Pathophysiology of a Fall in Arterial Oxygen Saturation During Sputum Induction

To the Editor:

We were very interested to read the article by Castagnaro et al (October 1999), who have precisely measured, by pulse oximetry, the fall in arterial oxygen saturation (SaO₂) during sputum induction by the inhalation of hypertonic (3%) saline solution. We were surprised by the fact that the fall in SaO₂ was also significant in healthy subjects. In their discussion, the authors suggest that this may be due to a mismatching between ventilation and lung perfusion. Very interestingly, these authors did not find a significant fall in FEV₁, which indicates that no significant obstruction could be considered as an explanation for a sudden oxygen desaturation during sputum induction.

Bhowmik et al studied the falls in FEV₁ and SaO₂ in patients with rather severe COPD and found only slight changes in SaO₂, despite significant falls in FEV₁. This would suggest that the fall in SaO₂ is greater when no clear bronchial obstruction is observed. The hypothesis is that the effect of sputum induction on SaO₂ necessitates a widespread distribution of hypertonic saline solution through the small airways, which is impossible if the patient’s obstructive disease is too severe. In addition, the inhalation of hypertonic saline solution causes a marked fall in SaO₂ in HIV-positive patients who did not have bronchial obstructions and did not develop bronchospasms during the inhalation period. Taken together, these data suggest that the hypertonic saline solution acts by modifying the ventilation-perfusion ratio through, modulating the vascular tone. Hypertonic saline solution has been shown to influence the release of neuropeptides and to induce modifications in the metabolism of arachidonic acid derivatives, which could explain the vasoactive modifications of small blood vessels in the lung. Consequently, an investigation of the eventual change in lung perfusion should be performed using lung scans of healthy subjects made during the inhalation of hypertonic saline solution.

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To the Editor:

We appreciate the positive comments by Drs. Cataldo and Luis about our study on oxygen desaturation during sputum induction in asthmatics, smokers, and healthy subjects. Furthermore, following the same study protocol, we recently assessed the oxygen desaturation during sputum induction in COPD patients. In nine COPD patients with mild to moderate airways obstruction, we found that the baseline arterial oxygen saturation (SaO₂) values (mean ± SD), the fall in SaO₂, and change in SaO₂ after sputum induction were 96 ± 2%, 92 ± 3% (p < 0.05), and 4 ± 2%, respectively. Moreover, COPD patients had a small fall in FEV₁ levels (percentage of predicted value) after sputum induction (82 ± 15% vs 77 ± 18%). Like asthmatics, smokers, and healthy subjects, COPD patients had oxygen saturation fall, with no changes in airway obstruction. We think that this drop could be caused by direct deposition of saline solution into peripheral airways, which induces abnormalities of ventilation-perfusion ratios throughout the lung.

To further explain the pathophysiology of SaO₂ fall during sputum induction, Drs. Cataldo and Luis speculated that the hypertonic saline solution might modify the ventilation-perfusion ratio by modulating vascular tone with a pro-inflammatory mechanism. However, we found that all subjects recovered the SaO₂ fall within 5 min of the cessation of sputum induction, without requiring supplemental oxygen. The transient and self...
reversing oxygen desaturation after sputum induction seems, therefore, to be in contrast with a mechanism involving mediators release.

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Angiotensin-Converting Enzyme Inhibitors, Angiotensin II Receptor Antagonists, and Symptomless Dysphagia

To the Editor:

Symptomless dysphagia is one of the main causes of pneumonia in elderly people with stroke, and swallowing or the cough reflex can prevent aspiration pneumonia.1 The article by Nakayama and colleagues (May 1999),2 concerning angiotensin-converting enzyme (ACE) inhibitors and the swallowing reflex, was a fascinating and timely study. We previously reported that ACE inhibitors may cure symptomless dysphagia in hypertensive patients with stroke.3 ACE inhibitors and angiotensin II receptor antagonists (Ang II) are very important drugs for hypertensive patients. We investigated the prevention of symptomless dysphagia and treatment with different antihypertensive drugs in hypertensive patients with stroke. We investigated whether a correlation existed between patients with symptomless dysphagia with stroke and the elimination of low serum substance P concentration by ACE inhibitors and Ang II.4 We excluded the immunocompromised patients.

The subjects were 53 patients with hypertension, symptomless dysphagia, and history of stroke. They were divided into group A (32 patients; 13 men and 19 women) and group B (21 patients; 10 men and 11 women). We obtained informed consent from the patients or their families.

To determine the occurrence of symptomless dysphagia, we gave 1 mL technetium tin colloid (99mTc) to patients in groups A and B during sleep via a nasal catheter.5 At 9:00 AM the next day, we checked for symptomless dysphagia by imaging.

We gave all patients in group A an ACE inhibitor (indapamid hydrochloride), 5 to 10 mg qd orally, and all patients in group B received Ang II (losartan potassium), 50 to 100 mg qd orally. We measured serum substance P before and 12 weeks after administration. The mean serum substance P before drug administration was 26.5 pg/mL in group A and 26.36 pg/mL in group B. After 12 weeks, symptomless dysphagia improved in 23 of 32 patients in group A. In these 23 patients, the mean serum substance P was 82.91 pg/mL. In six patients, symptomless dysphagia did not improve (mean serum substance P, 50.62 pg/mL) and in four of them, serum substance P was not increased (mean serum substance P, 46.12 pg/mL). Imidapril hydrochloride was stopped in the remaining patients because of excessive cough (mean serum substance P, 109.83 pg/mL). On the other hand, in all 21 patients in group B, symptomless dysphagia did not improve, and in all of them, serum substance P did not increase (mean serum substance P, 30.49 pg/mL) after 12 weeks (p < 0.0001).

We concluded that ACE inhibitors have advantage over Ang II in prevention of symptomless dysphagia in patients with stroke.

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To the Editor:

We thank Dr. Arai et al for their interesting comments on our study.1 They report that the administration of angiotensin-converting enzyme (ACE) inhibitor could increase serum substance P (SP) and could improve the symptomless dysphagia in patients with hypertension and previous stroke, but that angiotensin II receptor antagonists (Ang II) could not. ACE inhibitors inhibit not only the activation of angiotensin II, but also the degradation of SP and bradykinin. We have shown, in a 2-year study,2 that ACE inhibitors could upregulate impaired swallowing reflex, and that they could also reduce the risk of pneumonia by about one third, compared with results of other antihypertensive drugs used in treatment of patients with hypertension and previous stroke. However, the effect of Ang II on the swallowing reflex has not yet been examined. Dr. Arai’s experience clearly showed that the effect of ACE inhibitors on improvement of symptomless dysphagia should be independent from the angiotensin II pathway. We agree that ACE inhibitors have an advantage over Ang II in preventing symptomless dysphagia in patients with stroke.

Despite the important antihypertensive effect, ACE inhibitors also cause a side effect of excessive cough in 5 to 10% of subjects, as shown in the comment by Arai et al. Therefore, ACE inhibitors would not be useful for patients who have developed hypotension or other side effects as a result of these drugs. Another way to increase SP is through the administration of dopamine, which