Intravenous Streptokinase for Treatment of Acute Myocardial Infarction in Small Hospitals

Richard Henry, MD, and Frank deGruy, MD, MSFM
Mobile, Alabama

S treptokinase has been available for the treatment of thrombolysis in acute myocardial infarction for over 25 years.1,2 The efficacy of streptokinase has been documented most convincingly when it has been infused by the intracoronary route,3-8 but intravenous infusion has also been shown to be effective.9-17 Although the drug is effective by either route if given within six hours after onset of the coronary event, the sooner the drug is administered after the onset of symptoms, the better the outcome.14,15

For patients in rural areas, transfer to a tertiary institution with cardiac catheterization facilities is necessary for intracoronary infusion, which may not be possible before the six-hour therapeutic “window” has passed.

In contrast, intravenous administration of streptokinase only requires access to a peripheral vein, the ability to monitor the patient for bleeding or overanticoagulation, a thorough knowledge of the actions and contraindications of streptokinase, and a protocol for its use. Simple protocols are available10; moreover, the safety and efficacy of streptokinase in the rural setting has been established in at least one study.17 Candidates for intravenous streptokinase generally include those with onset of symptoms within six hours and acute ST-segment elevation characteristic of myocardial infarction. The drug is contraindicated in patients currently on oral anticoagulants or with recent surgery or trauma (including cardiopulmonary resuscitation), recent bleeding or stroke, severe hypertension, known bleeding disorder, or a known adverse reaction to streptokinase. Heparin is generally infused for 48 or more hours after the dose of streptokinase, and the partial thromboplastin time must be monitored during the administration of both drugs. Thus, most patients presenting to the hospital with acute myocardial infarction would qualify as candidates for thrombolysis with streptokinase. One might expect, therefore, that the use of intravenous streptokinase would have rapidly become the standard of care in the small community hospital. The study reported here was designed to assess the extent to which streptokinase has become a therapy for acute myocardial infarction in this setting.

METHODS

A questionnaire was mailed to all 76 primary care physicians (family physicians, general practitioners, and general internists) practicing in nine counties in southern Alabama. These physicians use 16 hospitals ranging in size from 30 to 99 beds (mean, 58 beds); all hospitals are equipped to manage patients with acute myocardial infarction.

The questionnaire inquired about the physicians’ management of acute myocardial infarction, with particular reference to their use of intravenous streptokinase.

RESULTS

Of the 76 questionnaires mailed, 52 were returned, for a 68 percent return rate. In Table 1 are shown the sample and response rates by specialty, and in Table 2, the responses to the questions on the questionnaire. Nearly all responding physicians perform initial evaluation and management of patients with acute myocardial infarction, and most (90 percent) manage at least some of these patients throughout their hospitalization. Of those 47 who continue management, about one half do so with uncomplicated cases only. Thirty-six respondents answered the question concerning their consultants’ use of intravenous streptokinase, and of these, 30 (83 percent) responded positively. This finding contrasts with the finding that of the 47 physicians who themselves continue management of acute myocardial infarction, only 21 (45 percent) have ever used streptokinase. The differences between specialties are not significant (Table 3). Two thirds of these physicians are affiliated with hospitals having a protocol for
intravenous streptokinase, whereas one third practice in hospitals where such a protocol is not established.

**DISCUSSION**

These results indicate that treatment with intravenous streptokinase has found its way into the smaller hospital setting, but not to the extent that its advantages and indications would suggest is appropriate. While nearly all the primary physicians' consultants are experienced in the use of intravenous streptokinase, less than one half of the primary physicians themselves are experienced with its use, and one third of them practice in hospitals where protocol for the use of this drug is unavailable. Why is this apparently efficacious drug neglected by such a sizable percentage of rural physicians?

One reason is lack of knowledge about and experience with the drug. Most of the literature on the efficacy of streptokinase is recent and was not available when most of the physicians in the field today were in medical school or residency training. The use of this drug, therefore, should be the focus of continuing medical education efforts made available to rural physicians.

There may be a more fundamental reason. While this drug seems to be efficacious in the hands of research-oriented subspecialists based in tertiary care referral centers, its efficacy is less certain in the rural setting. The generalizability of the studies done so far is limited. Until more studies on intravenous streptokinase for the treatment of acute myocardial infarction are done in the rural setting by primary care physicians, the present findings should be interpreted with caution. If and when such results become available, the use of this modality may become more universal.

**References**

INTRAVENTRAN STREPTOKINASE

continued from page 439


PENNELL CORP.
WINDSOR TOWNSHIP,
BLOOMSBURG, PA 17815

MICROX®
(metolazone) 1/2 mg Tablets

DO NOT INTERCHANGE: MICROX® TABLETS ARE A RAPIDLY AVAILABLE FORMULATION OF METOLAZONE FOR ORAL ADMINISTRATION. MICROX® TABLETS ARE NOT THERAPEUTICALLY EQUIVALENT TO ZAROXOLYN® TABLETS. FORMULATIONS BIOEQUIVALENT TO MICROX AND FORMULATIONS BIOEQUIVALENT TO ZAROXOLYN SHOULD NOT BE INTERCHANGED FOR ONE ANOTHER.

INDICATIONS AND USAGE Microx Tablets are indicated for the treatment of hypertension, alone or in combination with other antihypertensive drugs of a different class.

USAGE IN PREGNANCY

Diuretics do not prevent development of toxemia of pregnancy, and there is no evidence that they are useful in the management of pregancy-induced hypertension.

The routine use of diuretics is inappropriate and exposes mother and fetus to unnecessary hazard. Diuretics do not prevent development of toxemia of pregnancy, and there is no evidence that they are useful in the management of pregnancy-induced hypertension.

PRECAUTIONS

Microx Tablets are indicated for the treatment of hypertension, alone or in combination with other antihypertensive drugs of a different class.

MICROX TABLETS HAVE NOT BEEN EVALUATED FOR THE TREATMENT OF CONGESTIVE HEART FAILURE OR EDEMA DUE TO RENAL OR HEPATIC DISEASE. MICROX TABLETS SHOULD NOT BE USED WHEN DIURETICS ARE NOT INDICATED.

CONTRAINDICATIONS

Anuria, hepatic coma or pre-coma, known allergy or hypersensitivity to metolazone.

WARNINGS

Metolazone, the rapid onset of severe hypertension and/or hypokalemia has been reported following initial doses of thiazide and non-thiazide diuretics. When symptoms consistent with electrolyte imbalances appear rapidly, drug should be discontinued and supportive measures should be initiated immediately. Additional electrolyte imbalances may be required. Appropriate therapy with this class of drugs should be carefully re-evaluated. Hypokalemia may occur with consequent weakness, cramps, and cardiac dysrhythmias. Serum potassium should be determined of regular intervals, and dose reduction, potassium supplementation or addition of a potassium-sparing diuretic instituted whenever indicated. Hypokalemia is a particular hazard in patients who are digitalized or who have or have had a ventricular arrhythmia. Large doses or total doses may be precipitated. Hypokalemia is dose related.

In general, diuretics should not be used concomitantly with thiazide because they reduce its renal clearance and add a high risk of electrolyte loss. Usually large or prolonged losses of fluids and electrolytes may result when metolazone is administered concomitantly to patients receiving furosemide (see DRUG INTERACTIONS). When Microx Tablets are used with other antihypertensive drugs, particular care must be taken to avoid excessive reduction of blood pressure, especially during initial therapy with these drugs. Therapy with Microx Tablets should not be interchanged for one another. All patients receiving therapy with Microx Tablets should have their serum electrolyte determinations monitored at regular intervals and be observed for clinical signs of fluid and/or electrolyte imbalance. namely, hypokalemia, hypochloremic acidosis, and hypokalemia. In patients with severe edema, concomitant conduction defects, or renal disease, a diuretic may be induced, especially with hot weather and a low-salt diet. Serum and electrolyte determinations are particularly important when the patient has been treated previously for severe renal disease, or is receiving potassium-sparing diuretics. Microx Tablets are contraindicated in patients with severe renal disease, azotemia, and this possibility should be considered with Microx Tablets.

Microx Tablets are contraindicated in patients known to be allergic to sulfonamide-derived drugs, thiazides, or quinethazone.

Drug Interactions: Diuretic-induced hypokalemia can increase the sensitivity of the myocardium to digitalis; serious arrhythmias can result. Corticosteroids or ACTH may increase the risk of hypokalemia. Diuretics do not prevent development of toxemia of pregnancy, and there is no evidence that they are useful in the management of pregnancy-induced hypertension.

Parenteral electrolytes may be required. Appropriateness of therapy with this class of drug must be considered carefully, especially in patients with severe renal disease, azotemia, and this possibility should be considered with Microx Tablets. Rarely, the rapid onset of severe hyponatremia and/or hypokalemia has been reported.

Parenteral electrolytes may be required. Appropriateness of therapy with this class of drug should be carefully re-evaluated. Hypokalemia may occur with consequent weakness, cramps, and cardiac dysrhythmias. Serum potassium should be determined at regular intervals, and dose reduction, potassium supplementation or addition of a potassium-sparing diuretic instituted whenever indicated. Hypokalemia is a particular hazard in patients who are digitalized or who have or have had a ventricular arrhythmia. Large doses or total doses may be precipitated. Hypokalemia is dose related.

In general, diuretics should not be used concomitantly with thiazide because they reduce its renal clearance and add a high risk of electrolyte loss. Usually large or prolonged losses of fluids and electrolytes may result when metolazone is administered concomitantly to patients receiving furosemide (see DRUG INTERACTIONS). When Microx Tablets are used with other antihypertensive drugs, particular care must be taken to avoid excessive reduction of blood pressure, especially during initial therapy with these drugs. Therapy with Microx Tablets should not be interchanged for one another. All patients receiving therapy with Microx Tablets should have their serum electrolyte determinations monitored at regular intervals and be observed for clinical signs of fluid and/or electrolyte imbalance. namely, hypokalemia, hypochloremic acidosis, and hypokalemia. In patients with severe edema, concomitant conduction defects, or renal disease, a diuretic may be induced, especially with hot weather and a low-salt diet. Serum and electrolyte determinations are particularly important when the patient has been treated previously for severe renal disease, or is receiving potassium-sparing diuretics. Microx Tablets are contraindicated in patients known to be allergic to sulfonamide-derived drugs, thiazides, or quinethazone.

Drug Interactions: Diuretic-induced hypokalemia can increase the sensitivity of the myocardium to digitalis; serious arrhythmias can result. Corticosteroids or ACTH may increase the risk of hypokalemia. Diuretics do not prevent development of toxemia of pregnancy, and there is no evidence that they are useful in the management of pregnancy-induced hypertension.

Acute renal failure and this possibility should be considered with Microx Tablets. Rarely, the rapid onset of severe hyponatremia and/or hypokalemia has been reported.