Editorial

THE CLINIC AND PATHOGENIC SIGNIFICANCE OF HYPERGLYCAEMIA DURING ACUTE MYOCARDIAL INFARCTION

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Hyperglycaemia occurring in patients admitted in intensive care units for acute myocardial infarction, whether previous known as diabetics or not, had gained much attention in the recent years because its association with higher in-hospital morbidity and mortality[1,2]. Consequently, understanding the possible mechanisms through which hyperglycaemia worsens the prognosis of a patient with acute MI, as well as the effectiveness of its control during the in-hospital period seems to be of great relevance[3].

In the present study of R. Lichiardopol and col., hyperglycaemia of diabetic or prediabetic level has been detected in 69% of patients admitted in an intensive care cardiology unit with acute MI during one year; remarkably, about 50% of all patients had altered glucose tolerance without being previously known as diabetics. Besides this very high incidence, there are several points which were underlined in the above cited paper and should be commented in the light of last developments of this topic: the mechanisms connecting the glyco-metabolic status of the acute MI patients to in-hospital morbidity and mortality; the causes and the effects of under-diagnosing and under-treating this metabolic disturbance.

The most important issue, however, is whether elevated glucose is a direct mediator of adverse outcomes in acute MI patients or just a marker of greater disease severity/high risk. The second important is the need for specific guidelines for evaluation and management of the glycaemia in critically ill patients, especially in cardiology departments.

Is hyperglycaemia a marker of high risk or a mediator of adverse outcomes?

Important studies in humans have linked in the last years hyperglycaemia to the endothelial disfunction, evidenced through an abnormally low flow-mediated vasodilatation. Specifically, in a recent study[4] a higher incidence of the "no flow" phenomenon has been shown by myocardial contrast echo-cardiography in patients with elevated glucose levels after successfull reperfusion procedures. In another study, hyperglycemic patients with ST elevation acute MI (STEMI) had lower rates of spontaneous reperfusion[5]. Post-prandial hyperglycaemia is associated also with defects in myocardial perfusion due to microvascuscular disfunction, condition that improves with better glycemic control[6].

Some studies have shown that hyper-glycaemia is related to a prothrombotic state in humans; the possible mechanisms of this relationship are an increased platelet aggregation and higher levels of thromboxane A2 and von Willebrand factor[7].

A third possible mechanism linking hyperglycaemia to cardiovascular risk might be the inflammatory sub-clinical syndrome; the effectors of vascular inflammation, which were associated with hyperglycaemic status in both human and experimental studies, are interleukin-6 (IL-6) and tumor necrosis factor-α (TNF- α)[8]. TNF- α had been also shown to extend infarct size and induce myocardiocyte apoptosis[9].

Diabetic hyperglycaemia is associated with higher free fatty acids plasma levels and an impaired glucose utilization by the heart, resulting an increased oxygen consumption (worsening ischemia) and a higher risk for ventricular arrhythmias[10].

Finally, hyperglycaemia has been linked in several relatively small studies to an impaired immune response, rising the relative risk of cardiogenic shock.

A scientific statement from the AHA Diabetes Comitee of the Council of Nutrition, Physical Activity and Metabolism

Given the relatively controversial data from the prospective studies finished on this topic, the above mentioned Comitee has released a Scientific Statement[11] by which the specific areas to be addressed by future prospective studies were defined; some of these areas are:

- establish whether persistent hyperglycaemia has greater impact on prognosis than admission hyperglycaemia; the present study (R. Lichiardopol and col.) has evidenced the relationship between admission hyperglycaemia and the relative risk of death and LV failure;
- define target glucose levels associated with the best outcomes in acute MI patients whether are they known diabetics or not; in the discussed study the relative risk began to rise from blood glucose values of about 150 mg/dl and is highest at mean values of 250 mg/dl;
- establish if clinical benefits (and their relevance) are realized achieving the targets through the meanings of intensive glucose control, in terms of improved survival, in-hospital complications rate, LV function, etc.;
- establish the therapeutic protocols for intensive glucose control in acute MI in-hospital patients and demonstrate their feasibility, effectiveness and safety.

REFERENCES

1. O'Sullivan JJ, Conroy RM, Robinson K, et al., (1991): In-hospital prognosis of patients with fasting hyperglycaemia after first myocardial infarction, Diabetes Care, 14: 758-760

2. Mak KH, Mah PK, Tey BH, et al., (1993): Fasting blood sugar level: a determinant for in-hospital outcome in patients with first myocardial infarction, Ann. Acad. Med. Singapore, 22:291-295

3. Cerriello A (2005): Acute hyperglycaemia: a "new" risk factor during myocardial infarction, Eur. Heart J., 26: 328-331

4. Iwakura K, Ito H, Ikushima M et al., (2003): Association between hyperglycaemia and the no reflow phenomenon in patients with acute myocardial infarction, J. Am. Coll. Cardiol., 41: 1-7

5. Timmer JR, Ottervanger JP, de Boer MJ, et al., (2005): hyperglycemia is an important predictor of impaired coronary flow before reperfusion therapy in

ST segment elevation myocardial infarction, J. Am. Coll. Cardiol., 45: 999-1002

6. **Scognamiglio R, Negut C, de Kreutzenberg SV et al.,** (2006): Effects of different insulin regimes on postprandial myocardial perfusion defects in type 2 diabetic patients, Diabetes Care, 29: 95-100

7. **Gresele P, Guglielmini G, De Angelis M, et al.,** (2003): Acute, short term hyperglycemia enhances shear-stress induced platelet activation in patients with type 2 diabetes mellitus, J. Am Coll. Cardiol., 41: 1013-1020

8. **Morohoshi M, Fujisawa K, Uchimura I, et al.,** (1996): Glucose dependent interleukin 6 and tumour necrosis factor production by human perioheral blood monocytes in vitro, Diabetes, 45: 954-959

9. **Li D, Zhao L, Liu M, et al**., (1999): Kinetics of tumour necrosis factor alpha in plasma and the cardioprotective effect of a monoclonal antibody to tumour necrosis factor alpha in acute myocardial infarction, Am Heart J., 137: 1145-1152

10. **Oliver MF** (2002): metabolic causes and prevention of ventricular fibrillation during acute coronary syndromes, Am. J. Med., 112: 305-311.