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Intracoronary versus intravenous streptokinase in acute myocardial infarction

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To assess the relative efficacy of coronary thrombolysis using intracoronary versus intravenous streptokinase, 32 patients with acute myocardial infarction were randomly assigned to receive intracoronary ($n = 17$) and intravenous streptokinase ($n = 15$). All patients underwent selective coronary arteriography before and after administration of streptokinase by either route within 4 hours of the onset of symptoms. Intravenous streptokinase was given as 750,000 units over 30 minutes, while a mean dose of 180,000 units was required for thrombolysis in the group having intracoronary delivery. Recanalization occurred in 71.4% (10 of 14) of patients receiving streptokinase, by the intracoronary group in contrast to only 25% of patients (3 of 12) who received the drug intravenously ($P < 0.05$). Spontaneous thrombolysis was seen in 17.6% and 20% of the patients in the groups having intracoronary and intravenous delivery, respectively. Bleeding complications were few in both groups. Thus, when baseline coronary arteriography is performed, recanalization with intracoronary streptokinase is more effective in the treatment of acute myocardial infarction than intravenous streptokinase.

Key words: Intracoronary; Intravenous; Streptokinase; Thrombolysis; Myocardial infarction

Introduction

Thrombosis of an atherosclerotic coronary artery occurs in most patients having transmural acute myocardial infarction [1]. Since the demonstration by Rentrop and

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his colleagues [2] that thrombolysis can be produced with intracoronary infusion of streptokinase, the management of acute myocardial infarction has modified considerably. Intracoronary streptokinase, when given early in acute myocardial infarction, rapidly lyses coronary thrombus and achieves myocardial reperfusion in 75% of patients [3,4]. Intracoronary streptokinase, however, requires trained personnel for its administration and catheterization equipment available around the clock. Intravenous streptokinase is simple to administer and offers the advantage of quicker initiation of therapy. Early reports suggest that rapid intravenous delivery of high doses of streptokinase can dissolve coronary clots in 73 to 96% of patients [5–7]. But, when pre-intervention angiograms are done, these recanalization rates drop considerably [6–8]. Few studies have been conducted using baseline angiograms to compare the effects of streptokinase given by intravenous and intracoronary routes in the treatment of acute myocardial infarction. We present a randomized trial comparing the efficacy of intravenous and intracoronary streptokinase given by these different routes within 4 hours of acute myocardial infarction after visualisation of the blocked coronary artery related to the infarction.

Materials and Methods

We studied 32 patients with acute myocardial infarction, considering only patients less than 70 old years with ischaemic chest pain of more than 30 minutes duration which was not relieved by sublingual nitroglycerin or nifedipine. In addition, at least 2 mm ST segment elevation in two or more standard frontal plane leads or 2 mm in two or more precordial leads had to be present. Patients were excluded if they met any of the following criteria: (1) systolic blood pressure less than 80 mm Hg; (2) severe hypertension; (3) bleeding diathesis; (4) cerebrovascular accident; (5) major surgery or gastrointestinal bleeding during the previous 3 months; (6) prolonged cardiopulmonary resuscitation.

After obtaining informed consent, the patients were transferred from the emergency ward to the catheterization laboratory. They were assigned randomly to receive either intracoronary or intravenous streptokinase. All patients received 100 mg of hydrocortisone intravenously to prevent allergic reactions. Number 7 French side arm sheaths with backflow adaptors were introduced into the femoral artery and sutured into place. A number 7 French pacing catheter was positioned in the apex of the right ventricle. The coronary artery thought to be involved in the myocardial infarction was selectively injected using a No. 7 French pre-formed Judkins femoral catheter. Only patients with complete occlusion of the suspect coronary artery were subjected to interventional therapy. Two-hundred micrograms of nitroglycerin diluted in 2 ml of saline were given as an intracoronary bolus to prevent vasospasm. Patients with severe stenosis and poor antegrade flow were considered to have lysed spontaneously and did not receive any streptokinase. The left anterior descending coronary artery was considered the artery responsible for anterior acute myocardial infarction, and either the right or circumflex coronary artery the infarct-related vessel in inferior myocardial infarction.

Intravenous streptokinase (750,000 units in 50 ml of saline) was given over 30 minutes. Intracoronary streptokinase was given as an initial bolus of 40,000 units,

followed by an infusion of 6 to 8000 units per minute. Injections with contrast material were repeated in both groups every 15 minutes for 1 hour only. Intracoronary streptokinase was continued for 60 minutes if the clot did not dissolve. Intravenous heparin infusion (800 units/hour) was begun 3 hours after successful lysis and continued for 72 hours. The sheath was removed from the femoral artery after 24 hours. Patients with recanalization were maintained on antiplatelet agents for 3 months. Statistical analysis was performed using the standard and chi-square tests.

Results

A total of 32 patients were randomized, 17 to intracoronary and 15 to intravenous streptokinase therapy. The clinical profile of the two groups is shown in Table 1. There were no major differences in sex ratio, age or location of infarction.

The mean time from onset of symptoms to the emergency department was 150 minutes. A further 45 minutes elapsed before the onset of streptokinase infusion. The latter period involved transfer to the catheterization laboratory, further evaluation by the cardiologist and institution of catheterization. There were no significant differences in the time sequence between the two groups, as both required pre-intervention visualization of the coronary arteries (Table 2).

TABLE 1

Patient profile.

Characteristics	Intracoronary	Intravenous
Number	17	15
Mean age	52.4	54.5
(Range)	(30–70)	(40–70)
Male	13	15
Myocardial infarction		
Anterior	9	7
Inferior	8	8
Previous	0	0

TABLE 2

Time intervals and streptokinase.

	Intracoronary	Intravenous	*P* value
No. of patients	17	15	
Symptom onset to emergency	160	140	NS
Symptom onset to streptokinase	205	185	NS

NS = not significant.

TABLE 3

Recanalization rate by selective arteriography.

Coronary artery	Intracoronary		Intravenous		*P* value
	No.	%	No.	%	
Left anterior descending	5/7	71.4	2/7	28.61	–
Right coronary	5/7	71.4	1/5	20	–
Circumflex	0/0		0/0	–	
Total	10/14	71.4	3/12	25	< 0.05

Spontaneous recanalization was seen in 3 of 17 patients (17.6%) in the intracoronary group. Reperfusion with intracoronary streptokinase was achieved in the remaining 10 of 14 patients with 100% block (71.4%). Four (28.6%) vessels remained occluded after 60 minutes continuous infusion of intracoronary streptokinase. Two of these were right coronary arteries and the remainder were the left anterior descending. The time from onset of intracoronary streptokinase infusion to reopening was 20 minutes.

As opposed to intracoronary streptokinase, intravenous streptokinase was successful in only 3 of 12 patients (25%). Two patients exhibited lysis after 45 minutes and one opened in 15 minutes (Table 3). Three of 15 patients in the intravenous group had a patent infarct-related coronary vessel in the initial injection (20%).

The total dose of intracoronary streptokinase used was 180,000 units versus 750,000 units of streptokinase required in the intravenous group.

Ventricular ectopics were noted in all 32 patients during the administration of streptokinase. Accelerated idioventricular rhythm was seen in nine of 13 recanalized patients, but was also seen in 5 of 13 non-reperfused patients (*P* NS).

There were no major bleeding complications in either group. No patients required blood transfusion. Two patients in the intravenous streptokinase group developed bleeding from the gums. Two patients from each group had minor bleeding at the puncture site which was controlled by local pressure.

Two patients in the intracoronary streptokinase group had reinfarction, and one of these died during the hospital stay.

Discussion

This randomized trial suggests strongly that reperfusion with intravenous streptokinase in acute myocardial infarction is unsatisfactory. Intracoronary streptokinase is almost three times as effective, with recanalization occurring in 71.4% of the patients studied. A variety of studies using short-term intravenous streptokinase given in high doses have shown efficacy rates comparable to intracoronary streptokinase [5–7]. The dosage used was similar to ours. Reperfusion was based on indirect evidence such as arrhythmias, rapid resolution of ST segments, relief of chest pain and early peaking of cardiac enzymes. Coronary angiography was usually performed after a week or at discharge from the hospital. But, whenever baseline

coronary angiograms are performed, the recanalization rates plummet to only 10 to 60% [6,8–10]. The lysis rate does not improve when the dose of intravenous streptokinase is increased to 1.5 million units and time of injections extended to 90 minutes [11].

Data without pre-intervention angiograms are likely to be inflated, as spontaneous lysis occurs from 15 to 30% in the initial hours of acute myocardial infarction [12,13]. This may increase to as much as 77% after 14 days [14]. With such a high rate of autolysis following acute myocardial infarction, coronary angiography should be attempted in the first 60 to 90 minutes following streptokinase intervention. Visualization done after a week appears highly unreliable.

Cardiac arrhythmias are too common in the early hours of acute myocardial infarction to be taken as serious markers for reperfusion. Idioventricular rhythm is not specific and ventricular tachycardia cannot be used to distinguish between reperfused and totally occluded vessels [15]. Cardiac enzymes can also be quite non-specific [12,17].

We believe that the only reliable marker for reperfusion is direct visualization by selective angiography of the concerned coronary artery. We initiated therapy within 4 hours of onset of symptoms, but our results with intravenous streptokinase are not very encouraging. We selected only totally occluded vessels for thrombolytic therapy, and managed to recanalize only 25% of patients using intravenous streptokinase. This is a disconcerting piece of information because the majority of patients with acute myocardial infarction would never have access to a catheterization laboratory.

Other points remain to be clarified. Only one randomized trial has shown improvement in left ventricular function after streptokinase therapy [16]. It is still disputed as to whether thrombolysis translates into improved survival [18]. Reduced mortality has been shown in the Washington trial, although there was no change in the infarct size [19]. Greater mortality has been reported with intravenous streptokinase, when used after 9 hours of acute myocardial infarction, in the large Italian trial. In the same study, patients with lateral infarction and ST segment depression did worse than controls [20]. This is interesting because Dewood and his colleagues [21], in yet another landmark trial, have indicated that the rate of thrombus formation increased steadily in the first 7 days after a non-transmural myocardial infarction. One would have expected better results with streptokinase in the subset of patients with ST segment depression in the GISI trial [20].

We took the end point as good antegrade flow in a coronary artery which was previously completely blocked, and did not lay emphasis on mortality or left ventricular function. This was a prospective randomized study with two groups having comparable clinical features and location of myocardial infarction. Both groups received streptokinase within $3\frac{1}{2}$ hr of onset of symptoms.

The trial indicates clearly the superior results obtained by using intracoronary streptokinase for thrombolysis in acute myocardial infarction. We believe non-invasive markers of reperfusion can be misleading and unreliable. Results cannot be extrapolated from coronary arteriography done more than 1 week to 40 days after the acute event [22]. Considering the conflicting data being reported, more rando-

mized trials using larger numbers are warranted to identify the precise clinical role of intravenous streptokinase in acute myocardial infarction.

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