Letters to the Editor

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Clinical trials with ST-segment elevation myocardial infarction

It is with great interest that we read the article ‘Outcomes of patients in clinical trials with ST-segment elevation myocardial infarction among countries with different gross national incomes’ by Orlandini et al.1 We feel obliged to point out that at least what regards Poland as one of the countries with medium gross national income (GNI), some of the data presented are of purely historical value only. The authors state that in the years 1995–2002, only 10.9% of patients participating in clinical trials in medium GNI countries underwent PCI. In Poland, since 2001, the number of STEMI patients treated with primary PCI soared, reaching 22 706 per year in 2005,2 which constitute 34% of all PCI procedures. Given that—according to a recent survey—the incidence of hospitalized STEMI in Poland is between 1000 and 1200 cases per million people each year3 and that the country’s population is ca. 38 million, this means that nowadays between 50% and 60% of all hospitalized patients with STEMI are reperfused with primary PCI. As of April 2006, there were 59 Cathlabs throughout our country that provided round-the-clock PCI service, many of them with an yearly volume of 600–700 primary PCI. Pooled data from Poland’s hospitals performing primary PCI in year 2003 demonstrate 30-day mortality of 7.0% including patients with cardiogenic shock and 4.7% in patients with no shock.2 It is, at present, unlikely that there could be any underuse of invasive treatment of STEMI in Poland to adversely affect the outcome as compared with high GNI countries. Still, the authors may be right when speculating (p. 531) that in medium- or low-GNI countries, investigators may be ‘including a higher risk subset of patients’ and that ‘significantly greater proportion of patients (…) were randomized’ as compared with high-GNI countries. As a matter of fact, this brings any clinical trial closer to real life and should make its results more relevant for clinical practice.

References


Goyal et al.1 reported that higher plasma glucose levels after acute myocardial infarction (AMI) predicts higher mortality in non-diabetic patients, which is not surprising as glucose is pro-inflammatory and insulin has anti-inflammatory actions. Glucose–insulin–potassium (GIK) regimen improves myocardial function during endotoxic shock2,3 and this beneficial action has been attributed to insulin2,4 because of its inhibitory action on tumour necrosis factor-α (TNF-α), macrophage migration inhibitory factor (MIF), superoxide anion production, and increase in the synthesis of eNO4,5 and anti-inflammatory cytokines.2 CREATE-ECLA Trial failed to reproduce the beneficial effects of GIK regimen in AMI,6 as the mean serum glucose levels were 162, 187, and 155 mg% in the GIK infusion group at baseline, 6 h, and 24 h after randomization when compared with 162, 148, and 135 mg% in the control, respectively. The higher serum glucose levels in the GIK group could be responsible for the negative results observed in the CREATE-ECLA trial, as glucose has pro-inflammatory actions, whereas insulin is anti-inflammatory in nature.2,4,5 In fact, lack of increase in mortality in the GIK group, despite the higher serum glucose levels could be due to the anti-inflammatory actions of insulin. Based on the results from the CARDINAL study, I propose that GIK regimen should be given in such a manner that not only plasma glucose levels are maintained ~80–100 mg%, but also production of thrombolytics (inclusion criteria) and not with PCI.

Finally, our analysis shows the differences among different countries in the context of clinical trials and stresses the importance of running them worldwide.

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Glucose, insulin, and acute myocardial infarction

I would like to thank Dr Maciej Karcz and Dr Adam Witkowski for their interest in our article. Their data are based on registries of the Polish Cardiac Society where an increase in Primary Percutaneous Coronary Intervention (PCI) has been observed in patients with STEMI. Nevertheless, we believe that these data do not affect our conclusions because our manuscript was only about mortality in STEMI patients included in clinical trials and our data should not be extrapolated to all STEMI patients in a whole country. Besides, we believe that the differences we observed among different GNI are related more to the biases of the population selected than to a real difference in the whole population. Moreover, it is likely that the proportion of patients treated with PCI in Poland was different from that observed in our analysis at all the trials in our article but one (randomization to control or Glucose-Insulin Potassium) required patients to be treated with