Doxapram and Perception of Dyspnea

To the Editor:

Evidence suggests the relationship between the perceptibility of dyspnea and the hypoxic ventilatory response.1,2 Doxapram, a potent ventilatory stimulant, is known to affect primarily the receptors.3 Although the ventilatory effect of doxapram has been reported, it has been demonstrated that the drug augments the perception of dyspnea with resistive load.4 Because doxapram can improve both dyspnea sensation and hypoxic chemosensitivity, it is of interest to investigate the effect of a drug like doxapram on dyspnea perception in patients with inspiratory resistive loading.

Hypoxic ventilatory response and perception of dyspnea during inspiratory resistive load (20.0 cm H₂O/L/s and 30.9 cm H₂O/L/s) was measured using the rebreathing circuit with a Validyne pressure transducer (Validyne Engineering, Northridge, CA) as previously described.5 In seven healthy male volunteers (age range, 26 to 46 years) who did not know the procedure, the effect of doxapram on the sensation of dyspnea has not been investigated. Therefore, we investigated the effect of doxapram on the perception of dyspnea during inspiratory resistive load.

Dyspnea scores of individual subjects during breathing with resistances increased during doxapram infusion (p < 0.05 for both by paired t test; Fig 1). The Borg scores of individual subjects during breathing with resistances of 20.0 cm H₂O/L/s and 30.9 cm H₂O/L/s also significantly increased during doxapram infusion (p < 0.01 and p < 0.05, respectively, by paired t test).

These results showed that doxapram administration augments the dyspnea sensation as well as the hypoxic ventilatory response. Although we could not clarify the mechanisms by which doxapram augments the perception of dyspnea with resistive load, our finding provides some clinical implications. Since doxapram is occasionally used for the treatment of patients with respiratory failure, one should be aware that this drug possibly increases dyspnea. However, it has been reported that the blunted perception of dyspnea as well as lowered hypoxic chemosensitivity play a role in some pathologic conditions such as death from asthma and respiratory failure in Parkinson disease.1,2 Because doxapram can improve both dyspnea sensation and hypoxic chemosensitivity, it is of interest to investigate the effect of a drug like doxapram on these patients.

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Figure 1. Top, A: Individual (closed circles) and mean (open circles) [± SD] values of the ventilatory response to hypoxia after the placebo and doxapram infusions. The left panel shows the slopes of the ventilatory response to hypoxia (ΔV̇e/ΔSpO₂), and the right panel shows the P₀.₁ slope (ΔP₀.₁/ΔSpO₂). The absolute values of both slopes were significantly increased after the doxapram infusion (p < 0.05 in both). Bottom, B: Individual (closed circles) and mean (open circles) [± SD] values of the Borg score when the subject breathed with an external inspiratory resistance of 20.0 cm H₂O/L/s (left panel) or 30.9 cm H₂O/L/s after placebo (saline solution) and doxapram infusion. Mean Borg score values were significantly increased after the doxapram infusion (p < 0.01 for 20.0 cm H₂O and p < 0.05 for 30.9 cm H₂O/L/s).