ACUTE MYOCARDIAL INFARCTION SURVIVAL RATE AND COMPLICATIONS AFTER STREPTOKINASE THERAPY IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN - A COMPARATIVE STUDY

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ABSTRACT

Thrombolytic therapy is a well-established therapy in acute myocardial infarction (AMI), reducing mortality and infarct size. This study is a retrospective analysis of survival and complications after the use of streptokinase at Hospital Universiti Sains Malaysia.

Streptokinase was first used here in March 1990. Between then and February 1992, 126 patients were admitted to the Coronary Care Unit . Thirty-two patients who fulfilled our criteria for thrombolytic treatment were given an hour intravenous infusion of 1.5 MU streptokinase, and started on aspirin. A control group of 64 patients selected from before March 1990, and matched for age, sex and site of infarct, was given standard therapy. The survival at 4 weeks post-AMI was 91% in the streptokinase therapy group and 91% in both groups (p> 0.05). The complications encountered were reperfusion arrhythmias (2 patients), hypotension(1), maculopapular rash(1) and gum bleeding(1). None of these complications were statistically increased when compared to the control group and none resulted in the death of a patient.

We conclude that streptokinase therapy can be given safely in a rural Malaysian setting. Our survival and complication rates are comparable with other published series.

Keywords: *myocardial infarction, survival, complications, streptokinase, fibrinolytic therapy*

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INTRODUCTION

The past decade has witnessed the rapid development of an array of fibrinolytic agents and the rediscovery of the oldest agent, streptokinase, in the treatment of acute myocardial infarction (AMI)[1]. The recent Gruppo Italiano per lo Studio della Streptokinase nell' Infacto Miocardico (GISSI-1)[2], Anglo-Scandinavian Study of Early Thombolysis (ASSET)[3] and Second International Study of Infarct Surivival (ISIS-2)[4] trials have unequivocally demonstrated that administration of fibrinolytic agents early in the course of an evolving MI reduces in-hospital mortality. The ISIS-2 trial established that the combination of aspirin and a fibrinolytic agent reduces acute mortality by as much as 40%[4]. Those patients allocated the combination of streptokinase and aspirin had significantly fewer reinfarctions, strokes and deaths than those allocated neither[4]. The above trials have demonstrated that high dose intravenous streptokinase achieved re-canalisation of the affected coronary artery in 35-55% of patients. Thus thrombolytic therapy is now a well accepted therapy for acute myocardial infarction in patients presenting within the first few hours.

This study reviews the use of short-term intravenous streptokinase in combination with long-term aspirin in acute myocardial infarction at the Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian. The survival rate of the patients after 4 weeks, and the complications encountered during streptokinase therapy, are documented. A historical control group treated in our unit is also reviewed for comparison.

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METHODS

Patients

The subjects in this study were patients admitted to the Coronary Care Unit (CCU) in HUSM for AMI between March 1990 and February 1992. Of the 126 patients admitted to our CCU during this period, 33 patients were given streptokinase after satisfying the following criteria:

Criteria for inclusion

i) Chest pain which was compatible with acute myocardial infarction of less than six hours' duration
ii) ECG showing ST elevation of 2 mm or greater in V1 - V6 or 1 mm or more in the limb leads.

Criteria for exclusion were

i) Age more than 70 years.
ii) Severe hypertension (> 200/120 mmHg)
iii) Recent peptic ulcer bleeding
iv) Bleeding disorder
v) Anticoagulation therapy
vi) Stroke within the preceding 6 months
vii) Major surgery within the preceding 6 weeks
viii) Recent severe trauma including external cardiac massage
ix) Streptococcal infection, or use of streptokinase in the last 3 months.

One patient was excluded from analysis as he was subsequently found to have had unstable angina and not myocardial infarction. A control group of 64 patients was selected (2 controls for each streptokinase-treated patient) from prior to the streptokinase therapy era at HSUM, matched for age (same decade of life), sex and site of infarct. Patients were diagnosed to have hypercholesterolemia (in patients less than 55 years of age) if their cholesterol concentration was greater than 240 mg/dL or triglyceride concentration was greater than 250 mg/dL[5]. Patients with a diastolic pressure greater than 90 mmHg were diagnosed to have hypertension[6] while diabetic patients were diagnosed following the revised criteria of the National Diabetes Data Group of the National Institute of Health (1979):

Table I - Age and racial distribution of patients with acute myocardial infarction treated with streptokinase and in the control group

	Streptokinase group (n=32)	Control group (n=64)
Age (years)		
30 - 39	6	12
40 - 49	11	22
50 - 59	12	24
60 - 69	3	6
Race		
Malay	29	59
Chinese	2	4
Indian	1	1

(1) Fasting (overnight):Venous plasma glucose concentration 140 mg/dL on at least two separate occasions. (2) Following ingestion of 75 g of glucose: Venous plasma glucose concentration $\geq$ 200 mg/dL at 2 hour and on at least one other occasion during the 2 hour test (ie two values $\geq$200 mg/dL must be obtained for diagnosis)[7]. These patients were diagnosed to have hypercholesterolemia, diabetes mellitus or hypertension during previous admissions or subsequent follow-ups or during the present admission itself. Patients were defined as smokers if they smoked more than one cigarette a day for at least a year[8].

Procedure And Treatment Protocol

Before the infusion of streptokinase, all patients had a twelve-lead ECG. This was repeated soon after completion of the infusion, every 6-hourly for 24 hours, and then daily for a least 3 consecutive days. The patients were assessed to be in cardiogenic shock if they fulfilled some of the following criteria: (i) systolic arterial blood pressure < 90 mmHg; (ii) clinical signs of peripheral circulatory insufficiency, eg cold, moist skin, cyanosis; (iii) dulled sensorium; (iv) oliguria with urine flow of less than 20 mL/h; and (v) failure of improvement following relief of pain and administration of oxygen[9]. Blood was taken for grouping and cross-match in case of emergency complications.

Prior to the administration of streptokinase, intravenous hydrocortisone 100 mg was given as a precaution for allergic reactions. Streptokinase 1.5 megaunits was then added to 100cc of normal saline and infused over one hour. The patients were also started on long-term oral aspirin 150 mg daily.

For the control group, treatment included isosorbide dinitrate (55 patients), aspirin(32), calcium channel blockers(5) and beta-blockers(3).

Statistics

Statistical comparison between the two groups was performed using the chi-square test.

RESULTS

Thirty-two patients who were admitted for AMI were treated with intravenous streptokinase. The majority of patients were Malays (91%), followed by Chinese (6%) and Indians (3%). There was only one female patient while the others (97%) were male. The youngest patient was 31 years old while the oldest patient was 67 years with a mean age of 49.2 years (Table I).

As for the control group (64 patients) , the majority of patients were also Malays (92%), followed by Chinese (6%) and Indians (2%). There were 2 female patients (97% were males). The youngest patient was 33 years old while the oldest was 65 years with a mean age of 47.9 years (Table I).

Table II - The site of infarcts which occurred in the streptokinase and control groups

Site of infarct	Streptokinase No of patients (%)	Control No of patients (%)
Anterior	13 (41%)	26 (41%)
Inferior	11 (34%)	22 (34%)
Anteroposterior and/or anteroinferior	6 (19%)	12 (19%)
Anterolateral	2 (6%)	4 (6%)
Total	32	64

Table III - The complications which occurred in the streptokinase and control groups.*

Complications	Streptokinase No. of patients (%)	Control No. of patients (%)	p
Arrhythmias	2 (6%)	6 (9%)	>0.05
Hypotension	1 (3%)	1 (2%)	>0.05
Maculopapular rash	1 (3%)	0	>0.05
Gum bleeding	1 (3%)	0	>0.05

*There was no significant difference in the incidence of the any of the complications between the two groups.

Of the 32 patients given streptokinase, 22 were smokers, 15 were hypercholesterolaemic, 9 were diabetic, 8 were hypertensive and 3 had a family history of ischaemic heart disease.

In the control group of 64 patients, 48 were smokers, 16 were hypercholesterolaemic, 14 were diabetic, 21 were hypertensive and 6 had a family history of ischaemic heart disease.

Of the patients given streptokinase therapy, anterior infarcts occurred in 13 patients (41%), another 11 patients (34%) had inferior and/or posterior infarcts, while 6 patients (19%) had anteroposterior and/or anteroinferior infarcts. Two patients (6%) had anterolateral infarcts (Table II).

In the control group, anterior infarcts occurred in 26 patients (41%), 22 patients (34%) had infarcts and/or posterior infarcts while 12 patients (19%) had anteroposterior infarcts. Four patients (6%) had anterolateral infarcts (Table II).

Characteristics of patients on admission

In the streptokinase group, 26 patients (81%) had clinical evidence of left ventricular failure and/or radiological upper lobe diversion or pulmonary oedema on admission; 4 patients (13%) had arrhythmias and 3 (9%) had cardiogenic shock, as defined in 'methods'.

Of the patients in the control group, 58 (91%) had clinical left ventricular failure and/or radiological upper lobe diversion or pulmonary oedema on admission; 9 (14%) had arrhythmias while 6 (9%) had cardiogenic shock.

Complications occurring after therapy

The complications encountered following streptokinase therapy in the 32 patients receiving streptokinase were: (a) reperfusion arrhythmias - 2 patients (6%) - one developed ventricular fibrillation midway through the streptokinase therapy and was defibrillated while the other patient developed ventricular tachycardia and was given a lignocaine bolus followed by infusion; in the control group 6 patients (9%) had arrhythmias following 'standard therapy'; (b) hypotension - one patient (3%) as compared to one patient (2%) in the control group; (c)

masculopapular rash - one patient (3%), but no patient in the control group; and (d) gum bleeding - one patient (3%) with no patient in the control group (Table IV). None of these complications noted in the streptokinase group were statistically increased when compared to the control group. Also, none of these complications following streptokinase therapy resulted in the death of a patient.

In the control group, arrhythmias (14%) and hypotension (9%) were present on admission. Following standard treatment - which included the use of morphine, isosorbide dinitrate, aspirin, beta blockers or nifedipine - arrhythmias and hypotension were noted in an additional 6 patients (9%) and one patient (2%) respectively. Of the 32 patients given streptokinase, 3 died within 4 weeks (91% survival) as compared to 6 out of the 64 control patients (also 91% survival) ($p > 0.05$).

DISCUSSION

Coronary heart disease is one of the leading causes of death in Malaysia. It is the premier cause of all medically-certified hospital death[10]. In 1982 cardiovascular causes accounted for 31% of reported deaths in Peninsula Malaysia[11]. Within Malaysia, prevalent risk factors for coronary heart disease include smoking, hypertension, diabetes mellitus, hyperlipidemia and 'lifestyle[12].

Short-term intravenous infusion of streptokinase has been found to be safe and clinical results are encouraging[2,3,13-15]. Thrombolytic therapy has been demonstrated to recanalise occluded coronary arteries and reduce infarct size, thereby limiting cardiac dysfunction and reducing mortality[2,3,9,13,14,16]. However, the problems of persistent coronary occlusion, reocclusion following successful thrombolysis and occasional serious bleeding complications remain in some patients. Concomitant use of other pharmacological agents may improve thrombolysis and/or reduce myocardial injury, and hence may decrease the required dose of the thrombolysis agent, and the risk of serious bleeding. These agents, which include platelet inhibitors, thrombin inhibitors, beta-blockers, angiotensin-converting enzyme inhibitors, nitrates and calcium antagonists act by improving coronary blood flow, improving cardiac loading conditions or limiting myocardial injury[17].

The early administration of low dose aspirin in combination with thrombolytic agent has become an established treatment in acute myocardial infarction[2]. Thus, at HUSM, we use low dose oral aspirin in combination with streptokinase for all patients admitted to CCU who fulfil our criteria for thrombolytic therapy. This study reviews the complications and survival rate in patients given streptokinase. A historical control of 64 patients, who matched the streptokinase group patients for age, sex and site of infarct, was also reviewed.

Patients aged between 50-59 years were found to be the majority in this study: the mean age was 49.2 years for the streptokinase group and 47.9 years in the control group. The majority of patients in both groups studied were Malays and males as seen in Table I. The racial distribution of our patients is approximately that of Kelantan, which is a predominantly Malay society. The patients exhibited a typical Malaysian risk factor profile, which was very similar in the two groups. The most common site of infarct group was anterior (41%), followed by inferior (34%), anteroposterior and/or anteroinferior (19%) and anterolateral (6%). On admission, arrhythmias were noted in 13% and 14% in the streptokinase and the control groups respectively, while hypotension was noted in 9% of patients in both groups.

The complications after streptokinase therapy seen in our patients were reperfusion arrhythmias (6%), hypotension (3%), maculopapular rash (3%) and gum bleeding (3%). None of these complications were statistically increased when compared to the control group. These complications were all minor, had a low incidence rate and did not result in any deaths. These findings are comparable with previous studies[2,4]. In the control group, after standard treatment was given, both arrhythmias (9%) and hypotension (2%) were also noted. A much larger number of patients would need to be studied to estimate the incidence of rare serious complications, such as intra-cranial haemorrhage[2,4,15,18].

Our survival rate of 91% four weeks after streptokinase therapy also compares well with those of other studies[2,4]. However when compared to the control group, also with a survival rate of 91%, there was no difference, probably due to the small number of patients studied.

In the streptokinase group, 2 of the 3 deaths occurred in patients with extensive myocardial infarction who developed ventricular fibrillation 2-3 days after streptokinase therapy. The other death (one patient died at home, 21 days after therapy) was most likely due to reinfarction. In the control group, 2 of the 6 deaths were due to ventricular fibrillation as a terminal event. One patient died at home and the other 3 patients died of cardiogenic shock. Unfortunately, the causes of death could not be substantiated as no post mortems were performed.

We concluded that in a rural Malaysian setting, intravenous streptokinase seems to be a safe drug for routine administration in early myocardial infarction. There is a low incidence of complications, and none of the complications observed in our patients led to a fatal outcome.

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