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CORRESPONDENCE

Angiotensin II blockers in obstructive pulmonary disease: a randomised controlled trial

To the Editors:

In a recent issue of the *European Respiratory Journal*, ANDREAS *et al.* [1] explored the effect of the angiotensin II type-1 receptor blocker irbesartan on skeletal and respiratory muscle strength in Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage III and IV chronic obstructive pulmonary disease (COPD) patients.

Although I agree that there is only sparse evidence of any systemic or pulmonary effect of angiotensin-converting enzyme (ACE) inhibitors in COPD, there are some indications that increased rennin–angiotensin system activity may contribute to the pathogenesis and progression of COPD. Captopril, at a dose of 25 mg, is associated with lower exertional pulmonary artery pressure, lower pulmonary vascular resistance, higher mixed venous oxygen saturation, and lower lactate levels in selected COPD patients [2]. In several studies, KANAZAWA and co-workers [3–5] demonstrated that these effects might be ACE genotype dependent. Based on the presence (insertion) or absence (deletion) of some alleles, they demonstrated that increased pulmonary arterial pressure is associated with the angiotensin deletion allele, which was confirmed by an independent Slovakian group [6]. The deletion allele is also associated with greater quadriceps strength in COPD patients [7].

So if we want to study the effects of angiotensin-converting enzyme blockers on the exercise capacity in chronic obstructive pulmonary disease patients, we should not only power the study to detect modest changes in maximal oxygen uptake, but also stratify for angiotensin-converting enzyme gene polymorphism as this could potentially effect the oxygen delivery to the working muscle.

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REFERENCES

1 Andreas S, Herrmann-Lingen C, Raupach T, *et al.* Angiotensin II blockers in obstructive pulmonary disease: a randomised controlled trial. *Eur Respir J* 2006; 27: 972–979.
2 Kanazawa H, Hirata K, Yoshikawa J. Effects of captopril administration on pulmonary haemodynamics and tissue oxygenation during exercise in ACE gene subtypes in patients with COPD: a preliminary study. *Thorax* 2003; 58: 629–631.
3 Kanazawa H, Okamoto T, Hirata K, Yoshikawa J. Deletion polymorphisms in the angiotensin converting enzyme gene are associated with pulmonary hypertension evoked by exercise challenge in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000; 162: 1235–1238.
4 Kanazawa H, Otsuka T, Hirata K, Yoshikawa J. Association between the angiotensin-converting enzyme gene polymorphisms and tissue oxygenation during exercise in patients with COPD. *Chest* 2002; 121: 697–701.
5 Kanazawa H, Hirata K, Yoshikawa J. Influence of oxygen administration on pulmonary haemodynamics and tissue oxygenation during exercise in COPD patients with different ACE genotypes. *Clin Physiol Funct Imaging* 2003; 23: 332–336.
6 Tkacova R, Joppa P, Stancak B, Salagovic J, Misikova S, Kalina I. The link between angiotensin-converting enzyme genotype and pulmonary artery pressure in patients with COPD. *Wien Klin Wochenschr* 2005; 117: 210–214.
7 Hopkinson NS, Nickol AH, Payne J, *et al.* Angiotensin converting enzyme genotype and strength in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004; 170: 395–399.

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From the authors:

I would like to thank M. Meysman for raising the interesting aspect of the angiotensin-converting enzyme (ACE) genotype in chronic obstructive pulmonary disease (COPD) patients. I fully agree that the activation of the rennin–angiotensin system is likely to contribute to inflammation, cachexia, pulmonary hypertension and skeletal muscle dysfunction in COPD [1]. M. Meysman cited interesting studies by KANAZAWA and co-workers [2, 3] and HOPKINS *et al.* [4] pointing to an effect of the ACE genotype on pulmonary hypertension and muscle strength in COPD patients.

My study group evaluated the effects of an angiotensin-receptor blocker in patients with COPD and found no significant effect on the primary end-point, maximum inspiratory pressure. However, total lung capacity and haematocrit were affected [5]. It was reasoned that well-known cardiovascular drugs can produce unanticipated effects in COPD patients. Pulmonary haemodynamics were not evaluated because this was a noninvasive study. However, echocardiography was used without noticing a significant effect of angiotensin I inhibition on right ventricular dimension. Furthermore, the rennin–angiotensin system is unlikely to be a major determinant of pulmonary vascular pathology in therapeutic trials [6].

Albeit it must be acknowledged that there is a clear benefit of angiotensin-converting enzyme and angiotensin I inhibition in