Role for insulin in acute myocardial infarction: ruled out or hard to prove?

The only large randomized trials to investigate treatment focused on hyperglycaemia in MI patients were the Diabetes Insulin–Glucose in Acute Myocardial Infarction (DIGAMI) studies. In the first DIGAMI, the combination of insulin–glucose infusion followed by intensive insulin treatment resulted in both better glucose control and a reduction in hospital mortality from 11.1 to 9.1% (NS) and an absolute mortality reduction of 7.5% after 1 year.1 However, DIGAMI 2 could not confirm either the beneficial effect of early or sustained insulin treatment.2 During the first 24 h, intensive insulin treatment resulted in a decrease in glucose level from 12.7 to 9.1 mmol/L vs. 12.7 to 10.0 mmol/L in control patients.3 Nevertheless, positive effects of insulin treatment resulted in both better glucose control and a reduction in hospital mortality from 11.1 to 9.1% (NS) and an absolute mortality reduction of 7.5% after 1 year.1 However, DIGAMI 2 could not confirm either the beneficial effect of early or sustained insulin treatment.2 During the first 24 h, intensive insulin treatment resulted in a decrease in glucose level from 12.7 to 9.1 mmol/L vs. 12.7 to 10.0 mmol/L in control patients.

Is the role for insulin in acute MI ruled out? Yes, based on the current literature there is no evidence to support insulin treatment. Nevertheless, positive effects of insulin during myocardial ischaemia have been described in experimental studies.3 They depend on the influence on reduced fatty acid oxidation, increased glucose oxidation, and diminished apoptosis of myocardial cells to induce myocardial survival. These effects, however, could only be obtained soon after the initiation of myocardial ischaemia.4 Furthermore, there is a large amount of clinical evidence to support the concept that hyperglycaemia has an unfavourable effect.2,5,6 Hyperglycaemia during MI is short lived and strict glucose control should be obtained as soon as possible after symptom onset. Unfortunately, in the DIGAMI 2, the time delay between hospital admission and randomization, i.e. insulin treatment, averaged 8.6 h.

Is the role for insulin hard to prove? Yes, in MI patients, it is not easy to obtain glucose levels within the set range of 7.0–10.0 mmol/L within 24 h after admission.1,7,8,11 In critically ill patients, strict glucose was obtained,9 although it took ~24 h to reach target levels.10

Another striking aspect of the DIGAMI 2 study may be important to explain the results. Only one out of five hyperglycaemic/diabetes patients was treated with either coronary artery bypass grafting or primary percutaneous coronary intervention. To finally answer the question whether or not insulin therapy is of benefit in acute MI, MI patients should be treated with optimal modern reperfusion therapy and randomized to early, goal-directed insulin treatment. For instance, aiming of a glucose level of 7.0 mmol/L within 4 h after presentation and a more strict control thereafter.

References


Iwan C.C. van der Horst
Felix Zijlstra
Department of Cardiology
University Medical Center Groningen
PO Box 30001
9700 RB Groningen
The Netherlands
Tel: +31 50 3612355
Fax: +31 50 3611347
E-mail address: i.c.c.van.der.horst@thorax.umcg.nl

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Recurrent pericarditis: therapy of refractory cases

We read with interest the excellent Editorial by Maichi1 referring to the article by Artom et al.2 in which we are co-authors. We take this opportunity to comment on a minor point that anyway might be clinically relevant. Maichi writes that in refractory cases, azathioprine (75–100 mg/day) or cyclophosphamide can be added. This is also suggested by the European Guidelines recently published3 and has been quoted by authoritative reviews.4 Unfortunately, there is only one old article describing the use of azathioprine in this condition in two patients,5 and those authors acknowledged that ‘to suggest that azathioprine therapy is indicated in the treatment of steroid responsive pericarditis would indeed be presumptuous on the basis of these two cases’; other authors described other three cases.6,7 Moreover, there is no single article concerning cyclophosphamide (only one case described by Marcolongo et al.8), whereas Raatikka et al.9 reported five cases treated with methotrexate and one with cyclosporine and Peterlana et al.10 described four cases treated with intravenous immunoglobulin. Rheumatologists commonly use azathioprine, cyclophosphamide, cyclosporine, methotrexate, hydroxychloroquine, and intravenous immunoglobulin; we agree that azathioprine is the preferred choice if tolerated (at the common dosage of 2–3 mg/kg/die), but we suggest that it would be more prudent to state that probably immunosuppressive agents and steroid sparing agents might be used very rarely in

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