

Different types of statins might act differently in reducing plasma asymmetric dimethylarginine levels

To the Editor We read the article by Szpak et al.¹ with interest. The authors investigated whether active or passive tobacco smoking may affect endothelial dysfunction markers such as asymmetric dimethylarginine (ADMA), thrombomodulin (TM), plasminogen activator inhibitor-1 (PAI-1), and cotinine levels in patients with advanced coronary artery disease. Patients were divided into 2 groups according to the smoking status. The plasma levels of ADMA, TM, and PAI-1 were found to be elevated in smokers when compared with those of nonsmokers. In addition, serum cotinine levels were found to be independently associated with ADMA, TM, and PAI-1 levels in the whole study population.

ADMA is an important endogenous competitive inhibitor of nitric oxide synthase, and elevated levels of ADMA have been identified as an independent risk factor for progression of atherosclerosis.² Statin treatment has been shown to reduce circulating ADMA levels.² In the study by Szpak et al.,¹ the use of statin between smokers and nonsmokers was similar ($P = 1.00$). However, it should be stated that different types of statins might indeed act differently in altering plasma levels of ADMA. Specifically, rosuvastatin treatment in patients with hypercholesterolemia led to a significant reduction in plasma ADMA levels, which also appears to be related to the improvement in endothelial function.² Atorvastatin treatment in patients with nonischemic congestive heart failure had no clear effect on plasma ADMA levels.³ However, a recent study by Nishiyama et al.⁴ found that atorvastatin treatment resulted in a significant decrease in ADMA levels in patients with ischemic stroke.⁴ Simvastatin also had no effect on ADMA levels.⁵ In conclusion, the type of statin should be considered when assessing the plasma levels of ADMA because different types of statins might act differently even if the use of statin is similar between the groups.

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Authors' reply We appreciate the comments regarding our article,¹ especially those concerning the issue as to whether the type of statins could modulate the effect of cigarette smoking on endothelial function markers in patients with coronary artery disease (CAD). In our study, CAD patients were treated with simvastatin or atorvastatin. Drug doses were the same in both groups and ranged from 20 to 40 mg/d. In the smoker group, 14 patients received atorvastatin and 45 patients were on simvastatin. Simvastatin was administered to 50 nonsmoking patients and atorvastatin to 14 nonsmokers. The differences between the proportions of patients treated with the 2 statins in the nonsmoker and smoker groups were not statistically significant, and there were no differences in ADMA concentrations associated with the type of cholesterol-lowering

agents or their doses.¹ The available data indicates that a decrease of ADMA concentrations was not observed in the group of patients treated with high doses (80 mg) of simvastatin.^{2,3} The effect of atorvastatin on ADMA concentrations seems to be weaker,⁴ which may suggest that statin-induced improvements in endothelial function are likely mediated by alternative pathways.⁵

Although the differences in pleiotropic effects of statins depending on their type and dose are plausible even in patients with advanced CAD, our results¹ suggest that current cigarette smoking, as evidenced by serum cotinine levels, is a much more potent modulator of plasma ADMA concentrations as well as other markers of endothelial injury as compared with the type of statins. A larger interventional study is needed to specifically address the impact of various statins on the synthesis and degradation of ADMA in subjects with cardiovascular disease.

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Corrections

Papierska L, Ćwikła JB, Misiorowski W, et al. Unusual case of phosphaturic mesenchymal tumor. *Pol Arch Med Wewn.* 2013; 123: 255-256.

In the sentence “Somatostatin receptor scintigraphy (SRS) showed increased octreotide uptake in the right mandibular sinus” on page 256 and in figure legend on page 255 “mandibular sinus” should read “maxillary sinus”.

The article is correct at www.pamw.pl.

Starzyńska A, Szmuda T, Słoniewski P, et al. New minimally invasive therapeutic method in chronic back pain. *Pol Arch Med Wewn.* 2013; 123: 421-422.

Legend to Figure 1 should read “Patient with heterogenic oral leukoplakia” instead of “Patient with heterogenic oral leukoplakia of the buccal mucosa”.

The article is correct at www.pamw.pl.