Streptokinase Infusion in the Treatment of Acute Myocardial Infarction: A Review

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Abstract

Recent studies indicate that Streptokinase therapy early in Acute Myocardial Infarction can successfully produce coronary thrombolysis in approximately 80% of such patients. Reperfusion is frequently accompanied by relief of chest pain and normalization of ST segments. Cineangiography has shown myocardial salvage of the infarct region, improved LV function, and lowered mortality rates. The untoward effects of Streptokinase treatment appear to be manageable and the benefits of recanalization with Streptokinase outweigh the risks and side effects involved.

Introduction

An acute thrombosis immediately proximal to a high-grade atherosclerotic lesion is the usual cause of myocardial infarction.[1] The removal of the obstructing coronary clot and restoration of blood flow to the ischemic, potentially viable myocardium represents a logical means of limiting infarct size and consequent morbidity and mortality.[2] Since it is rarely possible to accomplish surgical reperfusion by coronary bypass grafting in the optimal period of less than three to five hours following acute myocardial infarction (AMI), other methods of reperfusion of the ischemic myocardium have been investigated. Current studies indicate that intracoronary thrombolysis and restoration of coronary flow can be achieved in AMI by the infusion of streptokinase (STK).[3]

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Current Studies

STK is an enzyme found during the growth of hemolytic streptococci which binds to and converts endogenous plasminogen, a plasma globulin, to plasmin.[4] The plasmin generated constitutes a nonspecific proteolytic enzyme that converts fibrin into its degradation products and results in thrombus dissolution.[5] Following the infusion of STK, coronary blood flow is thus re-established to jeopardized myocardium following AMI.

The efficacy of STK in the treatment of AMI by intracoronary thrombolysis was demonstrated by Rentrop, et al[6] in 1979. The Food and Drug Administration approved the use of STK in May 1982, for the treatment of coronary artery thrombosis associated with AMI.

The major untoward effects following STK therapy are hemorrhagic complications related to the total dosage of STK and are associated significantly with a decline of serum fibrinogen concentrations below 100 mg/dl.[7] Furthermore, since anticoagulation with high doses of heparin after STK therapy appears valuable in reducing early reocclusion, the bleeding tendency is increased.

In light of the potential bleeding problems, STK is generally administered by direct intracoronary infusion to deliver the smallest optimal dose required for thrombolysis. The greatest success has

been achieved by this technique.[5] However, since intravenous or intra-aortic infusion can be initiated earlier following the onset of symptoms without the requirement for coronary artery catheterization, these routes may prove to be favored.[3,5] The speed with which flow is re-established affects the preservation of the jeopardized myocardium. Rapid intravenous administration thus quickly returns blood flow to the potentially viable myocardium.[5]

Several factors influence the efficacy of coronary thrombolysis by STK. The interval between symptom onset of AMI and the initiation of STK therapy appears to be a critical determinant of success. Findings indicate a 73% rate of coronary thrombolysis by intracoronary STK in patients treated within 3 hours following the onset of symptoms.[5] The rapidity of thrombolysis is also related to the earliest institution of STK therapy. Lysis was achieved in less than one hour in patients receiving treatment less than 5 hours from the onset of AMI symptoms.[5] The rate of intracoronary STK administration and the total dose administered also appears to influence the success of the treatment. The optimal rate and dose is unclear at the present time; but ranges from an average total dose of 220,000 IU to 303,600 IU over an average time of 60 to 120 minutes.

A major benefit of STK therapy is improved left ventricular (LV) function. The degree of improvement depends on such factors as severity of acute ventricular impairment, continuing thrombolysis, rethrombosis, and the dose and timing of administration of STK.[8] Timmis, et al[8] found that the most significant improvement was noted in patients whose LV ejection fraction was less than 50% prior to STK administration. There also appears to be a significant relationship between LV function changes after STK therapy and the duration of chest pain prior to STK administration. The critical time interval for preservation of LV function is within the first 4 hours after the onset of AMI symptoms.

Several clinical features are noted at the time of effective recanalization according to Lee, et al.[5] A large proportion of patients were reported with reperfusion ventricular tachyarrhythmias which were managed by antiarrhythmic drugs such as procainamide and lidocaine. Patients who experienced chest pain prior to STK infusion had immediate relief following successful STK reperfusion. ECG ST segment elevation also rapidly normalized following coronary thrombolysis. Patients in whom STK therapy was unsuccessful or in whom STK was not administered had continuing chest pain, persistent ECG ST segment elevation, and absence of reperfusion arrhythmias. These positive clinical features are consistent with decreased myocardial ischemia and preservation of the myocardium following successful STK reperfusion.[5]

Long range effects of STK therapy are unclear and continued management of patients following successful thrombolysis is required. Lee, et al[9] report that although patients with AMI receive immediate and early benefits from STK therapy, such patients are still susceptible to chronic angina, reinfarction, and sudden coronary death. Short-term risks of reinfarction have been reported as high as 10% to 15% among patients recanalized with STK. The importance of coronary artery bypass grafting and anticoagulation therapy is stressed to prevent recurrent ischemia, reinfarction, and reocclusion following reperfusion.[9] The main concern following STK therapy should be directed to the relief of the remaining high-grade coronary stenosis. Results of aorta-coronary bypass grafting following intracoronary thrombolysis indicate that the morbidity and mortality is no greater among patients treated in this manner than those undergoing elective coronary artery bypass.[10]

The hemorrhagic complications following STK treatment do not appear to affect the overall morbidity and mortality associated with coronary artery bypass surgery. It should be noted, however, that bleeding disorders due to coagulation factor consumption may be present in those patients presenting for emergency bypass grafting following unsuccessful STK therapy. The Activated Coagulation Time and heparin dose-response may be atypical. Adequate heparinization is essential to preserve the remaining coagulation factors. The inclusion of Fresh Frozen Plasma as a prime constituent for the heart-lung machine should be considered to replace the factors. Finally, careful monitoring of the fibrinogen concentration and coagulation screen (Thrombin Time, Prothrombin Time and Activated Partial Thromboplastin Time) will guide the perfusion team in restoring coagulation potential after cardiopulmonary bypass.

A review of current studies reveals that STK therapy provides essential myocardial reperfusion during the first few critical hours following AMI. Though complete data is not yet available, it appears that STK therapy followed by bypass grafting of the occluded coronary arteries provides successful treatment for many patients. This combined therapy offers a realistic expectation of improving LV function prior to surgery and of prolonging life.

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