Letters to the Editor

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Statins and percutaneous coronary intervention

We have read with interest the article by Briguori et al.,1 and we have several comments for the authors. The paper is a randomized study on pre-treatment with statins before percutaneous intervention, showing reduction of post-procedural myocardial infarction (MI). The ARMYDA (Atorvastatin for Reduction of Myocardial Damage during Angioplasty) trial,2 was recently published and, by highlighting the differences between the two studies, we would like to point out some flaws in the paper by Briguori et al.

ARMYDA was the first randomized, prospective, multi-centre, double-blind, placebo-controlled trial, in which a fixed dose (40 mg) of a specific drug (atorvastatin) was given for a well-defined period (7 days) before elective intervention in a selected patient population with the same clinical syndrome (stable angina). The diagnosis of peri-procedural MI was made according to the Joint ESC/ACC Committee definition of MI for clinical trials on Percutaneous Intervention3 (i.e. CK-MB >2 times above the upper normal limit). This protocol allowed the detection of a significantly lower occurrence of peri-procedural MI in the atorvastatin arm, with an average risk reduction of 80% at multivariate analysis.

Conversely, Briguori’s study used a multitude of different statins (atorvastatin, pravastatin, simvastatin, and fluvastatin) at variable doses, given for variable times before the procedure (between 3 and 31 days), and left to the physician’s discretion; thus, it is not clear how the prospective randomization protocol was ‘designed’, in particular which drug treatment was specifically being investigated. This is quite unusual for a clinical randomized trial.

In Briguori’s study, a significant difference in peri-procedural Mls was found only for those with CK-MB >5 times above the upper normal limit, and there was no attempt to analyse the data according to the Joint ESC/ACC guidelines indicated above. Moreover, the incidence of such large Mls was remarkably higher in Briguori’s study vs. ARMYDA (16 vs. 5% in the untreated arm, 8 vs. 0% in the treated arm): the reason for this is also unclear.

Finally, the sizable procedural complications rate (9 vs. 0% in ARMYDA) reported by Briguori, somewhat unusual in a stable elective patient population, makes the incidence of unexplained peri-procedural Mls, and the potential impact of a structured protective pharmacological intervention, difficult to evaluate in such study.

References


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Statins and percutaneous coronary intervention: reply

Both our study1 and that by Pasceri et al.2 support the beneficial role of pre-procedural statin administration on lowering the rate of peri-procedural myocardial infarction.

The purpose of our study was to assess in a randomized fashion whether statin treatment, started at least 3 days before stenting, is useful in preventing peri-procedural cardiac enzyme elevation. Our study was not designed to test: (i) a specific statin, (ii) a pre-defined dosage of a specific statin, or (iii) a specific delay between statin administration and the procedure. Statin benefits may be explained not only by their lipid-lowering potential but also by non-lipid-related mechanisms (pleiotropic effects). In our opinion, only with a complete knowledge of the exact mechanism, can one design a study with (i) a specific statin (why atorvastatin?), (ii) a specific dose (why 40 mg?), and (iii) a specific time interval (why 1 week?).

Our study was not blinded. It was not feasible for us to conduct a blind study without support from a sponsor. This fact is a clear limitation overcome by the study of Pasceri et al.

We used the definition of large non-Q-wave myocardial infarction (CK-MB elevation, >5 times ULN) generally considered clinically useful in the field of interventional cardiology, as also reported in the Joint ASC/ASS Committee definition of myocardial infarction for clinical trials of percutaneous intervention.3 The rate of large non-Q-wave myocardial infarction (as defined in our study) reported in the literature is ~12%. We reported 15.6% in the control group and 8% in the statin group. The reality is that with a small number of patients, as in the Pasceri study, the percentage of events has large confidence intervals.

We reported an angiographic complication rate of 9% in the statin group and 5% in the control group. This includes the cumulative rate of major/minor dissection, abrupt closure, slow/no reflow, thrombus formation, side branch closure/compromise, and distal embolization. A
number of these complications did not have any clinical consequence, still we assumed it was important to highlight their incidence. Pasceri et al. stressed their 0% rate of angiographic complication and had concerns about our unusually 'high' rate of angiographic complication in a stable elective patient population. We would like to point out that the rate of angiographic complication reported in the ESPRIT trial,4 enrolling stable patients undergoing elective stenting was 10.1% in the eptifibatide group and 12.2% in the control group.

References

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Relations of plasma total TIMP-1 levels to cardiovascular risk factors and echocardiographic measures: the Framingham Heart Study

Johan Sundström et al.1 presented their very interesting data linking TIMP-1 levels to cardiovascular risk factors, including left ventricular hypertrophy. As the authors mentioned, TIMP-1 levels were previously measured in a number of cardiovascular diseases, such as hypertension, coronary disease, and heart failure, but the groups studied were smaller and results were inconsistent. Plasma TIMP-1 levels seem to be more often used than other possible biochemical parameters of collagen metabolism, at least in cardiovascular patients.2–5 However, not only increased left ventricular mass, but also increased intima media thickness of the common carotid arteries (IMT) can serve as an independent risk factor for cardiovascular events. Increased IMT may be related to the accumulation of extracellular proteins due to altered metabolism of collagen. Comparing patients with untreated essential hypertension with healthy controls, we found not only increased IMT in the former, but also significantly elevated plasma TIMP-1 levels. Moreover, we found a significant, positive correlation between IMT and the levels of TIMP-1 in hypertensives, but not in healthy subjects.6 We think that TIMP-1 level may be a biomarker of the remodelling of the entire cardiovascular system, not only the left ventricle of the heart.

References
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We thank Dr Szmiłeks and colleagues for their thoughtful comments. We agree with them that circulating TIMP-1 levels may reflect vascular as well as left ventricular remodelling. Their findings are interesting.