Controlling the Variability of Air-Pulses to Determine the Thresholds of Laryngeal-Pharyngeal Reflexes using a Novel Device

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***Abstract*— Factors determining the variability of air-pulse pressure to determine the thresholds of laryngeal-pharyngeal reflexes, which are related to swallowing and airway protection, were explored. Potential factors affecting the reproducibility of air-pulses were experimentally evaluated and included in a multiple linear regression model. A novel device controlling these factors and minimizing variability was designed. Its reproducibility was assessed by the coefficient of variation (CV) of the pressures and duration of air-pulses, and its validity was assessed by comparing obtained pressures and durations with desired pressures and durations. Differences in the pressures of air-pulse categories were assessed by a one-way ANOVA of repeated measures, a Tukey test and a box and whisker plot. The distance and angle between the exit of the tube conducting the pulses and the surface to be impacted, the diameter of the tube, the feeding pressure of the system, and the duration of air-pulses significantly affected the accuracy of air-pulses. The novel device incorporated electronic valves and a telemeter for use during the fiberoptic endoscopic evaluation of swallowing. The differences between the desired and obtained pressures and durations were below 3%. The CV of the air-pulse pressures of the novel device was 0.02. The CV of air-pulse duration was 0.05. The one-way ANOVA, Tukey test and box and whisker plot showed that the outlet pressures of air-pulse categories had statistically significant differences between them without overlap between categories, which helps to obtain an accurate threshold.**

INTRODUCTION

Clinical exploration of the laryngeal adductor reflex (LAR) threshold by air pulse stimuli was introduced by Aviv as part of the Functional Endoscopic Evaluation of Swallowing. This technical modification led him to change the test's name to "Fiberoptic Endoscopic Evaluation of Swallowing with Sensory Testing (FEES-ST)" [1], [2]. It has been shown that this test reaches good intra-observer reproducibility when performed by skilled observers but not when performed by novel observers; additionally, inter-observer reproducibility has been poor even with skilled observers [3]. With skilled observers, this technique has shown good predictive capacity for outcomes, such as penetration, aspiration and pneumonia [4], [5]. However, this finding has not been replicated in some studies, which could be related to the reproducibility problems already mentioned [6], [7].

The problems that compromise the reproducibility of this sensory test are likely related to factors that induce variation in the pressure of the air-pulse over the laryngeal mucosa. This variation could happen because of unnoticed changes in the distance or angle between the tip of the endoscope and the point of impact of the air pulse on the mucosa. In fact, the distance and the point of impact need to be calculated without sight or any other visual aids, and the patient's discomfort could lead him to move the structures where the pulse has to be delivered. Furthermore, the air-pulses have being generated by compressors of different specifications and conducted to the mucosa through tubes of different diameters.

The technological aids for controlling the factors compromising reproducibility should include a device to adjust air-pulse pressures at a fixed duration with millimeter of mercury precision in the range of 0 to 30 mmHg [1]−[4], [8]−[11] and a component improving the precision in the distance and angle of the pulse impact on the mucosa.

An experiment was performed to elucidate the factors affecting the reproducibility of air-pulses. A novel device controlling these factors was designed, and its reproducibility and validity were evaluated.

METHODS

A. Experimental design

An air-pulse generator is an electronic device with a proportional pressure regulator (VPPE Festo, Denkendorf, Germany) and a solenoid valve (MHA1, Festo, Denkendorf, Germany), which is regulated by modifying the potential difference applied to the pressure regulator from 0 to 10 V with PLC software (EasyVeep software package from Festo, Didactic GmbH & Co. KG, 73770 Denkendorf, Germany, 2003).

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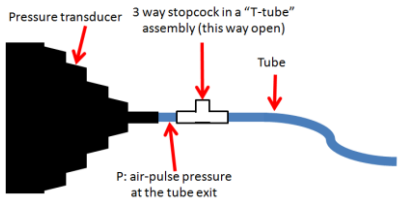
In summary, the experimental assembly consisted of a tube conducting the air-pulses from an air-pulse generator to a pressure sensor through a 3-way stopcock (Baxter International Inc., Deerfield, IL, USA). All the 3-ways were left open (Fig. 1) to measure the outlet pressure. The superficial pressure on the surface of impact was measured at different distances (1 to 10 mm) and angles.



(a)

(b)

Figure 1. (a) Assembly of components to measure the outlet pressure at the tip of the tube. (b) 3-way stopcock

The first step was to determine the required voltage to reach each of the desired air-pulse pressure categories at the exit of the tube. The desired pressures corresponded to what has been required to explore the LAR threshold, which is a series of air-pulses ranging from 1 to 10 mmHg (see Table I). The duration of the valve opening for each pulse was set to be constant at 50 ms, 100 ms and 135 ms [2], [10].

TABLE I. VOLTS REQUIRED TO REACH EACH OF THE DESIRED PRESSURE LEVELS

Volts	*Desired pressure at the tube exit (mmHg)*	*Mean measured pressure at the tube exit (mmHg)*
0.95	1.00	1.16
1.60	2.00	2.12
2.40	3.00	2.94
3.20	4.00	4.05
3.70	5.00	4.80
4.35	6.00	5.83
5.00	7.00	6.99
5.45	8.00	7.85
6.00	9.00	8.96
6.50	10.00	9.99

B. Variables selected to evaluate the device's reproducibility

Because pressure and duration of the air-pulse were the variables determined to elicit LAR, they were chosen to assess the validity and reproducibility of the device. Both variables were measured at the tube exit.

All the measurements were taken using a high sensitivity pressure transducer (Kistler, type 5015, Kistler Group, Winterthur, Switzerland) and its specific software (charge meter 5015 A measure, RS-232C, V1.33, Kistler Group, Winterthur, Switzerland).

The validation aimed to demonstrate:

1) The factors determining the outlet and superficial pressures.

2) Good repeatability of air-pulse pressures within each category of air-pulse pressure, including a small dispersion of pressures and similar values for mean, median and mode of air-pulse pressures.

3) The mean pulse pressure obtained for each air-pulse category being close to the desired air-pulse pressure for that category.

4) Good repeatability of air-pulse duration, including a small dispersion of air-pulse durations and similar values for mean, median and mode of air-pulse durations.

5) The mean air-pulse duration being close to the desired air-pulse duration.

6) Statistically significant differences and no overlap between the air-pulse pressures of adjacent categories.

C. Statistical methods

The pressure and duration of air-pulses were the dependent variables. They were analyzed as quantitative continuous variables, and their results were presented as the mean ± standard deviation (SD), median and mode. To assess validity, these results were compared with the desired values. Potentially relevant factors determining outlet and superficial pressure were experimentally evaluated and introduced in a multiple linear regression model (including the feeding pressure of the system, feeding voltage, tube (or catheter) diameter, the duration of air-pulses and the distance and angle between the tube exit and the surface to be impacted).

The presence of correlation between the SD and mean of the air-pulse pressure and duration was evaluated to determine the reproducibility of the pressure and duration variables. This correlation was determined by calculating the Kendall's (τ) correlation coefficient between the SD and mean of each of the pressure and duration variables [12]. Because there was correlation between the mean air-pulse pressure and its SD (τ=0.60, P=0.016) and between the mean air-pulse duration and its SD (τ=0.539, P=0.031), the reproducibility of air-pulse pressures and duration was determined by the coefficient of variation.

The coefficient of variation ($\boldsymbol{CV_i}$) for each category of air-pulse pressure (1 to 10 mmHg) was calculated by the following equation:

$$\mathrm{CV_i} = \frac{s_i}{\bar{x}_i}$$

where $\boldsymbol{CV_i}$ corresponds to the CV for the air-pulse category, $\boldsymbol{S_i}$ corresponds to the SD of the variable for the category, and $\bar{x}_i$ corresponds to the mean of the variable for the category.

The global CV was calculated by the following equation:

$$CV = \frac{\sum_{i} CV_i}{n}$$

where ***n*** corresponds to the number of air-pulse pressure categories.

The CV of air-pulse durations was calculated in a similar form for each air-pulse duration category (50 ms, 100 ms and 135 ms) and globally.

Because obtaining an accurate threshold requires clear differences in the pressures of air-pulse categories, one-way ANOVA of repeated measures and a Tukey test were performed.

A sample size of five measurements for each air-pulse pressure category was used to detect differences of 0.1 mmHg in the air-pulse pressures between adjacent categories of air-pulses with a standard deviation of 0.027, a confidence level of 99%, and a power of 90%.

RESULTS

The mean, median and mode were very close, and the differences among them were below 10% of their values.

The multiple linear regression model showed that the determinants of the outlet pressure were the feeding pressure of the system, the feeding voltage of the pressure regulator and solenoid valve, the tube diameter and the duration of air-pulses. The principal determinant of the superficial pressure was the outlet pressure, but this pressure was also significantly affected by the tube diameter and the distance and angle between the exit of the tube and the surface. All these factors reached statistically significant differences with $P < 0.003$.

The validity evaluation of the novel device, which aimed to control these variability determinants, showed average differences of 1% between the desired and measured pressures. The outlier value was for the category of 1 mmHg (P01), which had a difference between the desired and measured value of 20% (Table II). The difference between the desired and the measured duration of air-pulse was 1.36 ms (2.7% of the desired value) (Table IV).

The reproducibility evaluation showed a global CV for air-pulse pressures of 0.02. The category of 1 mmHg of desired pressure had the highest CV (0.05), but the categories of 2 to 10 mmHg of desired pressure had CVs below 0.03 (Table III). The global CV of air-pulse duration was 0.05 (Table IV).

An ANOVA test and a Tukey test (Table V) showed a statistically significant difference between air-pulse pressure categories, and a box and whisker plot (Fig. 2) showed the absence of the overlap of pressures between adjacent categories.

TABLE II. CHARACTERIZATION (CENTRAL TENDENCY AND DISPERSION) AND VALIDITY OF AIR-PULSE CATEGORIES

Category of air-pulse	*Desired pressure (mmHg)*	*Mean pressure at the tube outlet (mmHg)*	*SD (mmHg)*	*Median pressure at the tube outlet (mmHg)*	*Mode pressure at the tube outlet (mmHg)*	*Difference between obtained and desired pressures (%)*
P01	1.00	1.20	0.06	1.20	1.10	20%
P02	2.00	2.10	0.07	2.10	1.90	5%
P03	3.00	2.90	0.07	2.90	2.80	-3%
P04	4.00	4.00	0.12	4.10	3.80	0%
P05	5.00	4.80	0.11	4.80	4.50	-4%
P06	6.00	5.80	0.09	5.80	5.60	-3%
P07	7.00	7.00	0.10	7.00	7.00	0%
P08	8.00	7.80	0.13	7.80	7.80	-3%
P09	9.00	9.00	0.18	8.90	8.90	0%
P10	10.00	10.00	0.12	10.00	9.90	0%
Mean						1%

TABLE III. COEFFICIENT OF VARIATION OF AIR-PULSE PRESSURES AT THE TUBE OUTLET BY AIR-PULSE CATEGORY

Category of air-pulse	*CV of air-pulse pressures*
P01	0.05
P02	0.03
P03	0.02
P04	0.03
P05	0.02
P06	0.02
P07	0.02
P08	0.02
P09	0.02
P10	0.01
Pooled (global)	**0.02**

Notes: CV: coefficient of variation.

TABLE IV. AIR-PULSE DURATION IN MS AT THE TUBE OUTLET

	Duration of air-pulses (ms)
Desired duration	50.00
Mean	48.64
Median	48.00
Mode	48.00
Standard deviation	2.38
Difference between obtained and desired duration	2.70%
Global CV	**0.049**

Notes: CV: coefficient of variation

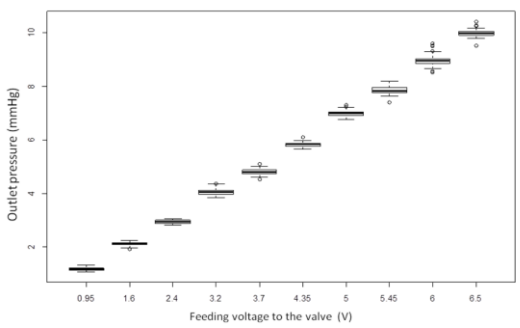


Figure 2. Box and whisker plot of the outlet pressure (tube exit) according to the feeding voltage of the valve (V) for the 700 □m internal diameter tube

TABLE V. TUKEY TEST FOR POST-HOC CONTRASTS BETWEEN AIR-PULSE CATEGORIES

Air-pulse Category	Tukey Test	Feeding Voltage (V)	Mean Outlet Pressure (mmHg)
P10	A	6.50	9.99
P09	B	6.00	8.96
P08	C	5.45	7.85
P07	D	5.00	6.99
P06	E	4.35	5.83
P05	F	3.70	4.80
P04	G	3.20	4.05
P03	H	2.40	2.94
P02	I	1.60	2.12
P01	J	0.95	1.16

DISCUSSION AND CONCLUSIONS

The principal determinants of the superficial pressure, which is the pressure responsible for the elicitation of LAR, were the feeding pressure of the system, the feeding voltage of the valves, the duration of air-pulses, the diameter of the tube conducting the air-pulses, and the distance and angle between the exit of the conducting tube and the surface.

The novel device showed good reproducibility with a CV of air-pulse pressures at the exit of the tube of 0.02 and a CV of air-pulse duration of 0.05. The validity was also good, with average differences of 1% between the desired and measured pressures and of 2.7% between the desired and measured duration. These results permit an accurate exploration of the LAR threshold, whose normal threshold is 2.97 ± 0.78 mmHg and requires a device capable of administering air-pulses of 50 ms duration at 1 to 10 mmHg of pressure at the tube tip without the overlap of pressure between adjacent categories [1], [2], [9].

This new device generates air-pulses with the pressure and duration of a commercial device (Pentax AP-4000), which was recently retired from the market and not substituted by any alternative. The advantages of this new device include: 1) the absence of drift compared with a 10% mean drift for the previous device, 2) a CV below 3% compared with 20% for the previous device, 3) an error magnitude below 0.2 mmHg compared with more than 2 mmHg for the previous device and 4) no failure to generate a stimulus compared with a 17% failure rate for the previous device [10].

There is another device designed by Hammer to overcome the limitations of the previous commercial device [10]. Unfortunately, the validation publication of Hammer's device did not include its reproducibility and validity measures. Additionally, it has only been tested in a few healthy and sick people and obtained LAR thresholds different from those obtained by the commercial device. These differences in the air-pulse characteristics and LAR thresholds of Hammer's device compared with those of the commercial device prevent the extrapolation of the results of the clinical validation of the commercial device to Hammer's device. Furthermore, the flexibility of the air-pulse duration of Hammer's device [10] could affect the accuracy of air-pulse pressures because this study found that the air-pulse duration is one of the most important determinants of air-pulse pressure accuracy.

The reliability of the pressure and duration of air-pulses generated by our device, in addition to the ease of handling provided by the software, should improve the reproducibility of the clinical exploration of the LAR, but this device has to be tested in a clinical validation study.

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REFERENCES

[1] J. E. Aviv, J. H. Martin, T. Kim, R. L. Sacco, J. E. Thomson, B. Diamond, *et al.*, "Laryngopharyngeal sensory discrimination testing and the laryngeal adductor reflex," *Ann Otol Rhinol Laryngol,* vol. 108, pp. 725-30, Aug 1999.

[2] J. E. Aviv, J. H. Martin, M. S. Keen, M. Debell, and A. Blitzer, "Air pulse quantification of supraglottic and pharyngeal sensation: A new technique," *Annals of Otology, Rhinology and Laryngology,* vol. 102, pp. 777-780, 1993.

[3] J. J. Cunningham, S. L. Halum, S. G. Butler, and G. N. Postma, "Intraobserver and interobserver reliability in laryngopharyngeal sensory discrimination thresholds: a pilot study," *Ann Otol Rhinol Laryngol,* vol. 116, pp. 582-8, Aug 2007.

[4] J. E. Aviv, R. L. Sacco, J. Thomson, R. Tandon, B. Diamond, J. H. Martin, *et al.*, "Silent laryngopharyngeal sensory deficits after stroke," *Ann Otol Rhinol Laryngol,* vol. 106, pp. 87-93, Feb 1997.

[5] J. E. Aviv, J. Spitzer, M. Cohen, G. Ma, P. Belafsky, and L. G. Close, "Laryngeal adductor reflex and pharyngeal squeeze as predictors of laryngeal penetration and aspiration," *Laryngoscope,* vol. 112, pp. 338-41, Feb 2002.

[6] P. K. Ku, A. C. Vlantis, S. F. Leung, K. Y. Lee, D. M. Cheung, V. J. Abdullah, *et al.*, "Laryngopharyngeal sensory deficits and impaired pharyngeal motor function predict aspiration in patients irradiated for nasopharyngeal carcinoma," *Laryngoscope,* vol. 120, pp. 223-8, Feb 2010.

[7] P. W. Perlman, M. A. Cohen, M. Setzen, P. C. Belafsky, J. Guss, K. F. Mattucci, *et al.*, "The risk of aspiration of pureed food as determined by flexible endoscopic evaluation of swallowing with sensory testing," *Otolaryngology - Head and Neck Surgery,* vol. 130, pp. 80-83, 2004.

[8] J. E. Aviv, R. L. Sacco, J. P. Mohr, J. L. Thompson, B. Levin, S. Sunshine, *et al.*, "Laryngopharyngeal sensory testing with modified barium swallow as predictors of aspiration pneumonia after stroke," *Laryngoscope,* vol. 107, pp. 1254-60, Sep 1997.

[9] J. E. Aviv, "Sensory discrimination in the larynx and hypopharynx," *Otolaryngology - Head and Neck Surgery,* vol. 116, pp. 331-334, 1997.

[10] M. J. Hammer, "Design of a new somatosensory stimulus delivery device for measuring laryngeal mechanosensory detection thresholds in humans," *IEEE Transactions on Biomedical Engineering,* vol. 56, pp. 1154-1159, April 2009.

[11] P. R. Kearney, C. J. Poletto, E. A. Mann, and C. L. Ludlow, "Suppression of thyroarytenoid muscle responses during repeated air pressure stimulation of the laryngeal mucosa in awake humans," *Ann Otol Rhinol Laryngol,* vol. 114, pp. 264-70, Apr 2005.

[12] J. M. Bland and D. G. Altman, "Statistics Notes: Measurement error proportional to the mean," *BMJ,* vol. 313, p. 106, July 13, 1996 1996.