CARBON DIOXIDE CAPNOMETRY TO ASSESS THE EFFECT OF OZONE INHALATION ON THE PERIPHERAL AIRSPACES

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INTRODUCTION

The inhalation of ozone (O_3), a ubiquitous air pollutant, may lead to chronic health effects in well individuals and may exacerbate health problems in people with preexisting lung disease. An important challenge in laboratory studies of human O_3 exposure is the noninvasive determination of adverse alterations in lung function. Whereas forced expired flow and specific airway resistance are well-established indicators of O_3-induced decrements in conducting airway function [3], measurements specific to the peripheral airspaces are lacking. The purpose of the current research was to evaluate a noninvasive measurement of peripheral airspace response that was based on CO_2 capnometry.

Farmery [1] developed a model of the CO_2 expirogram in which the slope of the alveolar plateau is attributed to the continuing accumulation of CO_2 in a well-mixed peripheral region as expiration proceeds. In particular,

$$dF/dV = F_M\theta/(V_{MP}+V_T/2) \quad (1)$$

where dF/dV is the slope of expired CO_2 fraction with respect to expired volume in the plateau region, F_M is the mean expired CO_2 fraction, θ is fraction of the breathing period occupied by expiration, V_T is the expired tidal volume, and V_{MP} is the end-expiratory volume of the well-mixed peripheral lung region. In the present research, the effect of O_3 exposure on V_{MP} for a group of 47 healthy people was determined.

MATERIALS AND METHODS

Twenty-three women and twenty-four men, all healthy nonsmokers between the ages of 18-33, participated in two research sessions in which they exercised for one hour on a bicycle ergometer in order to elicit a total ventilation of 30 liters per minute. While exercising, the subjects breathed through a mouth-only mask through which they were exposed to room air during the first session and air containing 0.3 parts per million O_3 during the second session. The mask was instrumented such that respiratory flow and O_3 concentration could be monitored throughout each breath. The overall uptake of O_3 (OZU) was computed as the integral of the product of the respiratory flow and the respired O_3 concentration.

Measurement of the CO_2 expirogram was duplicated immediately preceding the air or O_3 exposure, 10 minutes following exposure, and 70 minutes following exposure. During this measurement, the subjects were at rest and breathed through a mouthpiece assembly that monitored respiratory flow and respired CO_2 fraction. The subjects were coached to breathe at inspiratory and expiratory flows of 250 ml/sec with an inspiration time of 3 seconds and an expiration time of 5 seconds. A separate value of V_{MP} was determined for each CO_2 expirogram using equation 1.

RESULTS

The average$\pm$sd of the pre-exposure values of V_{MP} among all subjects in the air and O_3 exposure sessions was 4330$\pm$1030 ml. The relatively large variation of V_{MP} was similar at all 3 measurement times and in both research sessions. Variations associated with the pre-exposure V_{MP} were evaluated by an ANOVA including a components-of-variance analysis that employed subject and session as random factors. The results indicated that between-subject, between-session, and within subject variations contributed 60%, 0%, and 40% of the total variance, respectively. Moreover, between-subject differences were significant ($p=0.000$) whereas between-session differences were not significant ($p=0.331$).

The V_{MP} values separately averaged for each subject over the two research sessions were significantly correlated with subject height ($r=0.596$, $p<0.001$) as well as with subject weight ($r=0.425$, $p=0.003$). This is similar to what has been observed for standard lung volumes such as functional residual capacity.

Although V_{MP} decreased slightly as a result of exercise alone (Fig. 1; Air), a two-tailed Student's t-test indicated that this effect was not statistically significant at 10 minutes ($p=0.226$) or 70 minutes post-exposure ($p=0.132$). On the other hand, the combination of exercise and O_3 (Fig. 1; Ozone) caused a dramatic decrement in V_{MP} that was significant at 10 minutes post-exposure ($p=0.000$) and remained

significant at 70 minutes post-exposure (p=0.000). The 10-minute and 70-minute post-exposure measurements were not significantly different from one another (p=0.527).

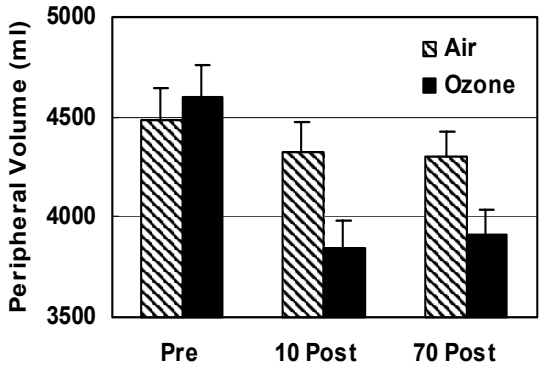

Figure 1. Changes in V_{MP} During Air and Ozone Exposures

The difference in responses between air+exercise and O_3+exercise was evaluated with a t-test that compared the post-pre exposure changes in peripheral volume (ΔV_{MP}) observed in the air and O_3 sessions. The results demonstrated that there were significant differences between air and O_3 responses both at 10 minutes post-exposure (p=0.000) and at 70 minutes post-exposure (p=0.000).

A possible dose-response relationship between ΔV_{MP} and OZU was examined using a Pearson's correlation of the post-pre exposure data obtained during the O_3 session (Fig. 2). Whereas ΔV_{MP} based on the 10-minute post-exposure measurement was significantly related to OZU (r=0.323, p=0.015), ΔV_{MP} based on the 70-minute post-exposure data was not (r=0.231, p=0.118).

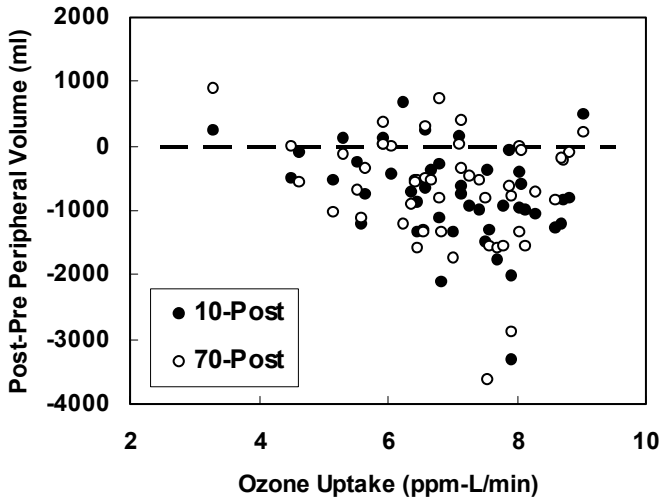

Figure 2. Dose-Response of the Peripheral Volume

The slope of the alveolar plateau of expired breath curves is frequently attributed to stratified inhomogeneities due to diffusion limitations or regional inhomogeneities due to mechanical effects. In the case of the CO_2 expirogram, in particular, the accumulation of CO_2 in the peripheral lung during the expired breath is a third source of the alveolar slope. Employing a single-path convection-diffusion model, Huang and associates [2] demonstrated that stratified inhomogeneities are neglible compared to the effect of CO_2 accumulation when the tidal volume is greater than 10 ml/kg; the average tidal volume in the present study was 18 ml/kg. Thus, V_{MP} values computed from equation 1 are due in part to a true, well-mixed, peripheral lung compartment but they must also be affected by regional inhomogeneities. This explains why the average pre-exposure V_{MP} value that we computed was nearly twice as large as a normal functional residual capacity. In spite of the influence of regional inhomogenities, we found that pre-exposure values of V_{MP} were correlated with height and weight, as one would expect if V_{MP} was related to lung size. Moreover, the goal of this study was to use changes in V_{MP} as a marker of physiological response so that baseline contributions of regional inhomogeneity should have a small influence on the results.

We observed a small but insignificant decrease in the average V_{MP} in the air exposure session when exercise alone was the physiological disturbance. However, only 60% of the subjects exhibited negative values of ΔV_{MP}, so that the individual responses were not consistently negative. With the combination of exercise and O_3 exposure, however, there was a significant and dramatic decrement in V_{MP} that was consistently observed in about 85% of the subjects.

The major problem with the measurement of V_{MP} is its large variability. This variability is amplified even more when one is trying to tease out the response in terms of a change in V_{MP}. Although measurements on different days contributed little to the overall variability, differences between subjects and between replicate measurements within the same subject contributed equally to variability. Thus, improvements in the precision of our instrumentation and in the reproducibility of a subject's breathing manuver during the expirogram measurement could markedly reduce variability, possibly eliminating some of the (inconsistent) positive changes in V_{MP} that were observed during O_3 exposure.

Finally, we were able to demonstrate that between-subject differences in ΔV_{MP} were related to OZU (Fig. 2). In particular, about 10% of the variation in ΔV_{MP} was explained by differences in OZU. The weakness of this relationship is not surprising for two reasons. First, changes in overall O_3 retention in the respiratory system may not parallel changes in O_3 uptake in the peripheral lung, the site of the ΔV_{MP} response. Second, other subject-specific factors such as antioxidant capacity and cell sensitivity may influence an individual's response to O_3 exposure.

ACKNOWLEDGEMENTS

This work was funded in part by Health Effects Institute research agreement #98-20.

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