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CORRESPONDENCE

CO_2-response in chronic obstructive pulmonary disease

To the Editor:

MONTES DE OCA and CELLI [1], in their paper on CO_2-responses, present data on the control of breathing in patients with normocapnic and hypercapnic chronic obstructive pulmonary disease (COPD), and in normal subjects. They conclude that the baseline ventilatory drive and CO_2-responses are preserved in most patients with severe COPD. However, effective ventilation is inadequate in the more severely obstructed patients, resulting in hypercapnia.

Apart from the incorrect conversion factors for cmH_2O into kPa, the paper leaves a number of open questions regarding the interpretation of the data.

Resting values of mouth occlusion pressure ($P0.1$) in controls (table 2) differ from those in COPD patients. Unfortunately, no data are given on the functional residual capacity (FRC) level of the controls. The FRC values of both patient groups seem likely to be elevated as compared to control subjects. Consequently the $P0.1$ could be higher due to the relative stiffness of the hyperinflated lungs and thorax or due to load-compensating mechanisms. The authors touch on this problem in the discussion, but do not really put this in perspective of the interpretation of this parameter for quantification of the ventilatory drive.

The authors have measured data on CO_2-responses from minute ventilation and from $P0.1$ by performing rebreathing experiments according to the Read rebreathing technique. It is not clear how the $P0.1$ response to hypercapnia was calculated: the methods section suggests that the $P0.1$ value itself was used (as an equivalent of tidal volume). Table 2 presents the $\Delta P0.1/\Delta(P_{ET,CO_2})$ in $cmH_2O \cdot min^{-1} \cdot torr^{-1}$, suggesting that the $P0.1$ value was multiplied by the respiratory frequency (as an equivalent for minute ventilation)?

The rebreathing technique is based on giving 7% CO_2 (inspiratory carbon dioxide tension (P_{I,CO_2})=7.0 kPa (53 mmHg)) in oxygen in the inspiratory air, in order to stop CO_2 excretion and thus increasing the arterial carbon dioxide tension (P_{a,CO_2}) as a stimulus to the chemoreceptors. The time course of this process will be different depending on the starting level of arterial P_{a,CO_2}. The arterial P_{a,CO_2} will be fairly representative for the stimulus to the peripheral chemoreceptor. However, the activity of this chemoreceptor will be low or even zero in the high hyperoxic range in this kind of experiment. Thus, the build-up of CO_2 at the site of the central chemoreceptor will be the principal stimulus for the increase in ventilation and $P0.1$ in these subjects. The eucapnic patients have a P_{a,CO_2} of 5.3 kPa (40 mmHg), whereas the hypercapnic patients have a P_{a,CO_2} of 7.3 kPa (55 mmHg). We are not informed about the P_{a,CO_2} of the normal subjects, but one may assume that this was in the normal range. Thus, the control subjects and normocapnic patients will build-up the central chemoreceptor CO_2-stimulus with a substantially shorter time constant than the hypercapnic patients. This means that there is a different relationship between P_{ET,CO_2} and the central chemoreceptor simulus in the three groups, which will be even greater due to different degrees of (mis)matching of ventilation and perfusion. Consequently, it is not very adequate to use the nonsteady state value of P_{ET,CO_2} as the ventilatory stimulus to compare the CO_2-responses in both patient groups and in the control subjects on the basis of this parameter of ventilatory stimulus. Steady state CO_2-response curves, with P_{a,CO_2} as the stimulus, might have been more adequate in this kind of investigation.

The authors speculate that "patients with severe COPD reach the top values of their neuromuscular drive and that, after this level is reached, no more increment in the $P0.1$ can be expected to maintain P_{a,CO_2} within normal limits". Surprisingly the authors do not discuss the findings of SCANO *et al.* [2] in the same patients and address the very same problem, using the same CO_2-rebreathing experiments. Their results showed that the response of the electrical activity in the diaphragm to hypercapnia was not significantly different in normocapnic and hypercapnic COPD patients or in control subjects. This experimental evidence suggests that there are still reserves in the neuromuscular drives of the severe COPD patients, and that impairment of respiratory muscle function prevents this drive to be converted into actual ventilation. If this is what MONTES DE OCA and CELLI [1] mean with "neuromechanical coupling failure", then the eventual interpretation of the findings of both groups may be similar?

I am unsure whether both groups of investigators may not be measuring effects of different relationships between P_{ET,CO_2} and the actual central chemoreceptor stimulus, combined with the net result of load on the respiratory muscles *versus* the working capacity of these muscles.

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