Optimal Dosage of Insulin and Glucose in Glucose-Insulin-Potassium Treatment of Acute Myocardial Infarction Remains to Be Established

To the Editor:

The dosage of insulin and glucose plays an important role for the efficacy of GIK (glucose-insulin-potassium) treatment. Until the ECLA study, only 4 trials in acute myocardial infarction (AMI) had used the GIK therapy required to achieve adequate suppression of plasma free fatty acids (FFAs).1 Pooled data from these trials demonstrated a 48% reduction in mortality. In the ECLA study, a significant survival advantage relative to the control group was demonstrated that this regimen reduced the level of plasma free fatty acids (FFAs).1 Pooled data from 421–428.

Hence, before large-scale prospective, randomized studies on the efficacy of GIK (glucose-insulin-potassium infusion) are done by Dr Rolf Ekroth and colleagues at Sahlgrenska University Hospital in Göteborg, Sweden, it has been shown that insulin and potassium administration is a somewhat limited perspective. This assumption fails to consider a number of other potentially beneficial effects of GIK therapy, including a favorable effect on potassium flux, lipid metabolism, hyperglycemia/osmolarity, and plasma volume/hemodynamics. In addition, the extrametabolic effects of acute insulin administration likely contribute to the efficacy of this therapy, including favorable effects on vascular tone, coagulation, arrhythmogenesis, and apoptosis.1

Although a dose-finding study could assess safety and feasibility of different regimens, it would be impractical to power such a study for efficacy assessment. Such a study would have to rely on surrogate markers of efficacy, such as suppression of plasma free fatty acids, as implied by Svedjeholm et al. Although physiologically sound, these measures have never been validated against clinical outcomes and suffer all the limitations of reliance on the “structure-function” relationship outlined in the previous paragraph. One could also make a similar argument that studies to define the optimal duration of therapy and studies of the patient selection parameters would be required. However, we feel that these studies are impractical, if not altogether impossible, due to the financial constraints of studying nonproprietary pharmacotherapy.

Higher insulin doses would potentially come at the expense of safety and tolerability. Higher insulin doses may be advisable.

Response

In their letter, Dr Svedjeholm and colleagues provide a concise summary of the topic of glucose-insulin-potassium (GIK) therapy. Their comments reflect the current understanding of the metabolic benefit of GIK therapy in acute myocardial infarction (AMI). The spirit of their letter is that dose-finding studies should be performed before a large-scale follow-up trial with GIK is done, with the implication that higher doses of insulin may prove more beneficial.

Should we consider a dose-finding study before the performance of a large-scale clinical trial?

Svedjeholm et al attribute the benefit of GIK in AMI to a metabolic mechanism. However, conceptually limiting the benefit of GIK therapy to its impact on anaerobic myocardial metabolism is a somewhat limited perspective. This assumption fails to consider a number of other potentially beneficial effects of GIK therapy, including a favorable effect on potassium flux, lipid metabolism, hyperglycemia/osmolarity, and plasma volume/hemodynamics. In addition, the extrametabolic effects of acute insulin administration likely contribute to the efficacy of this therapy, including favorable effects on vascular tone, coagulation, arrhythmogenesis, and apoptosis.1

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