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Validation by fluid volume of acoustic rhinometry before and after decongestant in normal subjects*

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SUMMARY

To validate the measurement of nasal volume by acoustic rhinometry, acoustic rhinometry (AR) measures before and after decongestion were compared to a reference volume measurement in 10 healthy volunteers over 3 visits each. The reference method was hydraulic infusion with manometry, involving slow constant-rate infusion of isotonic saline into each nasal cavity while the subject was appropriately positioned. Consecutive 10mm nasal segments were measured, and hydraulic volume derived. AR volume and hydraulic volume measures were compared. Within subject reproducibility of hydraulic volume and AR volume measures over 3 study days was better than 16% and 11%, respectively.

Pre-decongestant, highly significant correlations between AR volume and hydraulic volume in the 20-40 mm segment were found. The mean ratios of AR volume/hydraulic volume ranged from 1.01 – 1.14. Post decongestant, significant correlations were found in the 30-50mm segments. The mean AR volume/hydraulic volume ratios were significantly lower (0.88-1.03). Hence, the magnitude of the AR volume change after decongestant was less than the hydraulic volume change (ratio range 0.8 to 1.01), but there were still significant correlations between hydraulic volume and AR volume in the 20-50mm segments of the cavity.

Since hydraulic volume is expected to be similar to anatomical nasal volume, we conclude that changes in AR volume before and after vasoconstriction are similar to anatomical changes in nasal vasculature. AR volume measurements provide a sensitive, reliable and accurate assessment of vasoactive drugs in the nasal cavity.

Key words: acoustic rhinometry, decongestant, nasal volume, manometry, clinical trial

INTRODUCTION

Reliable and accurate measurement of the nasal cavity is important for the objective assessment of pharmacological or surgically induced changes in nasal anatomy. A common technique for making such measures is acoustic rhinometry (AR). This is a convenient, non-invasive tool that evaluates nasal dimensions by emitting broad band sound into the nasal cavity and analysing the echo. An assessment of nasal cavity cross-sectional area (CSA) and volume can be derived from this. The validity of this method is dependent upon several factors including rigid cavity walls, no sound loss, and symmetrical branching of the airways. In practice, these requirements may not be entirely satisfied (Fisher, 1997).

The usual AR measure of nasal dimensions is the cross-sectional area of the nasal valve, where the minimal cross-sectional area of the nasal cavity is located (MCA). However, several studies have shown that AR measures of nasal volume may be more sensitive and discriminatory in detecting changes in both congestion and decongestion studies (Rasp, 1993). We have recently reported that AR volume measures are more sensitive in detecting the effects of low doses of a decongestant, compared to MCA and nasal airway resistance (NAR) (Taverner et al., 1999). Furthermore, when double doses of decongestant are administered, significant changes in AR volume, but not MCA or NAR, were detected.

There are numerous studies which have shown that AR MCA measures are reproducible and accurate (Brooks et al., 1989; Fisher, 1997; Millqvist and Bende, 1998; Silkoff et al., 1999). On the other hand, the validity of AR volume measurements of drug induced changes is unproven, as their comparison against another measurement has not been published. A study using a

Abbreviations: AR: Acoustic rhinometry; CSA: Cross-sectional area; MC: Minimal cross-sectional area; NAR: Nasal airways resistance; CT: Computed tomography; MRI: Magnetic resonance imaging

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water displacement method to compare the relationship of hydraulic CSA and AR CSA showed high correlations between the measurements (Hilberg et al., 1989). We have developed a variation of this technique to provide an accurate and reliable method of assessing nasal volume repeatedly before and after nasal decongestant for comparison with AR volume. The aim of this study was to assess the relationship between AR volume and hydraulic volume in defined segments of the healthy human nasal cavity before and after decongestion.

MATERIALS AND METHODS

Subjects

Ethics approval for the study was obtained from the Royal Adelaide Hospital Research Ethics Committee. All subjects gave informed, written consent. All subjects were 18 years of age or older, healthy and free from upper airway disease, nasal deformity and obstruction. Subjects were not suffering from upper respiratory tract disease, or taking medications affecting the nose at the time of the study.

Measurements

Constant Rate Isotonic Fluid Infusion Manometry (CRIFIM)

Isotonic fluid was infused at a low constant rate into the anterior nares (one nostril at a time) while the position of the head was fixed.

A modified infusion pump (Model 600-900, Harvard Apparatus Co. Inc., Dover, MS, USA) was set at a calibrated infusion rate of 0.693ml.sec^{-1}. This flow rate was sufficient to fill the nasal cavity during comfortable breath holding. Left and right versions of an external nasal adaptor (Rhinometrics, Lynge, Denmark) were modified to contain separate infusion and pressure measurement ports. The infusion port was connected to the infusion pump, while the pressure port was connected to a digital manometer with a range of –2.0 to 10cm of water. The manometer provided an analogue output for real-time acquisition by computer via an analogue to digital converter (Strawberry Tree, Acjr Data Acquisition Board, Sunnyvale, CA, USA; resolution of 2x10^{-4} cm of water).

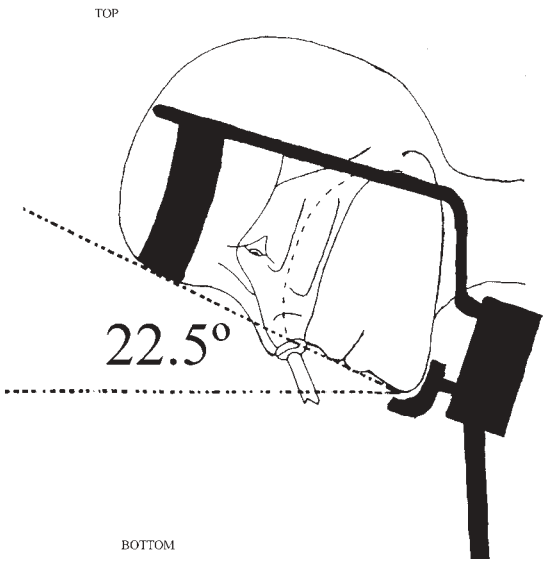

Figure 1. Position of subject's head during study. Indicating the position of the head holder, maintaining the sagittal plane of the subject's head at 22.5° to the horizontal.

The dashed line through the nasal cavity indicates the approximate acoustic axis of rhinometry measurements (Djupesland and Pedersen, 2000).

CRIFIM nose-piece is shown in position. The hydraulic axis runs vertically.

During the measurement procedure, the head of the subject was held comfortably on a sturdy ophthalmologic head holder assembly with the sagittal plane of the head (defined by the forehead and chin) fixed at a 22.5° angle above the horizontal (Figure 1). This angle ensured that the hydraulic level was orthogonal to the acoustic axis of the mid-portion of the nasal cavity, making measurements in the region 20-60 mm from the nares comparable with AR. Movement was minimised in this position. Soft white paraffin was used to obtain a watertight seal between the nasal adaptor and the nostril. Sterile isotonic saline at body temperature was used for infusions. To minimise the chance of sinus filling, the manometer contained an electronic cut-out to turn the infusion off when the pressure reached 6.4cm of water. The pressure in the water column at the bottom of the anterior nares was continuously measured. The infusion time took up to 20 seconds for each nostril and subjects were asked not to breathe, move or swallow during the recording. Recordings were repeated if this occurred.

As a control, a fixed tube with a known diameter was measured at different times during the study. The accuracy of hydraulic volume measurements (observed - expected/expected) was better than 5%, reproducibility (coefficient of variation (SD/mean)) was 5%.

Acoustic Rhinometry

Acoustic rhinometry measures of nasal dimensions were obtained from a SR-2000PC SR Electronics acoustic rhinometer (Lynge, Denmark). In line with current recommendations (Hilberg and Pedersen, 2000), daily calibration with a standard nose was carried out before use. For each nasal cavity measurement, three acoustic traces were recorded under standard conditions. The acoustic seal was broken and reformed between each trace. The recording that contained the median MCA measurement from sets with low variability was used.

Rhinomanometry

Rhinomanometry was performed to determine the influence of saline infusion on nasal function. Active posterior nasal airway resistance was measured using a NR6-2 rhinomanometer (GM Instruments, Glasgow, UK) at a reference pressure of 75Pa according to standard methods.

Study Design

The study was designed to compare two measurement systems assessing nasal volume before and after administration of a

nasal decongestant. On each study day, rhinomanometry and AR measures were performed in each nasal cavity, closely followed by CRIFIM measures (left and right nostril in random order). To determine the effect of saline infusion on nasal patency, AR and rhinomanometry measurements were made again within 5 minutes. The decongestant oxymetazoline hydrochloride nasal spray (Drixine, ScheringPlough, 50 µg each nostril) was administered and the same measurements of AR, CRIFIM and NAR were repeated 15 minutes later. Each study visit took no more than 90 minutes. All subjects attended for 3 study days and the three visits for each subject were completed within 14 days.

Data analysis

The CRIFIM curves were smoothed to remove transient small pressure peaks (< 0.1mm of water) by averaging the data. Smoothed time-pressure curves were converted to volume-vertical distance curves using the fixed infusion rate and density of the infusion fluid. The hydraulic volumes of consecutive 10mm segments of the nasal cavity were calculated (e.g. the volume between the nasal orifice and a point 10mm into the nasal cavity was expressed as segment 0- 10mm). The hydraulic CSA of the nasal cavity could not be reliably estimated because of low level noise in the pressure data.

For AR measures, the saved data files containing distance and CSA data were used to express the volume of defined segments from the nasal orifice (e.g. 0-10mm etc.). Left and right side data were analysed separately throughout. CRIFIM and AR data were assessed for mean intra-individual reproducibility (coefficient of variation, CV). Pearson's correlation coefficient (r) between AR and CRIFIM measures were derived and the significance of correlations was evaluated by two-tailed t tests.

To compare the changes in volume as measured by the two systems before and after decongestant, the ratio of AR volume/hydraulic volume was calculated for each segment. To compare the magnitude of change in AR and CRIFIM with decongestant, the ratio: (% change in AR volume)/(% change in hydraulic volume)) was derived. This data was log-transformed to ensure a normal distribution. Averages were calculated and the data was anti-log transformed for further analysis. All data are presented throughout as geometric ratios. Only when a significant correlation was found ($p<0.05$), was the associated ratio considered to be a valid descriptor of the AR volume and hydraulic volume measurements.

RESULTS

Eleven subjects were recruited, one failed to re-attend after visit 1. Ten subjects completed the study (5 males, 5 females; mean age 24.5 +/– 2.9 years). Comparisons of AR and NAR measures taken immediately before and after CRIFIM infusions showed that saline infusion did not alter nasal geometry or resistance significantly. The mean change in AR volume was –1.4% and the mean change in NAR was 0.8%. For all subsequent analysis the AR measures before CRIFIM were used.

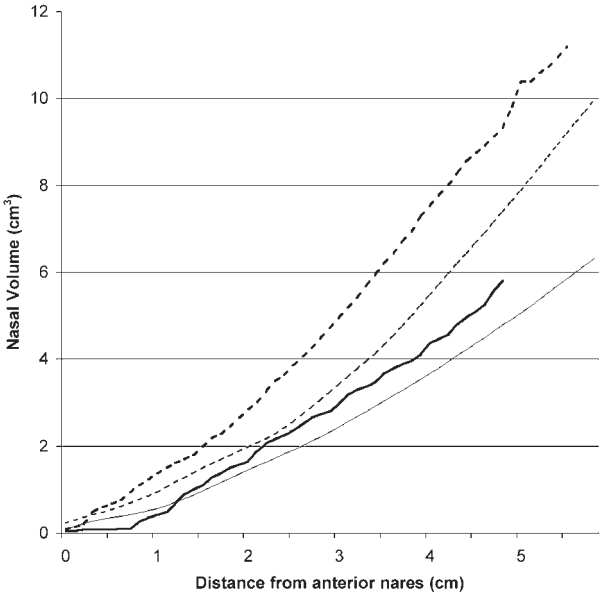

Figure 2. Nasal Volume (cm^3) measured by acoustic rhinometry and CRIFIM, pre decongestant and post decongestant (AR pre-decongestion (thin solid line); CRIFIM pre-decongestion (thick solid line); AR post-decongestion (thin solid line); CRIFIM post-decongestion (thick solid line)).

The MCA and volume measurements by AR were reproducible over the 3 study days in each individual, the mean CV for 0-40mm segments was 11% and 16% for AR and CRIFIM respectively. An example of AR and CRIFIM distance-volume data in one subject (Subject 9, Visit 3, left side) is shown in Figure 2. The increase in both AR volume and hydraulic volume after drug administration in all segments of the cavity is apparent.

The mean volumes before and after decongestant for all subjects showed similar and predictable changes, which were significant for all segments (Table 1). The volumes measured by AR and CRIFIM before and after decongestant were expressed as ratios and correlations between the measures were calculated (Table 2). Pre-decongestant, there were highly significant correlations in segments between 20-30mm and 30-40mm of the nasal cavity and the mean AR volume/hydraulic volume ratios ranged from 1.01 to 1.14. Post-decongestant, there were highly significant correlations between AR and CRIFIM measurements for segments 30-40mm, 40-50mm and 0-40mm. The mean AR volume/hydraulic volume ratios for the significantly correlated segments ranged between 0.88 and 0.94. The post decongestant ratios differed significantly from the paired pre-decongestant ratios ($p<0.0001$).

Volume changes following decongestion as measured by AR and CRIFIM, showed highly significant correlations between the segments 20-30mm, 30-40mm, 40-50mm (Table 3). The mean AR volume/hydraulic volume ratios for the significantly correlated segments between 20mm and 40mm ranged between 0.80 and 0.101. The change detected by hydraulic volume was significantly larger than the change detected by AR volume ($p<0.0001$).

Table 1. Mean volume (cm^3) of defined segments from anterior nares of left and right nasal cavities measured by acoustic rhinometry (AR) and CRIFIM (n=30). (pre = pre-decongestion, post = post-decongestion).

Segments		**10—20mm**		**20—30mm**		**30—40mm**		**40—50mm**		**0-40mm**	
	Side	**AR**	**CRIFIM**	**AR**	**CRIFIM**	**AR**	**CRIFIM**	**AR**	**CRIFIM**	**AR**	**CRIFIM**
Pre	**L**	0.78	0.57	0.66	0.63	0.80	0.93	0.97	1.47	3.12	3.03
	R	0.78	0.64	0.67	0.78	0.94	0.85 (n=27)	1.17	1.20 (n=24)	3.30	3.24
Post	**L**	0.76	0.93	0.82	1.21	1.15	1.38	1.27	1.46 (n=27)	3.58	4.72
	R	0.77	0.99	0.80	1.35	1.22	1.64	1.42	1.56 (n=24)	3.66	5.24

Table 2. Ratios and correlations between AR and CRIFIM volume measurements before and after decongestion. 95% confidence intervals of ratios expressed as AR/CRIFIM. *p*-value indicates the significance of the corresponding correlation. (pre = pre-decongestion, post = post-decongestion).

	Segment	**10-20mm**	**20-30mm**	**30-40mm**	**40-50mm**	**0-40mm**
	n	60	60	51	29	51
Pre	**95% CI**	1.10, 1.18	0.99, 1.07	0.97, 1.07	0.92, 1.1	0.99, 1.08
	***r* (*p*-value)**	-0.01(>0.05)	0.56 (<0.0001)	0.48(0.0003)	0.20 (>0.05)	0.43 (0.002)
	n	59	57	52	35	52
Post	**95% CI**	0.88, 0.95	0.79, 0.87	0.88, 0.96	0.88, 1.0	0.80, 0.92
	***r* (*p*-value)**	0.08 (>0.05)	0.12 (>0.05)	0.46(0.0006)	0.45 (0.007)	0.35 (0.01)

Table 3. Ratios and correlations between AR and CRIFIM changes in volume after decongestion. 95% confidence intervals of ratios expressed as AR/CRIFIM. *p*-value indicates the significance of the corresponding correlation.

Segment	**10-20mm**	**20-30mm**	**30-40mm**	**40-50mm**	**0-40mm**
n	59	56	48	19	48
95% CI	0.76, 0.84	0.76, 0.85	0.85, 0.95	0.87, 1.15	0.81, 0.90
***r* (*p*-value)**	-0.07 (>0.05)	0.36 (0.006)	0.62 (>0.0001)	0.61 (0.006)	0.26 (0.07)

DISCUSSION

A validation study in cadavers has shown significant correlations between computed tomography (CT) and AR measures of nasal volume (Mayhew and O'Flynn, 1993). In living humans with nasal obstruction, significant correlations between AR volume and high resolution CT volume occurred within the anterior portion of the nasal cavity (0-40mm) but not beyond (Prasun et al., 1999). To date, no validation studies of AR volume measurements have evaluated drug-related changes in the nasal cavity.

In our study, volume measurements by AR and CRIFIM both before and after decongestant were reproducible only for points beyond 20mm from the anterior nares.

In the proximal section of the cavity (0-20mm), reproducibility was low in both methods. A significant artefact was observed in the CRIFIM measures at the point when liquid reached the nasal cavity from the nosepiece. The infusion technique was not designed to assess the volume of the nares anterior to the nasal valve, since the direction of infusion was not orthogonal to the walls of the cavity. In addition, in AR measures, an arte-

fact is commonly observed from the anterior nares to about 10mm up the cavity due to distortion by the nosepiece or occlusion from the sealant (Hamilton et al., 1997).

In the current study, AR volume was highly predicted by hydraulic volume in the 20-40mm range of the nasal cavity before and after decongestant. To compare the accuracy of measurements by AR compared to CRIFIM, volumes were expressed as ratios of AR volume/hydraulic volume. Before decongestant, significant correlations were found between AR volume and hydraulic volume in the 20-40mm segment of the cavity. The mean ratio for nasal volume measured was close to unity, suggesting that the hydraulic volume at this point of the nasal cavity was equivalent to the AR volume. This is in contrast to a magnetic resonance imaging (MRI) study that found poor correlations between MRI measures and AR volume before decongestant (Corey et al., 1997). Corey considered that this poor correlation was due to inter-observer variation in the CSA as measured by the MRI used to determine volume. After decongestion in our study the mean AR volume/hydraulic volume ratio of 10mm cavity segments fell to less than unity, but the AR volume measures remained highly correlated to CRIFIM measures in the 30-50mm segment of the nasal cavity. This suggests that after decongestant, hydraulic volume was slightly underestimated by AR. Consequently, the absolute changes in AR volume associated with decongestion were lower than changes detected by hydraulic volume measures.
A similar phenomenon was noted when the ratio of change was noted before and after decongestion.

There are several possible reasons for the consistent differences between volumes seen after decongestion by AR and CRIFIM. One possibility is that hydraulic volume over estimates the anatomical volume of the nose after decongestion. Saline absorption in the nasal cavity during infusion is possible, however this is unlikely since AR volumes did not change before or after CRIFIM. The angle of the nasal cavity during infusion could lead to overestimation of the hydraulic volume. The direction of infusion of the fluid should conform to the direction of the acoustic wave for the estimates of volume to be comparable. The acoustic axis varies along the nasal cavity. In this study, the head was held at an appropriate angle to ensure that measurements were comparable in the region beyond the nasal valve. Alternatively, AR may have underestimated the real anatomical volume. Irregularities in the nasal mucosal surface may be more apparent after decongestant, leading to a failure of the assumption that the nasal cavity possesses a regular branching structure, resulting in possible underestimation of volume after vasoconstriction (Fisher, 1997). AR may underestimate the anterior CSA (3-24mm) compared with CT measurements in healthy volunteers after decongestant (Min and Jang, 1995).

In comparison to the congested state, the acoustic path into the nasal cavity is shorter and more direct in states of decongestion, when the inferior turbinate provides less obstruction to airflow (Tomkinson and Eccles, 1998). This may lead to errors in the comparison of nasal volumes at a given distance from the start of the cavity before and after decongestion, and our study has not excluded this. These authors also recommend caution in the interpretation of nasal volume changes distal to the constriction represented by the MCA after decongestion, since these changes may be artefactual. On the other hand our study suggests that the changes in AR volume with decongestant seen in the range 20-50mm from the nasal orifice distal to the MCA are genuine.

In summary, this study validating acoustic volumes before and after decongestion finds that they are closely correlated with, and almost identical to, hydraulic nasal volume. The principle of hydraulic nasal infusion provides an alternative measure of anatomical nasal volume and may be a suitable standard with which to compare AR volume measurements. The changes in AR volumes that occur with nasally active drugs are due to underlying changes in the anatomical volume of the nasal cavity. AR volume measurements are useful as a sensitive, reliable and accurate assessment of vasoactive drugs in the nasal cavity.

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