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Reduced incidence of left ventricular thrombi with intravenous streptokinase in acute anterior myocardial infarction: prospective evaluation by cross-sectional echocardiography

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Forty-five consecutive patients with transmural anterior acute myocardial infarction were prospectively studied to determine the effect of intravenous streptokinase on the incidence of left ventricular thrombi. Three patients died. The remaining patients were divided into 2 groups. Group 1 patients ($n = 22$) received 750,000 units of intravenous streptokinase within 6 hours of onset of symptoms. Neither thrombolytic therapy or anticoagulants were administered to 18 patients in group 2. Cross-sectional echocardiography was performed 8 to 10 days following acute myocardial infarction to detect left ventricular thrombus. Technically satisfactory echocardiography was not possible in 2 patients. Apical akinesia or dyskinesia was observed in all patients. No patient in the treated group developed left ventricular thrombus compared with 8 of 18 (44.4%) in group 2 ($P < 0.05$). One patient in the control group sustained an embolic cerebrovascular accident. Thus intravenous streptokinase significantly reduces the incidence of left ventricular thrombus formation in patients of transmural anterior acute myocardial infarction.

Key words: Anterior myocardial infarction; Intravenous streptokinase; Left ventricular thrombus

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Introduction

Left ventricular thrombi are a frequent and well-known complication following transmural anterior acute myocardial infarction. They may embolize into the central nervous system and systemic vessels, resulting in catastrophic and permanent defects [1–5]. Hence prevention of left ventricular thrombus becomes of great importance in the management of patients with anterior acute myocardial infarction. Early anticoagulation does not appear to prevent thrombi development [1,3,6,14]. Extremely few trials have evaluated the effect of thrombolytic therapy on left ventricular thrombus formation. We, therefore, undertook a prospective study, to determine whether intravenous streptokinase reduced the incidence of left ventricular thrombus in patients with anterior acute myocardial infarction, using cross-sectional echocardiographic examination.

Materials and Methods

This was a prospective study of 45 consecutive patients admitted with transmural anterior acute myocardial infarction. Patients with inferior, posterior and undefined myocardial infarction were not included. Patients less than 70 years old with ischaemic chest pain of more than 30 minutes duration, accompanied by at least 2 mm ST segment elevation in 2 or more precordial leads and typical evolutionary changes in the 12-lead electrocardiogram were considered. Patients were excluded if they had a contraindication to thrombolytic or anticoagulation therapy, previous acute myocardial infarction, major surgery or gastro-intestinal bleeding during the previous 3 months. The patients were divided into 2 groups.

Group 1

Patients in group 1 were assigned to receive intravenous streptokinase as they were admitted within 6 hours of onset of symptoms. All patients were given 100 mg of hydrocortisone intravenously to prevent allergic reactions.

This was followed by an infusion of intravenous streptokinase (750,000 units in 50 ml of saline) over 30 minutes. Intravenous heparin (800 units/hour) was begun 3 hours after completion of the intravenous streptokinase infusion. Heparin was continued for 3 to 4 days and the dosage adjusted to maintain whole blood clotting time between 16 and 18 minutes (normal less than 10 minutes). Heparin was followed by anti-platelet agents for 3 months.

Group 2

Patients constituted the control group. These patients had arrived in the coronary care unit after 6 hours of onset of symptoms. No anticoagulation or thrombolytic therapy was administered in this group.

Enzyme Evaluation

Total serum lactate dehydrogenase (LDH) activity was determined on admission, and daily for the next 3 days of hospital stay using a commercially available kit (LDH Autopak-Ames). The normal range is up to 450 IU/l.

Total creatine kinase (CK) and creatine kinase-MB (CK-MB) fraction were measured at admission and daily for the first 3 days. Separated CK-MB and total CK activity were analysed with a commercially available kit (CK-NAC KIT-Stangen). The normal range is 15 to 150 IU/l. A CK-MB level of greater than 5% when total CK activity is over 150 IU/l or a CK-MB isoenzyme value of greater than 8 IU/l when the CK level is less than 150 IU/l was considered positive for myocardial infarction.

Cross-sectional Echocardiographic Evaluation

Cross-sectional echocardiography studies were performed on a Diasonics Cardiovue 3400 R real time echocardiograph using a 2.25 MHz 80-degree wide angle transducer. All patients were examined in the left lateral decubitus position 7 to 10 days following the acute myocardial infarction. Images were obtained from parasternal long and short axis and apical two- and four-chamber views. All studies were independently reviewed by 2 observers and total agreement was a prerequisite for inclusion in the trial. Left ventricular thrombus was diagnosed when observers were in agreement that the following criteria were met: (1) associated wall motion abnormality, (2) apical location, (3) distinct thrombus margin, (4) appearance of the mass in 2 views, (5) acoustically distinct mass from underlying myocardium, (6) consistent size in different views and (7) attachment to left ventricular wall.

False positive or negative readings were minimized by optimal gain settings and care taken to recognize echocardiographic artifacts, papillary muscles, chordal structures, muscular trabeculae and tangential information for normal myocardium.

Apical wall motion abnormalities were analyzed and classified as hypokinetic, akinetic or dyskinetic. Dyskinesia was defined as systolic bulging towards the transducer.

Thrombi were classified as mural (concave free margin) or protruding (convex free margin).

Statistical analysis was done using the standard and chi-square test methods.

Results

Forty-five consecutive patients with transmural anterior acute myocardial infarction were divided into 2 groups. Group 1 patients received intravenous streptokinase and group 2 served as controls. There were 3 deaths – one patient from group 1 and 2 from group 2 expired in the coronary care unit. None of them had displayed evidence of clinical embolization prior to their deaths. No cross-sectional echocardiographic examination was performed in these patients.

Two patients had technically unsatisfactory echocardiograms.

TABLE 1

Characteristics of patients who received intravenous streptokinase (group 1) and those who did not (group 2).

	Group 1 ($n = 22$)	Group 2 ($n = 18$)	Significance
Age	54±16	56±11	NS
Male	18	14	NS
Female	4	4	NS
Apical dyskinesia	19	17	NS
Apical akinesia	3	1	NS
Thrombus	0	8	$P < 0.05$
CK (mean)	1348 IU/l	996 IU/l	NS
CK-MB (mean)	576 IU/l	398 IU/l	NS
LDH (mean)	820 IU/l	705 IU/l	NS

The clinical profile of the 2 groups who had a satisfactory cross-sectional echocardiographic study is shown in Table 1. There were no statistical differences in age, sex or the cardiac enzymes.

No patient in the treated group developed left ventricular thrombus compared with 8 of 18 (44.4%) patients in the control group ($P < 0.05$). There were 6 cases of mural thrombi and 2 of protruding type.

One patient of group 2 had a cerebrovascular accident on the ninth day following acute myocardial infarction. A bland infarction was detected by a computed tomographic scan and a mural left ventricular thrombus on cross-sectional echocardiographic examination. He was put on intravenous heparin (1000 U/hour) and surprisingly had a repeat cerebrovascular accident 3 days after the result, on heparin infusion. The second computed tomographic scan did not reveal intracranial haemorrhage and the cardiac thrombus was reduced in size on cross-sectional echocardiography.

Akinesia or dyskinesia was detected in all patients having left ventricular thrombus, with the thrombus being localized to the apex in each case. There were no bleeding complications.

Discussion

This prospective study demonstrates a clear reduction in the development of left ventricular thrombus when intravenous streptokinase is used in patients with acute anterior myocardial infarction. This is in contrast to data from the Western Washington trial and Friedman et al. [8,9]. Both concluded that intra-coronary streptokinase did not reduce the incidence of ventricular thrombus formation. Five of 45 patients treated in the first study developed cardiac thrombus while paradoxically no patient in the control group developed any. This was a randomized trial but the echocardiographic examination was done 8 weeks following acute myocardial infarction. Friedman et al. detected thrombus in 7 of 13 patients with successful reperfusion of the left anterior descending artery [9].

With systemic streptokinase, however, there is a significant reduction in the frequency of left ventricular thrombus formation [10]. Our trial, with twice the number of patients, is in accordance with Eigler's study. Systemic thrombolysis utilises more than twice the amount of streptokinase employed for direct administration into the coronary ostium. We used 750,000 units of intravenous streptokinase. This may have produced the necessary plasma lytic state to have direct action on the initial left ventricular thrombus.

The exact mechanism for reduction in the incidence of cardiac thrombus requires explanation. It is quite possible that with timely reperfusion there is salvage of myocardium, and reduction in infarction size [16]. We were, however, unable to demonstrate any significant difference in segmental wall motion as detected by cross-sectional echocardiography. Patients with cardiac thrombi had higher peak elevations of cardiac enzymes than those without thrombi, although the difference was not significant. Weinreich et al. [1], Keating et al. [5] and Arvan et al. [23] similarly did not find statistical difference in infarct size and wall motion score in patients with and without cardiac thrombi. Few randomized trials have demonstrated improvement in left ventricular ejection fraction following thrombolytic therapy following acute myocardial infarction [16].

Cardiac thrombi have been seen to develop in the initial hours following acute myocardial infarction [9], and may be susceptible to lysis at this point by streptokinase. Kremer et al. [24] were able to lyse large left ventricular thrombi using systemic urokinase in 10 of 16 patients. Eight of these 16 patients had cardiac thrombi despite full dose heparin and oral anticoagulants.

The incidence of left ventricular thrombi in patients with myocardial infarction ranges from 32 to 70% [1,3,5,14] as detected by serial cross sectional echocardiography and as high as 95% at surgery [8,10].

The incidence of clinical embolism, in patients diagnosed with cardiac thrombus by cross-sectional echocardiography, ranges from 0 to 36% [1,3,5,14,24]. Autopsy studies have reported a 22 to 64% incidence of embolic phenomena [1,3,5]. System embolization, especially into the central nervous system, becomes a particularly sinister problem in these patients. Hence the prevention of cardiac thrombus formation by intravenous streptokinase acquires an important status in the management of acute myocardial infarction.

The role of anticoagulants in preventing cardiac thrombus and embolization remains ambiguous. Results of studies yield conflicting data [1,5,7,18,22]. The Medical Research Council [20] reported a significant reduction in the frequency of clinical thromboembolic events in the high-dose anti-coagulation group, although at necropsy there was no difference from the low-dose group. The incidence of left ventricular thrombi was not studied clinically or on autopsy. The Veterans Administration study [21] did not elaborate on the type of thromboembolic events that were observed in the treated and control groups. The treated group did have a lower incidence of thromboembolic phenomena, but this was not statistically significant. There were 4 deaths because of bleeding in the treated group. No autopsies were conducted. Hilden et al. [22] in a controlled study of anti-coagulant therapy in acute myocardial infarction were unable to reduce significantly the frequency of clinical

thromboembolism, in the treated patients. On autopsy, however, cardiac thrombi were significantly less in the anticoagulated group. But the incidence of peripheral embolism in patients with mural thrombus was greater in the treated group. Anticoagulants, moreover, carry the inherent disadvantages of haemorrhagic complications, dosage monitoring, and problems of patient compliance [21,22].

Recently 2 prospective randomized trials have failed to show a reduction in cardiac thrombi formation by heparin and warfarin in acute myocardial infarction [6,23]. Recurrent emboli on optimal anticoagulation have been reported [7,18,23]. One patient in our series, from the control group sustained an embolic cerebrovascular accident. He recovered in 24 hours but had another embolic cerebrovascular accident after 3 days, despite being on high-dose heparin, with whole blood clotting time at twice normal. The computed tomographic scan was repeated and did not reveal intracranial haemorrhage.

We used cross-sectional echocardiography examination to detect left ventricular thrombus because it is quite sensitive (95%) and specific (86 to 93%) [15]. It is non-invasive, easy to perform, and gives quick information. A major limitation in our study is that we performed cross-sectional echocardiography on only one occasion, and that at 8 to 10 days after acute myocardial infarction. It is not possible to state the time of left ventricular thrombus development. We chose this point of time because 85% of left ventricular thrombi have formed in the first 7 days [22]. Doing an early examination is not predictive of embolization as spontaneous changes in left ventricular thrombus morphology are known to occur [22]. Our end point was to detect the frequency of thrombi occurrence.

This study was not randomized as we could not withhold thrombolytic therapy from any patient with acute myocardial infarction coming into the hospital within 6 hours of onset of symptoms. Another limitation may be false positivity with cross-sectional echocardiographic examination [15].

Reduced mortality has been reported with intravenous streptokinase in patients of transmural anterior acute myocardial infarction [17]. These are the patients most prone to develop left ventricular thrombus and may possibly embolize. Our trial strongly suggests that intravenous streptokinase prevents left ventricular thrombus formation in this group of patients. More prospective, and if possible, randomized studies are recommended to establish this additional advantage.

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