GIK Infusion Failed to Help Acute MI Patients

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW ORLEANS — An infusion of glucose, insulin, and potassium as an adjunct therapy for acute myocardial infarction was ineffective in a major study with more than 20,000 patients.

Thirty days after treatment, "GIK [glucose-insulin-potassium] had no impact on death, cardiac arrest, cardiogenic shock, or repeat infarction in patients with acute, ST-segment elevation myocardial infarction," Shamir R. Mehta, M.D., reported at the annual scientific sessions of the American Heart Association.

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The results suggested that the 24-hour GIK infusion used in the study may have had selected benefits for certain patient subgroups, but because these analyses were not prespecified end points, they couldn't be considered definitive conclusions.

For example, the 10,088 patients treated with GIK had a 5.6% rate of recurrent ischemia after 7 days, compared with a 6.5% incidence among the 10,107 patients treated with placebo, a statistically significant difference. But the study was not designed to test whether GIK affected the rate of recurrent ischemia. The finding suggested that GIK might be especially useful for patients with unstable angina, a clinical setter where recurrent ischemia is more common, said Dr. Mehta, a cardiologist at McMaster University in Hamilton, Ont.

The first report of GIK infusion use to treat acute MI was in 1962. A recent meta-analysis of 16 subsequent studies with a total of nearly 5,000 patients showed that those who received the infusion had an 18% relative reduction in the risk for death, compared with patients who did not receive GIK, said Dr. Mehta.

High-dose glucose is included in the infusion to boost the amount of carbohydrate substrate that's available for energy production in ischemic cells. Insulin is added to facilitate the penetration of glucose into ischemic cells and to reduce the level of toxic free fatty acids in the serum of acute MI patients. Potassium is included as a polarizing agent to minimize the risk of malignant arrhythmias.

The study was done at 470 centers, most of which were in India, China, and South America, and it received no commercial funding. Patients with acute MI were enrolled within 12 hours of symptom onset, and aside from randomization to receive GIK or placebo, their management followed local standards. Thrombolytic therapy was used in 74% of patients, and another 9% were treated with percutaneous coronary intervention (PCI). Virtually all patients also received aspirin.

The GIK infusion consisted of 25% glucose, 50 U/L of insulin, and 80 mmol/L of potassium. The rate was 1.5 mL/kg per hour, and it was continued for 24 hours. GIK and placebo infusions started within an hour of randomization for 90% of patients.

The results suggested that GIK might have been most beneficial to patients with the greatest likelihood of having their infarct-related arteries cleared by treatment. In the subgroup of 1,831 patients who were treated with PCI, GIK treatment led to about a 25% reduction in mortality, compared with those treated with placebo.

In a second subgroup of 2,562 patients treated with either PCI or tissue plasminogen activator, GIK infusion cut the death rate by 30%, compared with patients who received placebo. But these analyses were done on a post-hoc basis and are only hypothesis generating, cautioned Dr. Mehta.

The overall lack of benefit from GIK in this study may be explained by the low rate at which reperfusion was achieved in many study patients, commented Marc Cohen, M.D., chief of the cardiology division at Newark (N.J.) Beth Israel Medical Center. Although 74% of patients received lytic therapy, this treatment restores full coronary flow (Thrombolysis in Myocardial Infarction [TIMI] phase III flow) in only about half of treated patients. When coupled with the 18% of patients who received no reperfusion therapy, it's likely that "TIMI III flow was not achieved in more than half of the patients in the study. GIK may not work without early, successful reperfusion," Dr. Cohen said. ■