To the Editor:

The recent articles by Khaja, et al (1) and Anderson, et al (2) constitute a significant contribution to the experience with thrombolytic therapy in the management of acute evolving myocardial infarction. However, other reports consistent with these trials yielded disparate results and conclusions. The data presented by Anderson, et al (2) suggest favorable effects of streptokinase, but there are methodological problems: inclusion of subjects who had subtotal occlusion of the infarct artery, and random assignment of control patients to routine cardiac care unit management without angiographic characterization of coronary anatomy. In an accompanying editorial (3), Swan suggests that the time interval between the onset of chest pain and intervention with streptokinase may be the critical variable to explain the seemingly inconsistent findings in these two studies. This suggestion, which has been made previously (4), seems to be inconsistent with reports that streptokinase therapy is effective after mean times of 5.6 ± 4 hours (5) and 9.2 ± 4 hours (6).

Comparison with results from previous investigations is complicated by the use of different doses, routes, and times of administration of streptokinase (5-8), varied usage and modes of administration of anticoagulant therapy (5-8) and by occasional use of corticosteroids and plasminogen (7). Earlier trials lacked randomization and prospective controls (5-7); however, in even more recent studies selected patient groups were so dissimilar that valid comparisons were impossible.

An association has been demonstrated between spasm and the site of significant coronary stenoses (9). How does this observation relate to subjects with total versus subtotal coronary occlusion?

The occurrence of hemorrhagic myocardial infarction after successful reperfusion has been described both in experimental animal studies (10) and in humans (11). That this phenomenon may promote delayed infarct healing, increase susceptibility to rupture and aneurysm formation, and lead to infarct extension (10) merits concern (12). Could streptokinase be replacing an ischemic, “bland” infarct with a hemorrhagic one? If so, would it account for the absence of benefit in ventricular function after therapy?

Streptokinase is an effective agent for producing reperfusion through an occluded infarct artery. Its effect on the ischemic myocardium, however, is less well established. Identifying the clinical, laboratory, and angiographic features of patients likely to benefit from thrombolytic therapy is essential. Only rigorously designed, randomized trials with standardized protocols will resolve these crucial questions: Can streptokinase favorably influence infarct size without unnecessary potential risk? If so, what is its optimal timing and route of administration? What other therapeutic agents (e.g., nitrates, beta-blockers, calcium antagonists, anti-platelet drugs) can be combined with streptokinase for additional benefit? What are the long-term effects of successful reperfusion; and are there definite end-points indicating advantage or detriment? After successful reperfusion, what form of management is best to treat the remaining coronary artery disease? What is the optimal time for such intervention?

We agree with the dictum of Leroy and Snider (13) that “suspicion rather than certainty should govern the physician’s conduct.” Widespread application of thrombolytic therapy to acute myocardial infarction should await further demonstration of its unequivocal benefit.

David M. Lang, MD
Jan Rival, MD
Department of Internal Medicine,
Henry Ford Hospital

References

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