A NOVEL METHOD USING NORMAL SUBJECTS FOR THE EVALUATION OF NASAL DECONGESTANTS

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INTRODUCTION

An accepted standard for the measurement of airway resistance is whole body plethysmography. Techniques, other than plethysmographic, for the determination of airway resistance require the introduction of appliances into to oropharynx. Such non-physiologic intrusions are not readily tolerated by other than carefully trained subjects, and hence restrict their applicability to a large clinical population. To overcome these limitations, a

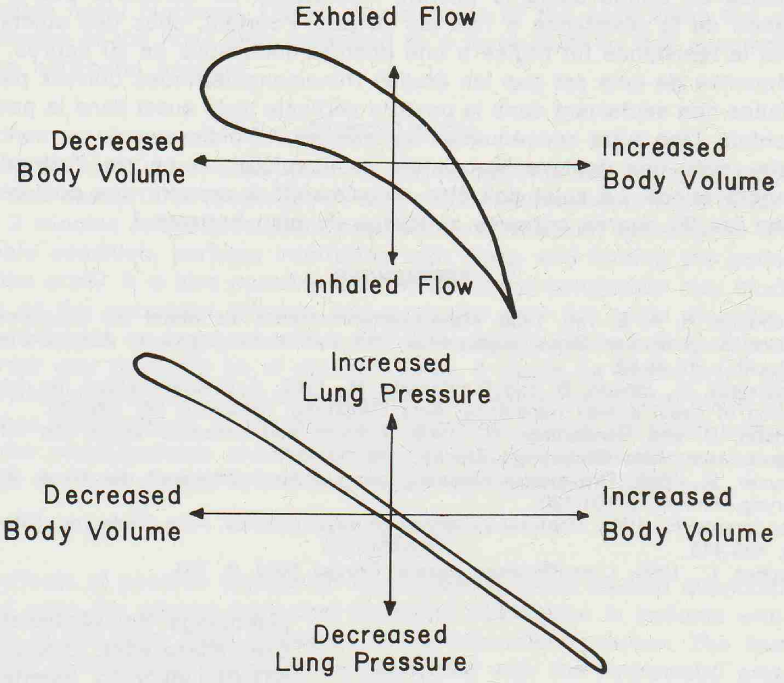

Figure 1. Representative lissajous patterns of respiratory data. Upper loop (open shutter); lower loop (closed shutter).

non-intrusive technique was devised employing whole body plethysmography for the determination of nasal airway resistance.

Technique

Resistance is the ratio of the pressure-drop across an airway to the flow through that airway. Since this ratio is a non-linear function of flow, it is necessary to know at which flows the determination is made. We have chosen 0.5 L/sec for both the inspiratory and expiratory phases of the respiratory cycle. Our extracorporeal technique utilizes sequential series of breaths (Figure 1). The first series (open shutter) permits the simultaneous measurements of flow and box pressure (body volume). The second series (closed shutter) permits the silmultaneous measurements of alveolar pressure and box pressure. Accordingly, airway resistance is the quotient of the closed to open shutter relationships, i.e.

$$\text{resistance} \quad \frac{\text{alveolar pressure/box pressure}}{\text{flow/box pressure}}$$

where box pressure, the common denominator, cancels out.
Traditionally, panting is preferred since small volume changes do not unduly influence the pressure times volume relationship (Boyle's Law). Resistance to nasal airflow is determined after the subject (with the mouth closed) executes a series of rapid and shallow breaths (through the nose) into a special anaesthetic face mask.

Study design

This study consisted of two parts. Part I comprised 6 normal adult volunteers in whom measurements were made at 2 hourly intervals during the course of a 10-hour day. Pre- and post-prandial measurements were recorded for two of three daily meals. Measurements were made when each nostril was sequentially occluded and also during normal nasal breathing (i.e. when neither nostril was occluded).
Part II utilized 3 of the 6 subjects examined in part I. Each subject received two activations of oxymetazoline hydrochloride (Afrin) (0.5 mg/cc) into each nostril. Duplicate measurement were made prior to and at post-drug times of 1/12, ¼, ½, ¾, 1, 1½, 2, 3, 4, 5, 6, 7, 8, 10, 11 and 12 hours. Determinations were made only when breathing was through both nostrils.

Discussion

Airway resistance of the left naris was defined as $(R_A)_{n.s.}$, and of the right naris as $(R_A)_{n.d.}$. When neither nostril was occluded, and the breathing was normal nasal breathing, the term ambinaric was applied and the corresponding symbol was $(R_A)_{n.a.}$. A mathematical combination (not physiologic) of the resistances of the individual nares when the contralateral naris was occluded was defined as binaric in character and the symbol used was $(R_A)_{n.u.}$. Measured data for these terms appear in the table and it is apparent that $(R_A)_{n.a.}$ does not equal $(R_A)_{n.u.}$ for either series or parallel combinations of $(R_A)_{n.d.}$ and $(R_A)_{n.s.}$. This conclusion appears valid regardless of the marked diurnal variations of the individual mononaric and ambinaric resistances.

Based on these finding, part II employed ambinaric measurements only. Figure 2 presents the results following medication and also shows the unmedicated, ambinaric, diurnal variations for each of 3 subjects as measured in part I. Significantly, the range of pre-medication values for each subject approximated that found for the individual during the part I study of diurnal variations — even though these data were obtained 16 weeks previously. The results following medication confirm the marked, long-acting, nasal decongestant effect of oxymetazoline hydrochloride. This methodology is of

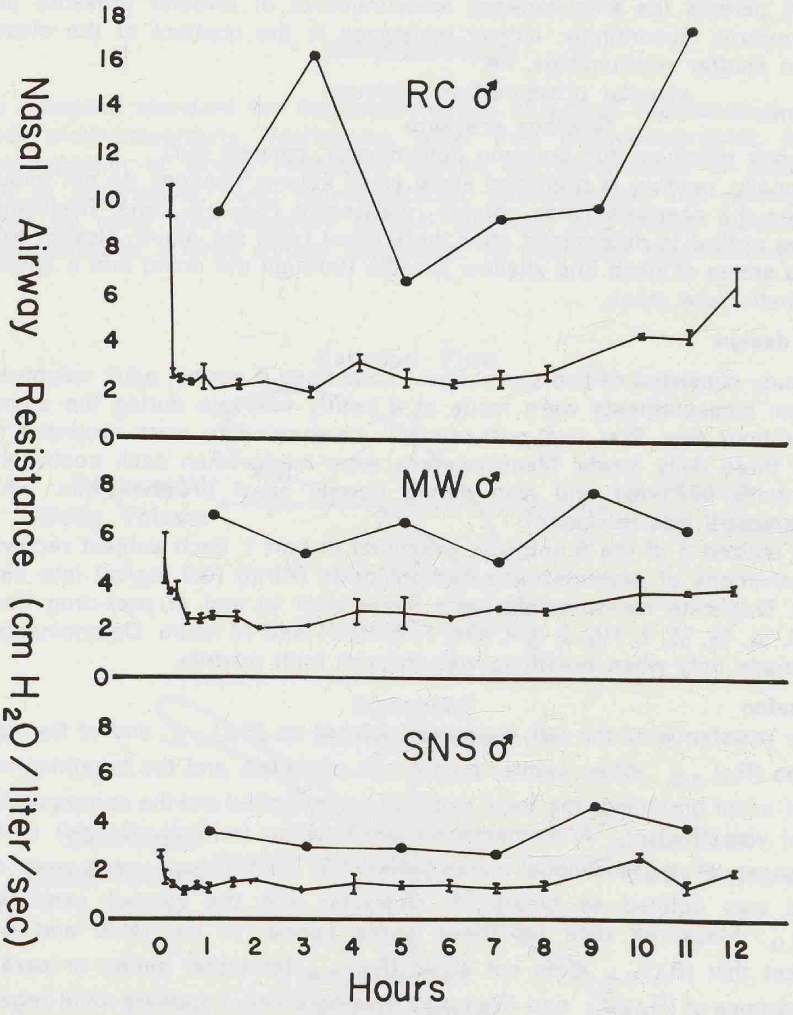

Figure 2. Upper plots - without medication; lower plots - with medication (v.: text).

practical importance in that it permits the evaluation of nasal decongestants in individuals who manifest neither signs nor symptoms of nasal congestion ("normal" subjects).

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