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THE MAGIC OF MAGNESIUM

Magnesium was once widely used by physicians in the management of acute myocardial infarction (AMI). It appeared to be safe, and cost less than \$5 per patient. Over time, interest waned because of negative results from the Fourth International Study of Infarct Survival (ISIS-4), a large, international trial. However, many physicians still believed in the value of magnesium.

A review of older data

Data on intravenous (IV) magnesium in animals confirms a significant benefit with smaller MIs when given early in experimental models. A meta-analysis of 12 small, randomized controlled trials (RCTs) demonstrated benefit, with a reduction in mortality. The Second Leicester Intravenous Magnesium Intervention Trial (LIMIT-2), a modest RCT, evaluated 2,000 patients with acute ischemic syndromes, and demonstrated a 24% reduction in mortality. Based on this information, many physicians, including myself, were commonly using IV magnesium in the management of AMI.

ISIS-4 evaluated over 50,000 patients with suspected AMI. One arm of the study looked at IV magnesium, and demonstrated no benefits; this came as

a surprise to many, in view of previous positive data and good experimental data in animals. Magnesium use fell dramatically. Many physicians still believed that high-risk patients were too few in ISIS-4, and that the agent may have been given too late following thrombolytic therapy. Therefore, magnesium, given early after AMI, might have a niche in older patients, or in those ineligible for reperfusion therapy.

A review of newer data

Dr. Elliot Antman of the New England Research Institute in Watertown, Mass., and primary investigator for the Magnesium in Coronaries (MAGIC) trial, presented his data for the first time at the European Society of Cardiology Congress in September 2002. MAGIC, sponsored by the National Heart, Lung, and Blood Institute (NHLBI), randomized 6,213 patients from 14 countries, including Russia and Bulgaria, to either IV magnesium or placebo. After 30 days, the primary end point of the trial, all-cause mortality, was identical in both study groups at 15%. No significant differences were seen in terms of the primary end point in any of the 21 subgroups analyzed, nor was there any particular benefit or harm seen in the secondary outcomes of need for heart failure therapy, defibrillation, or pacemaker implantation.

What can be said about the benefits of magnesium?

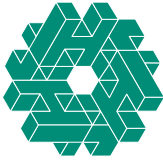
The latest, and most definitive, study of early magnesium use in AMI has failed to show that it can reduce short-term mortality in high-risk patients. The

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benefits of magnesium seen in the early studies were likely a product of inadequate sample size. Previous smaller studies, dating back several decades, have investigated the effects of magnesium in AMI, but produced confusing and conflicting results.

Physician's perspective

As stated by the investigators from the MAGIC trial, the routine use of IV magnesium, in both low-risk and high-risk patients presenting with AMI, has had no value in evidence-based medicine. A decade ago, expert opinion and clinical trials suggested that magnesium was valued in the management of AMI. The meta-analysis of the 12 small RCTs and the modest RCT featuring 2,000 patients all demonstrated clear benefits in mortality reduction. Although the confidence intervals were wide, I routinely used IV magnesium up until the results of ISIS-4. The MAGIC trial confirms the results of ISIS in high-risk patients, demonstrating no benefit. Physicians will have to debate over how much information is necessary to change clinical practice.


Physicians need to understand and interpret large and simple RCTs whenever possible. Many trials are now funded by the drug industry because they necessari-

tate an investment of millions of dollars. In addition to sample size, one must look at the totality of end points and the confidence interval. Ideally, more than one large scale RCT is necessary.

Most recently, the introduction of computerized data-

bases, with observational data on such topics as women taking hormone replacement therapy or patients at risk for vascular disease taking vitamin therapy, has demonstrated a 50% reduction in cardiovascular outcome.

Therefore, physicians are now practising evidence-based medicine, and it is important that we keep ourselves up-to-date. We must also realize that new information will change practice patterns, and we need to adapt quickly.

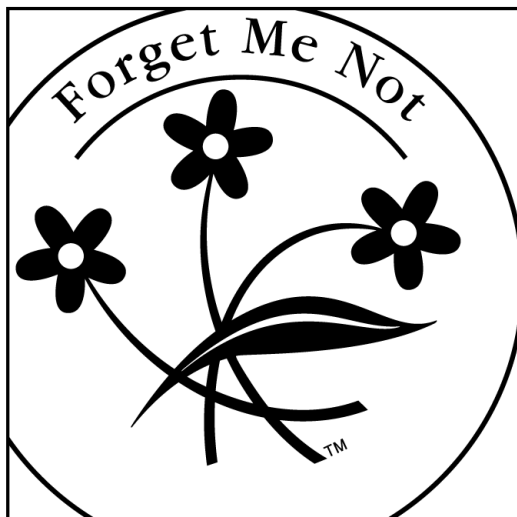
Magnesium has no role in the management of AMI on a routine basis. I will reserve IV magnesium for the management of ventricular arrhythmias, especially in patients with prolonged QT syndrome and torsades de pointes. 



**For a good move
see page 28**

Suggested Reading

1. Antman EM, Cooper H, Domanski M: Early administration of intravenous magnesium to high-risk patients with acute myocardial infarction in the Magnesium In Coronaries (MAGIC) trial: A randomized controlled trial. *Lancet* 2002; 360(9341):1189-96.



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