynx at 30 second intervals were performed for 40 minutes or until the dye was observed bilaterally. Times from introduction of the dyed saccharin to the first report of a sweet taste, and to appearance of the dye in the left and right nasopharynx were recorded.

The data available for analysis consisted of bilateral measures of nasal patency and clearance for the ten subjects on six different testing days. While it is recognized that the tests of patency and clearance were not performed simultaneously, the study design assured that reversals in the side dominance of nasal patency dit not occur during the performance of the clearance test. Consequently, the measures of patency and clearance for each day were treated as synchronistically paired observations. The means of the left (LNC), right (RNC) and total (TNC) nasal conductances for observations recorded before and after the clearance test were computed and used as measures of their respective nasal patencies. Clearance time was used as an inverse measure of the clearance rate. Combined clearance time (CCT) was defined as the time elapsed between introduction of the test solution and the first report of a sweet taste. Clearance times for the left (LCT) and right (RCT) sides of the nasal cavity were defined as the time elapsed between introduction of the test solution and the appearance of the blue dye in the ipsilateral nasopharynx.

RESULTS

Nasal clearance time was estimated by two different methods, the first measuring the clearance time of the combined nasal cavity and the second measuring the clearance time for the left and right nasal cavities individually. Prior to exploring the relationship between clearance and nasal patency, the correspondence between these measures of clearance rate was defined. To estimate the amount of information shared by these measures, correlation coefficients were computed for both the between subject mean data set and the between-session intrasubject data set. Figure 1A shows the mean values of the LCT and

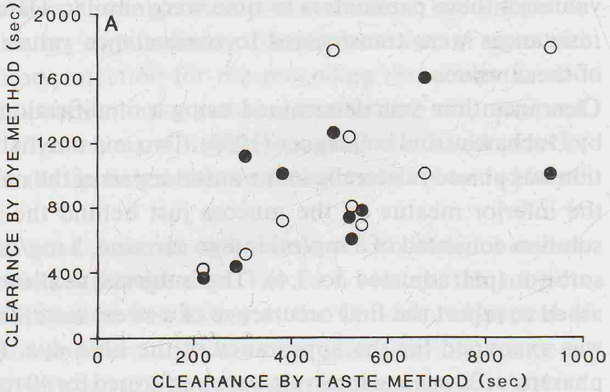

Figure 1 A. Distribution of clearance times estimated by the dye method for the left (open circles) and right (closed circles) nasal cavities as a function of the clearance time estimated by the taste method. Individual subject mean data.

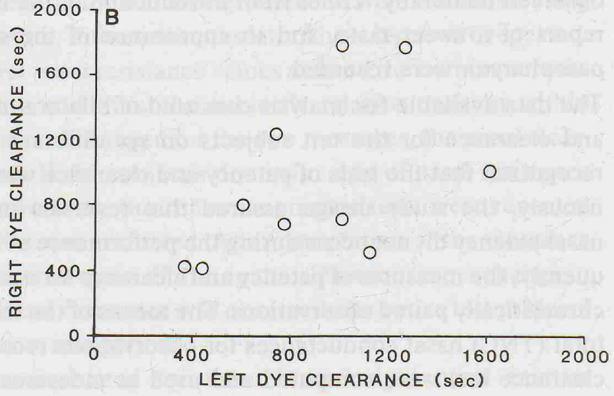

Figure 1 B. Distribution of clearance time for the right nasal cavity as a function of the clearance time of left nasal cavity. Individual subject mean data.

Table 1. Nasal clearance summary data[1] for the left (L), right (R) and combined (C) Nasal cavity.

						correlation			correlation
									differential
subject	side		mean	STD	range	left	right	min	values
1	L	1*	776	102	645-890	1			.44
	R	5	688	113	540-810	−0.17	1		
	C		547	97	435-734	0.77	0.17	0.77	
2	L	1	1610	810	580-2400	1			−.49
	R	5	1011	476	450-1860	−0.6	1		
	C		676	309	340-1260	0	0.64	0.53	
3	L	1	440	70	330-525	1			−.57
	R	3	412	92	330-550	−0.25	1		
	C		285	33	240-330	0.25	0.3	0.32	
4	L	3	1005	647	540-2400	1			−.40
	R	0	1790	862	540-2400	0.48	1		
	C		935	700	300-2400	0.99	0.58	0.99	
5	L	4	605	163	330-870	1			−.46
	R	1	806	219	540-1050	0	1		
	C		526	120	285-660	0.81	0.25	0.92	
6	L	2	1010	585	360-1700	1			−.57
	R	4	719	321	403-1350	−0.49	1		
	C		382	67	300-480	0.43	0.66	0.45	
7	L	0	1122	596	655-2400	1			−.88
	R	6	513	136	300-630	0.28	1		
	C		306	80	210-306	0.36	0.62	0.62	
8	L	4	366	81	240-510	1			−.17
	R	2	424	83	315-530	−0.43	1		
	C		219	34	180-270	0.81	0.14	0.54	
9	L	4	1265	644	540-2400	1			−.77
	R	2	1775	794	240-2400	−0.75	1		
	C		488	301	210-1100	0	0.57	0.73	
10	L	5	740	303	420-1320	1			0
	R	1	1240	581	510-1810	0.56	1		
	C		520	268	210-930	0.75	0.66	0.75	

[1] All data given in seconds.
* Number of observations when that side showed the more rapidly clearance rate.

RCT as a function of the CCT for each subject. The pearson correlation coefficients for these distributions are 0.47 for the LCT and 0.75 for the RCT. These are statistically significant and demonstrate that the respective functions are linear and characterized by positive slopes. Thus, the mean clearance times estimated by the dye method are related directly to the clearance times estimated by the saccharin taste method. Figure 1B shows the distribution of these mean data for the RCT as a function of the LCT. The pearson correlation coefficient for this distribution was 0.49 showing the mean clearance times of the left and right nasal passages of each subject to be positively related.

For the data available from the various test sessions, the correlation coefficients between the left, right, and total clearance times of each individual were determined. The values of these coefficients estimate the degree of association between the different measures of clearance times within a given subject and are reported in Table 1. The CCT of subjects, 1, 4, 5 and 8 was more highly correlated with the LCT, while for subjects 2, 6, 7 and 9 the CCT was more highly correlated with the RCT. For subjects 3 and 10, no side preference was noted. The correlation coefficients between the LCT and RCT were negative in six subjects, positive in three, and zero in one.

The larger degree of association between the CCT and either the LCT or RCT suggested that CCT may measure the clearance time of the more rapidly clearing nasal passage. This is supported by the fact that in six of the eight cases showing a preference, the preferred side had a lesser mean clearance time. To further define this possibility, the correlation coefficients between the CCT and the lesser value of the LCT or RCT for the six test sessions were computed for each subject. The value of these coefficients designated "min" are reported in Table 1. For eight of the ten subjects, these coefficients were less than those of the previously defined preferred side. These results suggest that for each individual, the CCT generally tracks the clearance time of that side of the nasal cavity characterized by the lesser mean clearance time, irrespective of the relative clearance rate at the time of testing.

The influence of test day on the measured parameters of nasal function was investigated. For each study day, the mean values of the various parameters were computed and examined for systematic fluctuations. The results are exemplified in Figure 2 for the CCT (a) and the TNC (b). The mean CCT ranged from 480 to 585 seconds and the mean TNC ranged from 0.35 to 0.52 L/sec/cmH_2O. The distributions of these data for the various study days were characterized by rather large standard deviations reflecting the intersubject variance. No systematic influence of test day on these parameters could be demonstrated. Interestingly, the function relating the mean CCTs to their respective mean TNCs was linear and characterized by a negative slope (Figure 2C). The pearson correlation coefficient for this data set was −0.88, indicating a statistically significant

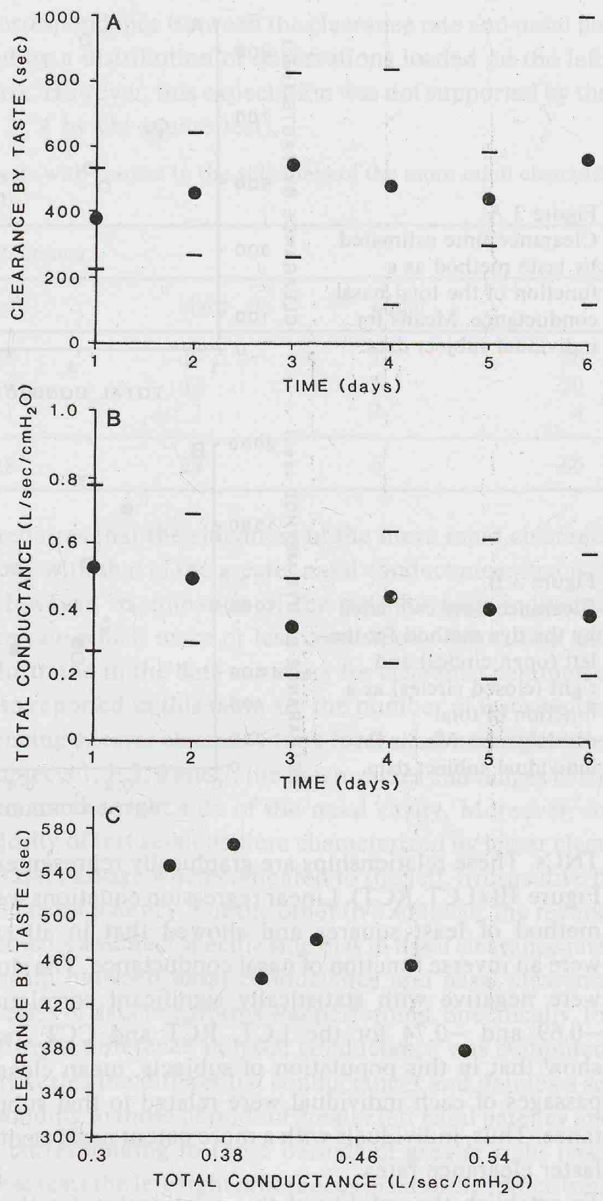

Figure 2 A.
Mean and standard deviations of the clearance times estimated by the taste method for the various study days.

Figure 2 B.
Mean and standard deviations of the total conductance for the various study days.

Figure 2 C.
Mean daily clearance time as a function of mean daily total conductance.

negative association ($p < .01$). Since clearance time is an inverse measure of clearance rate, these data support a direct relationship between the clearance rate and the patency of the nasal cavity.

To further explore this relationship, the mean values of the CCT, LCT and RCT for each individual were plotted as a function of their respective mean

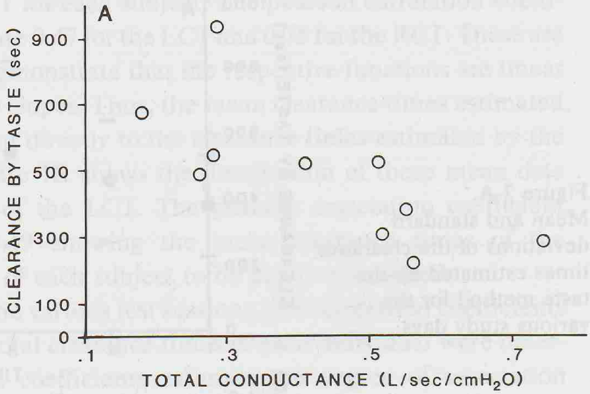

Figure 3 A.
Clearance time estimated by taste method as a function of the total nasal conductance. Means for individual subject data.

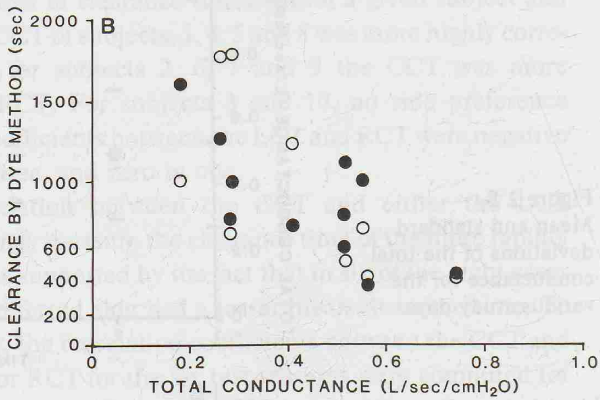

Figure 3 B.
Clearance time estimated by the dye method for the left (open circles) and right (closed circles) as a function of total conductance. Means for individual subject data.

TNCs. These relationships are graphically represented in Figure 3A (CCT) and Figure 3B (LCT, RCT). Linear regression equations were fitted to the data by the method of least squares and showed that in all cases the clearance times were an inverse function of nasal conductance. The slopes of the regression lines were negative with statistically significant correlation coefficients of −0.72, −0.69 and −0.74 for the LCT, RCT and CCT, respectively. These results show that in this population of subjects, mean clearance rates for both nasal passages of each individual were related to that subject's mean nasal conductance. Thus, individuals with a more patent nasal cavity also exhibited relatively faster clearance rates.

To establish the validity of this relationship for the intraindividual data, the results for all tests were examined for a correspondence between the side of the nasal cavity evidencing the more rapid clearance rate and that showing the greater nasal patency. In a preliminary analysis, the results for each test session were classified bivariatly with respect to these parameters. The resulting distribution for the 60 test sessions is reported in a three by three contingency table (Table 2).

A well defined positive correspondence between the clearance rate and nasal patency would be suggested by a distribution of observations loaded on the left-right diagonal of this matrix. However, this expectation was not supported by the observed distribution ($p > .4$ by chi square test).

Table 2. Distribution of tests with respect to the sidedness of the more rapid clearance and greater patency.

	clearance			
patency	left	right	equal	
left	18	17	1	36
right	6	11	3	20
equal	1	1	2	4
total	25	29	6	60

This test of relatedness requires that the sidedness of the more rapid clearance rate alternates in synchrony with that of the greater nasal conductance; that is, it tracks the nasal cycle. However, examination of the data for each individual shows a bias in clearance rate which more or less consistently favors one side over the other. This is illustrated in the data summary for clearance parameters presented in Table 1. Also reported in this table are the number of test sessions for each individual evidencing a lesser clearance time for the left and right sides of the nasal cavity. For subjects 1, 2, 3, 6 and 7, the mean values and ranges of the clearance times were less for the right side of the nasal cavity. Moreover, for these individuals the majority of test sessions were characterized by lesser clearance times for the right nasal passage when compared to the left, irrespective of the concurrent differential nasal patency. For the other five subjects, the reverse was true. This result documents a subject specific side bias in nasal clearance rate. To examine the relationship between nasal conductance and nasal clearance in this biased data set, a series of data transforms was performed. Specifically, for every test session the left-right difference in nasal conductance was computed. This procedure effectively scales the differential conductances and defines a set of positive values corresponding to those periods of greater left nasal patency and a set of negative values corresponding to those periods of greater right nasal patency. Similarly, for these tests the left-right differences in nasal clearance were computed. These differential clearance times were plotted as a function of their respective differential nasal conductance values for the data of each subject. Figure 4 shows this function for subject 7. A linear regression equation was fitted to these data by the method of least squares and the correlation coefficients were computed. These coefficients are reported in Table 1. In eight of the ten subjects, the functions relating differential clearance to differential conductance

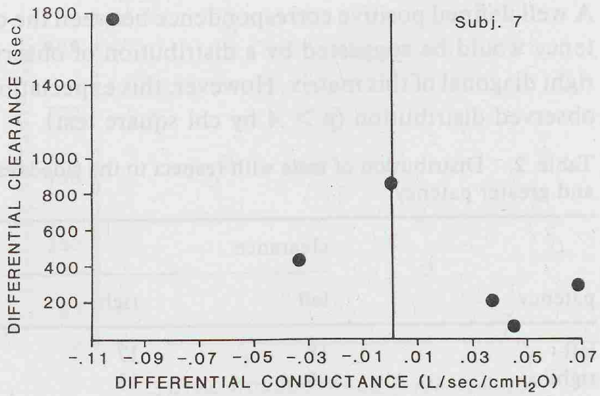

Figure 4.
Differential clearance time (left-right) as a function of differential conductance for the data set of subject 7.

were relatively linear with moderate to high correlation coefficients. Of these, the correlation coefficients were negative in seven subjects and ranged from −0.40 to −0.88. These functions were characterized by negative slopes indicative of a reciprocal relationship between the two variables. The data for the remaining two individuals (subjects 8 and 10) showed no well defined relationship between these variables as evidenced by their negligible correlation coefficients of −0.17 and 0.00. These results document that in the majority of subjects tested, the clearance times for a given side of the nasal cavity are relatively longer when the contralateral side is relatively more patent. Recognizing that clearance time is an inverse measure of clearance rate, these observations support the hypothesis that nasal clearance rate is directly related to the degree of ipsilateral nasal patency.

DISCUSSION

A variety of methods have been developed to measure the rate of mucociliary clearance in the nose (Proctor, 1982; Puchelle et al., 1981). In general, these methods utilize a tracer substance and a detector. One disadvantage of many of the methods is the inability to perform simultaneous bilateral assessments. As a consequence, information regarding the possible cyclic bilateral fluctations in clearance rate is largely lacking. Moreover, the influence of nasal patency on clearance function has not been addressed adequately. To obviate this deficiency, we used a modification of the previously described dyed saccharin technique which allowed for bilateral assessments. In a number of earlier studies, the dyed saccharin technique was reported to provide measurements well correlated with the results of other techniques (Duchateau et al., 1985; Puchelle et al. 1981; Van de Donk et al., 1982).

The introduction of the dyed saccharin into both sides of the nasal cavity presented no particular problems and in all patients the dye could be observed bilaterally in the nasopharynx on at least two trials. The ranges of nasal clearance times estimated by both the saccharin taste method and the dye method were similar to those reported in other studies (Duchateau et al., 1985; Andersen and Proctor, 1983). Clearance times estimated by the saccharin taste method were generally shorter than those recorded for the observation of dye in the nasopharynx. However, for the data available on each subject, good correlations between these measures were reported for at least one side of the nasal cavity.

In most previous studies, irrespective of the technique employed, a large inter-subject variation in measures of nasal clearance time has been reported. Also, a variety of factors which influence clearance rate have been identified (Proctor, 1977). Nonetheless, apriori assignment of a particular patient to either slow, normal or rapid clearance rate subclasses on the basis of these influencing factors has not been achieved. In this study we observed a large variability in mean clearance times for the ten study subjects. However, concurrent measurement of nasal patency as estimated by the total nasal conductance was shown to be strongly correlated with all measures of clearance rate. Using the square of the pearson product moment correlation coefficient as an estimate of explained variance, about 50 percent of the total variance in the mean values of the left, right and combined nasal clearance time could be attributed to the degree of nasal patency. This is a highly significant result and suggests that nasal patency should be evaluated and controlled in future studies designed to assess the influence of various factors on nasal clearance rate.

The results discussed above suggested that changes in nasal patency associated with the nasal cycle might be reflected in a change in the sidedness of the more rapidly clearing nasal passage. Indeed, Puchelle and colleagues (1981) reported a significant difference in mean clearance time between the "free" nasal cavity (18.6 min) and the "congestive" nasal cavity (37.0 min). However, that study used aluminium disks (.6 mm) as the tracer which may have been physically prevented from transversing the more congested nasal cavity. Further, the nasal patency assessments were subjective and not quantified. In the present study, these problems were overcome by using a dye as the tracer and the method of anterior rhinometry to objectively quantify differential nasal patency. Here, we could not document a relationship between the sidedness of the more rapid nasal clearance and that of the greater patency. Rather, for each patient a preferred side was identified which most often demonstrated the greater clearance rate. This side preference was not conditioned by the relative differential nasal patency. For a given individual the mean bilateral difference could average as much as 10 minutes. While the reasons for the existence of a side preference are not known, it clearly represents a source of variation in measures of an individual's nasal clearance rate when repeat measures are not limited to one nasal passage.

When the two sides of the nasal cavity are treated as individual data sets, a rather large intra-individual variance in clearance rate was also documented. This was reported for the results of a number of previous studies where individual subjects were treated as the experimental unit (Proctor, 1982; Andersen et al., 1971). In the present study, this large variance was most clearly documented in the data sets for the left side of the nasal cavity of subjects 2, 4, 7 and 9; and the right side of the nasal cavity of subjects 4 and 9 where at least one of the six observations showed no clearance of dye within the 40 minute time period. This variability could be partly explained as an effect of the relative patency of that nasal passage. This is supported by the fact that in general, the differential (left-right) nasal patency was positively correlated with the differential nasal clearance rate. This suggests that the clearance rate of a given side of the nasal cavity is dependent on the degree of patency of that side. Thus, clearance rate is influenced by the nasal patency cycle but this effect appears to be modulated by other factors, as yet, unidentified. Because of the potential significance of this observation to both nasal physiology and the methodology used in assessing nasal clearance function, experiments using each nasal passage as the experimental unit should be designed to specifically address this interesting phenomenon.

RÉSUMÉ

La conductivité nasale ainsi que la "clearance" nasale étaient mesurées dans les deux cavités nasales dans dix volontaires pendant six jours différents. La conductivité nasale était évalué par rhinomanométrie active antérieure et la clearance était évaluée par une technique employant de la saccharine colorée.

Les résultats du temps de clearance montrent de grandes variations intra- et interindividuelles.

Les temps de clearance mesurés à l'aide de la sensation de saccharine étaient plus courts que ceux déterminés par l'apparition du colorant dans l'oropharynx, mais ces mesures étaient correlées d'une manière positive.

Les moyennes des temps de clearance étaient aussi correlées avec la conductivité nasale moyenne.

Dans sept des dix sujets le temps de clearance pour un côté donné était plus court si la conductivité était plus grande de ce côté.

Ces résultats suggèrent que le temps de clearance est fonction de la conductivité de la cavité nasale et puisse aussi montrer des fluctuations cycliques alternées.

ACKNOWLEDGEMENT

This study was supported in part by Grant NS-16337 from the National Institutes of Health and a grant from Norwich Eaton Pharmaceuticals.

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