LETTERS TO THE EDITOR

doi:10.1093/eurheartj/ehn244
Online publish-ahead-of-print 3 June 2008

Possible involvement of advanced glycation end products in carry-over benefits of atorvastatin in ASCOT-BPLA

I read with interest the recent study by Sever et al.,1 which reported that patients originally assigned atorvastatin continued to demonstrate lower event rates in most cardiovascular endpoints after the termination of Lipid Lowering Arm of the ASCOT (ASCOT-LLA) trial, compared with those originally assigned placebo, although LDL-cholesterol levels were almost identical in the two groups during the 2 years extended follow-up period.2 These observations suggest sustained cardioprotective effects of atorvastatin after the cessation of active treatment in at-risk patients with hypertension. A similar outcome was reported in the DCCT-EDIC Research; it revealed that original intensive therapy for 6.5 years reduced the risk of cardiovascular events to about 50% of that of conventional treatment in diabetic patients 11 years after the end of the trial, although glycosylated haemoglobin values in the two groups had almost converged during the follow-up periods.2 These clinical studies strongly suggest that so-called ‘metabolic memory’ causes chronic vascular damage in high-risk patients with hypertension and diabetes that are not easily reversed, even by subsequent, relatively good control of LDL-cholesterol or blood glucose.

Reducing sugars can react non-enzymatically with amino groups of protein to form Amadori products.3,4 These non-enzymatically with amino groups of LDL-cholesterol or blood glucose. Subsequent, relatively good control of diabetes that are not easily reversed, even by memory’ causes chronic vascular damage in strongl suggest that so-called ‘metabolic progression of cardiovascular disease.3,4 Indeed, increased formation and accumulation of AGEs have been known to progress at an accelerated rate under diabetes or oxidative stress conditions, thus playing a role in the development and progression of cardiovascular disease.3,4 Indeed, increased serum or skin levels of AGEs are reported to predict future cardiovascular mortality or progression of diabetic microangiopathy, respectively, in patients with diabetes.3,4 Further, increased formation and accumulation of AGEs are a possible mechanism to explain the ‘metabolic memory’, a long-term beneficial influence of early metabolic control on cardiovascular outcomes. Since we have previously found that atorvastatin not only inhibits the AGE signalling to inflammation in vitro, but also reduces serum levels of AGEs in hypercholesterolemic type 2 diabetic patients,4,7,8 it is conceivable that carry-over beneficial effects of atorvastatin on cardiovascular events in Blood Pressure Lowering Arm of the ASCOT (ASCOT-BPLA) trial could be ascribed, at least in part, to its inhibitory effects on AGE formation and/or the downstream-signalling pathways. Therefore, it is an interesting issue to clarify whether circulating or skin AGE levels at the closure of ASCOT-LLA could predict cardiovascular events at the end of ASCOT-BPLA.

References

Sho-ichi Yamagishi
Department of Pathophysiology and Therapeutics of Diabetic Vascular Complications
Kurume University School of Medicine
67 Asahi-machi Kurume 830-0011
Japan
Tel: +81 942 31 7873
Fax: +81 942 31 7873
Email: shoichi@med.kurume-u.ac.jp

doi:10.1093/eurheartj/ehn245
Online publish-ahead-of-print 9 June 2008

Association of adiponectin with adverse outcome in coronary artery disease patients: results from the AtheroGene study

We read with interest the article by Schnabel et al.1 in which the authors assessed the prognostic value of baseline levels of adiponectin in patients with manifest coronary artery disease (CAD). They conclude that adiponectin concentration is predictive of cardiovascular death or non-fatal myocardial infarction (MI) at a median follow-up of 2.5 years.

Several considerations are worth noting before accepting these conclusions. First, the overall study population is markedly heterogeneous due to the inclusion of patients with stable angina (SA) and various sub-sets of patients with acute coronary syndromes (ACS) (e.g. ST-elevation and non-ST-elevation MI). While baseline adiponectin

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2008. For permissions please email: journals.permissions@oupjournals.org.