Supramaximal Flows: Comparison between Asthmatics and Patients with Chronic Obstructive Pulmonary Disease

Alejandra González Alejandra Fernández Sergio Guardia Hernando Sala

Hospital Alejandro Posadas, Buenos Aires, Argentina

Key Words

Asthma · Chronic obstructive pulmonary disease · Supramaximal flow

Abstract

Background: The major motive that prompted this study was to investigate whether or not the differences in supra-maximal flow (SF) behavior between patients suffering from asthma and patients suffering from chronic obstructive pulmonary disease (COPD) might aid in clarifying the differences in the physiopathology of the two diseases. **Objectives:** The aim of the present study was therefore to compare SFs in asthma and COPD patients with similar degrees of air-flow limitation. **Methods:** Twelve asthmatic patients were individually matched with 12 COPD patients by forced expiratory volume during the first second (FEV₁) as a percent ($\pm 5\%$) of the reference value (Δ FEV₁) and by age (± 4 years). The subjects performed baseline maximal expiratory flow-volume curves (MEFV) and then repeated the same maneuvers through a valve that occluded the air flow 6 times per second with an open/closed time ratio of 4/1. We then plotted an envelope of the expiration-interrupted curve passing through the SF peaks, measured the increase in flow at 50% of the forced vital capacity between the baseline curve and the envelope curves (Δ Vmax₅₀), and compared the FEV₁ of

the interrupted curve to the FEV₁ obtained from control MEFV curves (Δ FEV₁). **Results:** We found significantly higher values for Δ Vmax₅₀ ($p < 0.03$) and Δ FEV₁ ($p < 0.01$) in the asthmatics compared to the COPD patients. **Conclusions:** The differences reported here are best explained by a greater preservation of elastic recoil pressure at a similar degree of air-flow limitation in the asthmatics than in the COPD patients.

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Introduction

When a maximal expiratory flow-volume (MEFV) curve is performed starting from a volume lower than the total lung capacity, a transitory peak flow is observed that exceeds the flow in the MEFV curve for the same lung volume. This flow is referred to as the supramaximal flow (SF) and can occur during a cough, in submaximal expiratory curves, or after obstruction of the airway during a forced expiration. SFs have been described in normal subjects as well as in experimental animals, and they become increased in patients with increased air-flow limitation [1–3].

Diverse mechanisms have been proposed in an attempt to explain the genesis of these SFs. In 1974, Knudson et al. [4] attributed SFs to an emptying of the flow-

limiting segment downstream from the choke point of the airway during a forced exhalation. Pedersen et al. [5] measured the volume of air contained in SFs when induced by interrupted expiratory curves at 15 Hz and demonstrated that this volume was higher than the volume of the flow-limiting segment. Therefore, they postulated that mechanisms other than the emptying of the flow-limiting segment played a role in the occurrence of SFs and also suggested that changes in the configuration of the airway, from a transient unstable one leading to the peak expiratory flow, to a configuration that is more stable and permits a lower flow. This stable configuration then persists until the next interruption.

A third possible mechanism, referred to as *pendelluft*, could play a predominant role. This term applies to when the maximum forced lung evacuation becomes more heterogeneous, the fast pulmonary units lose more volume than the slow ones in a given exhalation period so that during the interruptions the former become refilled with air from the latter, which, in turn, at the moment of interruption have a greater volume and hence a higher elastic recoil pressure. Immediately after the flow is re-established, the fast units contribute to the generation of greater flow rates [6–8].

The physiopathologic mechanism that limits the expiratory flow in asthmatics and in COPD patients is different: with asthmatics, the predominant mechanism is an increase in resistance within the airway, whereas with COPD patients there is both an increment in that resistance and a reduction in the elastic recoil pressure because of the emphysema. Our hypothesis is that the SF pattern is different in the two diseases.

Materials and Methods

The study involved 12 stable asthmatics matched on an individual basis with 12 COPD patients. The patient pairing was done according to age and the degree of obstruction of the airway, such that the age discrepancy was lower than 4 years and the differences in the expiratory flow volume in one second (FEV_1) were less than 5%. The clinical pictures of the patients included were consistent with the clinical and functional criteria for asthma and for COPD outlined by the GINA [9] and GOLD [10] guidelines, and none of the subjects had previously used either short- or long-action bronchodilators within the previous 6 or 12 h, respectively. Patients with a worsening of their primary disease or with any other concomitant pulmonary disease were excluded from the study. All of the subjects accepted and signed a consent form included within their clinical records. The study protocol was approved by the Hospital Posadas teaching and research committee, and the ethics committee confirmed that the procedures used complied with all the criteria of proper clinical practice.

Fig. 1. Baseline maximal expiratory flow-volume curves (solid line) and 6-Hz interrupted curves (dotted line). The plotted envelope curve (dotted line) passes through the SF peaks. $\Delta V_{\max 50}$ = Increment in the flow at 50% of the forced vital capacity between the two curves.

The patients performed a baseline MEFV curve according to the criteria of the American Thoracic Society [11]. The maneuvers were performed through the use of a dry piston-type spirometer (Sensormedics, USA) with a linear-response frequency up to 7 Hz, a resistance of less than 2 cm of water at a flow of 12 l s^{-1} . The inertial characteristics of the spirometer were evaluated by means of an explosive decompressor (ATSOK, Argentina) [12].

Next, the subjects repeated the same maneuver, exhaling from their total lung capacity down to the residual volume by means of a specially designed circuit that contained an electromechanical valve. This valve consisted of a central axis with two wings having an alternating swinging movement that first opened and then closed the expiratory line. The movement was regulated by a potentiometer controlled by an electronic circuit. The cycling frequency and the percentage of time the valve remained closed was set at 6 Hz, a 4/1 ratio of open-to-closed time, and an aperture and closure time of 15 ms each. Owing to the effect of the cycling of the valve over the pressure transducers, the flow cannot be measured with a pneumotachograph [12].

After each interruption a transitory SF was observed. We plotted an envelope curve that passed through the SF peaks and measured the increment in flow between the baseline and those envelope curves. The flow increment measured at 50% of the forced vital capacity between both curves is the $\Delta V_{\max 50}$ (fig. 1).

Interrupted curves were deemed acceptable only if the difference in the forced vital capacity between the baseline and interrupted curves was $<5\%$. We first compared the FEV_1 (in absolute values) obtained from baseline curves and the FEV_1 from interrupted curves (i.e. the ΔFEV_1).

We then analyzed the morphologies of the curves and classified them as two types: type A if the flow recorded after the transitory peak value returned to baseline levels and type B if the SF persisted after the transitory peak flow as a supramaximal value until the following interruption always when compared to the uninterrupted curves and to similar lung volumes.

Fig. 2. ΔFEV_1 values in asthmatic and COPD patients. $p < 0.01$.

Fig. 3. ΔSF values in asthmatic and COPD patients. $p < 0.03$.

Table 1. Summary of the anthropometric and spirometric data from both groups

	Asthma	COPD	p
Age, years	59 ± 7.6	59 ± 7.7	0.9
Sex (M/F)	6/6	10/2	0.08
Height, cm	161 ± 9	162 ± 9	0.7
$FEV_1\%$	42 ± 20	40 ± 19	0.8
FEF_{25-75}	20 ± 13	17 ± 11	0.5
ΔSF	1.76 ± 0.4	1.43 ± 0.21	0.03
ΔFEV_1	6.16	-2.01	0.01

Since the quantitative data analyzed in all instances fell within a normal distribution, we could utilize the paired Student's t test for the comparison of the measurements. The prevalence of different types of curve morphologies between the asthmatics and the COPD patients was verified by the χ^2 test.

All the values presented are expressed as the mean $\pm$ the standard deviation.

Results

Table 1 summarizes the anthropometric and spirometric data from both groups.

The comparisons with respect to age (59 ± 7.6 vs. 59 ± 7.7 years) and the FEV_1 value (42 ± 20 vs. $40 \pm 19\%$) between the asthmatic and COPD groups, respectively, given the pairing, were not statistically different. Moreover, no patient evinced an adverse reaction to the technique applied.

Figure 2 shows the plot of ΔFEV_1 between the basal and interrupted curves for the asthmatics (6.16 ± 7.11) and the COPD patients (-2.01 ± 4.32). The difference here was highly statistically significant ($p < 0.01$).

Figure 3 compares the ΔV_{max50} between the two respective groups, with the asthmatics exhibiting significantly higher values (76 ± 40 vs. $43 \pm 21\%$; $p < 0.03$).

An analysis of the curve morphologies indicated that, of the 12 patients in each of the two groups, the curves from 9 of the asthmatics and 4 of the COPD patients were of type B morphology, but this difference in prevalence was not statistically significant.

Discussion

The existence of SFs has been described by different authors. Knudson et al., working with normal subjects, proposed that the origin of SFs is the displacement of gas volume from the flow-limiting segment owing to the expiratory collapse of the airway [4]. Pedersen et al. considered that the change in configuration of the airway consequent to the interruptions of flow was a contributing element and furthermore that a substitution of rigid tubes for the collapsible airway would eliminate the SF peaks [5].

Wellman et al. showed that the SF peaks obtained in partial maximal expiratory-flow curves decreased in successive maneuvers, thus implicating the involvement of the viscoelastic properties of the airway wall in the genesis of the SF peaks [13].

The SFs were seen to vary with the degree of air-flow limitation such that with greater degrees of limitation

higher SFs were observed [6, 7]. Likewise, working with normal subjects to obtain interrupted curves by means of a fast valve, we observed that the longer the valve-closure period, the greater became the magnitude of the SF [6]. We also noted that the SFs obtained correlated with the degree of air-flow limitation, SFs increase as FEV₁ and FEF_{25–75} decrease. This same phenomenon was later demonstrated in a subsequent study involving asthmatic patients [7].

When we induced an increment or decrement in the nonhomogeneity in the lung emptying with the respective drugs methacholine and salbutamol, we observed that the SFs followed a reproducible pattern: they increased after an inhalation of methacholine and decreased after an inhalation of salbutamol. In other words, they increased when the nonhomogeneity of lung emptying became enhanced and decreased upon the induction of bronchodilation [7]. We therefore proposed that the occurrence of an emptying of the fast units into the slow ones during the interruptions – the mechanism referred to as *pendelluft* – could be one of the principal elements involved in the genesis of the SFs.

When the interruption valve is open, the fast lung units – i.e. those of lower flow resistance – contribute more to the generation of flow than do the slow units. Upon closure of the valve, the slow alveolar units remain with a greater volume and hence a higher elastic recoil pressure than the fast units and thus fill those units up with air by emptying themselves into them.

In normal subjects the maximal expiratory flow down to a given lung volume depends on the driving pressure plus the resistance of the airway. The former is a function of the lung's elastic recoil pressure, while the latter is determined by the caliber of the airway.

The physiopathologic mechanism producing a limitation in expiratory flow in asthmatics is a narrowing of the airway through a contraction of the bronchial smooth muscle along with inflammation, edema, and secretions; while the reduction in pulmonary elastic pressure contributes significantly less [14, 15].

Green and Mead, working with normal subjects, described that the maneuver of maximal inspiration modifies the permeability of the airway, producing a bronchodilatory effect through the relaxation of the bronchial smooth muscle, whereas in asthmatics this response is variable [2]. Boni et al. studied the effect of the preceding inspiratory speed and the end-inspiratory pause in a forced expiratory maneuver with healthy subjects and COPD patients and found that the speed of the preceding inspiration did not influence the subsequent expiratory-

flow peak or the FEV₁ in either healthy subjects or COPD patients, unless the former became >2 s. By contrast, any end-inspiratory pause decreased these indices in all individuals [16].

In our study, the resistance of the airway could not be evaluated since even the forced oscillation technique is unable to measure airway resistance while the interruption valve is in operation. According to the bronchodynamic studies mentioned above, however, if the preceding deep inhale were to induce bronchodilation the SFs should diminish, whereas with bronchoconstriction the opposite effect would occur.

COPD patients exhibit ventilation-distribution disorders as a consequence of alterations in both the airway and the lung parenchyma. The limitation in flow occurs fundamentally because of an inflammatory effect in the small airway (mucosal edema, remodeling, and mucus impact) that modifies the latter's viscoelastic properties, while the diminution in the elasticity of the lung parenchyma is brought about by a loss of functional alveolar units that generates a decrease in the pulmonary elastic recoil pressure [14, 15].

The difference in the mechanism of flow limitation between asthma and COPD is what led us to suppose that if the interchange of gas volume between the units of different time constants upon sudden interruption of expiratory flow by a valve is one of the main contributory elements in the generation of SFs, then COPD patients and asthmatics should evince different responses: the emphysema in the former would reduce the ability of the alveolar units of different time constants to interchange gas volumes among themselves in *pendelluft* fashion and as a consequence would diminish the lung's capacity to generate SFs.

Accordingly, the present study has demonstrated that, with the same degree of pulmonary obstruction, the asthmatics exhibited significantly higher values for $\Delta V_{\max 50}$ and ΔFEV_1 than did the COPD patients. Neither an emptying of the flow-limiting segment of the lung nor changes in the configuration of the airway – two mechanisms proposed for the genesis of SFs [4, 5] – could account for this observation. The greater filling up of the fast units upon flow interruption in the asthmatics would appear to be the predominant mechanism responsible for both effects.

The morphology of the interrupted curves was different between the two groups as well. The curves from the asthmatics were predominantly of type B, with the SFs extending in time after the peak of air flow up to the next interruption – in contrast to the COPD curves, where the

type A morphology prevailed. This difference, however, was not significant, which we would attribute to an insufficiently large sample size. Even so, an investigation of curve morphology was not the primary objective of this study.

We conclude that the differences reported here are best explained by a greater preservation of elastic recoil pressure at a similar degree of air-flow limitation in asthma than in COPD. The increment in FEV₁ between the interrupted and uninterrupted curves in the asthmatics prompts us to investigate possible clinical applications of

this type of intervention to the differential diagnosis between these two illnesses as well as the role that rapid and transitory interruptions of expiratory flow might play in the treatment of the asthma exacerbations [17].

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