News
The University of Texas Health Science Center at Dallas
5323 Harry Hines Boulevard Dallas, Texas 75235 (214)688-3404

January 28, 1985

CONTACT: Susan Rutherford
OFFICE: 214/688-3404
HOME: 214/349-7820

****Two blood clot-dissolving drugs being tested for limiting the extent of a heart attack.

DALLAS--Saving heart attack patients may depend on how soon they are seen after heart pain begins and the availability of drugs to dissolve destructive blood clots, according to cardiologist Dr. Michael Winniford at The University of Texas Health Science Center at Dallas.

"It now appears that, at the latest, a patient must come into the hospital within three to four hours after the onset of severe heart attack pain in order to limit the extent of heart damage."

He explains that atherosclerosis, caused by cholesterol build-up inside arteries, can lead to angina (warning pain). However, a person generally does not have a heart attack until a blood clot forms at the site of the atherosclerotic placque, says Winniford.

"It is usually the blood clot that causes the myocardial infarction (heart attack)," he says. "In 90 percent of all heart attacks we find a blood clot. In the other 10 percent, the cause of the heart attack is unknown."

Winniford, along with Drs. George Revtyak, James Willerson and David Hillis, is participating in a National Institutes of Health-funded study of two drugs, called thrombolytic agents, known to dissolve blood clots. The drugs, streptokinase and tissue plasminogen activator (TPA), both work to restore blood circulation and can limit the damage to heart muscle. TPA is the newer drug and is more expensive to manufacture since it requires genetic engineering. But TPA may be safer to use.

As part of the three-year National Heart, Lung, and Blood Institute multicenter study, the researchers want to know if indeed one drug is better than the other. They are also looking at whether limiting the size of a heart attack with either drug will actually affect the patient mortality rate.

Winniford says that when a coronary artery becomes blocked the heart begins to die cell by cell in a wave-like manner. If the clot remains in the artery, the area of cell death grows until all the area supplied by the artery is dead.

The patient has a small or large heart attack depending on the amount of tissue supplied by the blocked artery, he says. The time course is tremendously variable. A heart attack may be complete in as little time as three to four hours or as long as eight to ten hours, depending on which artery is affected.

Three years ago standard treatment to control the extent of a heart attack was bedrest, relief of pain with an analgesic, oxygen and treatment of irregular heartbeats. "Treatment was not directed at a blood clot but at controlling the consequences of a blood clot.

"Now it has become clear we have the ability to treat the underlying problem of the heart attack and dissolve the clot, provided the clot can be dissolved in a timely way before the heart attack is finished. Ideally, drugs should be administered within the first two to three hours after the beginning of the heart attack."

Streptokinase is a drug that was first used for pulmonary blood clots and only recently was put to use for coronary clots. Injected into a coronary artery during cardiac catheterization, it has been shown beneficial in dissolving clots. But use of the drug involves a significant risk of bleeding, says Winniford.

Streptokinase, an enzyme produced by a strain of streptococcus bacteria, destroys and attacks a clot at many different levels. It depletes the body of factors needed

(more)

for clotting and remains active in the bloodstream for 24 to 48 hours after injection. During this time the patient is unable to form a blood clot anywhere in the body.

"It takes heroic efforts to stop bleeding during treatment with streptokinase," Winniford says. "The drug works not only in the clot but in the rest of the body as well.

"We are looking at TPA in hopes that it is safer and more effective. The nice thing about TPA is that it only works at the site of the clot. It doesn't destroy the body's ability to make clots after the drug has been administered. If the patient bleeds from an ulcer, we can stop TPA and blood clots quickly. After we have just dissolved a clot in a coronary artery we can treat with heparin to prevent a recurrence of the clot. Fortunately, the effect of heparin can be reversed very quickly if bleeding occurs."

A blood clot, made up of fibrin and plasminogen (protein), can be dissolved by TPA through its ability to change plasminogen to plasmin. Plasmin is the body's own way of dissolving fibrin. TPA is normally produced in the body by endothelial cells. In the heart it may be produced slowly or not at all.

The health science center drug study will locally involve 50 patient volunteers who enter Parkland Memorial Hospital for severe chest pain over a nine month period. Patients choosing to participate are taken to the cardiac catherization lab and a heart catheter is inserted within seven hours of the onset of chest pain. X-rays (coronary angiography) are taken to confirm the presence of a blood clot and then through an intravenous line one of the drugs is given. Over the subsequent two years an additional 100 to 150 patients will be treated in the emergency room at Parkland with a thrombolytic agent.

"In the past, patients have been reluctant to come to the hospital when they are having a heart attack. They have expressed feelings of hopelessness and resignation that nothing could be done medically to stop the process.

"Now if we are to dissolve the clots the patient must come in early. If they wait six or eight hours to enter the hospital it's too late to reduce the size of the heart attack," Winniford says.

##

DISTRIBUTION: AA,AB,AC,AF,AG,AH,AI,AK,SL