

Streptokinase used in general practice

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SUMMARY. Over a six-month study in general practice 43 patients were identified whose presenting symptom was chest pain thought to be cardiac in origin. The median time from the onset of pain to the general practitioner attending was 60 minutes.

On the basis of history, examination and initial electrocardiogram these patients were assessed as unlikely or likely to be infarcting. Of this latter group 15 fulfilled the inclusion criteria for intravenous streptokinase, four commencing treatment at home and 11 on admission to the local general practitioner medical ward. Each received 1.5 mega units over 60 minutes. The median time from the onset of pain to the start of therapy was 120 minutes. Of the 28 patients clinically suspected of having sustained a myocardial infarct 24 proved positive — an over-diagnosis rate of 14%. No major problems were encountered following streptokinase.

Introduction

STREPTOKINASE was first discovered in 1933 by Tillett and Garner.¹ However, its logical use in the treatment of myocardial infarction has only been possible in recent years with the understanding of the dynamics of coronary artery occlusion and the definitive establishment by DeWood in 1980 of a thrombus as the cause.² Recent trials have shown that intravenous streptokinase is effective when instituted early after the onset of pain, resulting in reduced infarct size and reduced mortality both at 21 days and 12 months.^{3,4} The benefit is greatest when streptokinase is given within the first three hours after the onset of symptoms.³

This paper examines the use of streptokinase in general practice for patients presenting over a six month period with chest pain thought to be cardiac in origin. The study recorded the time from the onset of pain until the general practitioner attended, the general practitioner's ability to select the correct patients for streptokinase therapy and the outcome of the treated cases.

Method

Stranraer and district, situated in the south-west of Scotland, is served by five practices working from a health centre and one rural group practice; 17 500 patients are cared for over an area of 400 square miles, mainly centred in Stranraer and six outlying villages.

The health centre is attached to the local hospital which has 20 medical and 24 surgical beds. The 20 bed medical ward is staffed by the general practitioners. All 14 principals agreed to participate in the study.

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During the study two packs each containing an infusion set, saline, streptokinase, hydrocortisone and syringes, protocol sheet and patient data sheet together with a defibrillator with monitor on constant charge were kept at the hospital casualty department. These were available for the two on-call general practitioners from the health centre at weekends, evenings and nights on call. The rural practice was similarly equipped.

Criteria for treatment

All patients presenting with chest pain thought to be cardiac in origin were included in the study. Patients were given streptokinase therapy if they fulfilled any of the following criteria:

1. Classical history with pain lasting for more than 20 minutes, unrelieved by sublingual nitrates.
2. Suggestive history plus ST elevation of 2 mm in chest leads.
3. Suggestive history plus ST elevation of 1 mm in limb leads.

Patients were not given therapy if any of the following applied:

1. More than six hours elapsed since the onset of pain.
2. Aged over 75 years.
3. Vascular disease present: transient ischaemic attack, cerebrovascular accident less than two weeks earlier, uncontrolled high blood pressure, dissecting aneurysm, valvular disease plus atrial fibrillation.
4. Systemic disease present: peptic ulceration, diabetes plus proliferative retinopathy.
5. Taking anticoagulants or antiplatelet drugs.
6. Bleeding disorders present.
7. Recent surgery (less than two weeks earlier).

In view of the general practice setting of the study the exclusion criteria were absolute.

Procedure

For patients fulfilling the above criteria, intravenous analgesia was given, blood was taken for grouping, hydrocortisone was given intravenously and streptokinase treatment was commenced (1.5 mega units in 100 ml saline infused over 60 minutes).

The patients were monitored in transit and in the ward. Serial enzyme tests and electrocardiograms (ECGs) were carried out over the first three days. For each patient the general practitioner recorded on a prepared data sheet the time from the onset of pain until the arrival of the general practitioner (access time), the time from the onset of pain until admission to the medical ward (admission time) and the time from the onset of pain to the instigation of streptokinase treatment (treatment initiation time). Also recorded were any complications and the eventual outcome.

Results

Information was provided about 43 patients, 15 of whom fulfilled the criteria for streptokinase treatment. Of the 43 patients 12 had contraindications to treatment. Five patients had had pain for more than six hours, four were over 75 years of age and three had previous gastrointestinal bleeding. Twenty patients (46.5%) were accessed by the general practitioner in the first hour and 31 (72.1%) in the first four hours (Figure 1). Twenty one patients (49%) were admitted in the first two hours and 30 (70%) in the first four hours. The median time for admission to the medical ward for the various groups are presented on Table 1 as are the median times to the instigation of treatment for the streptokinase group.

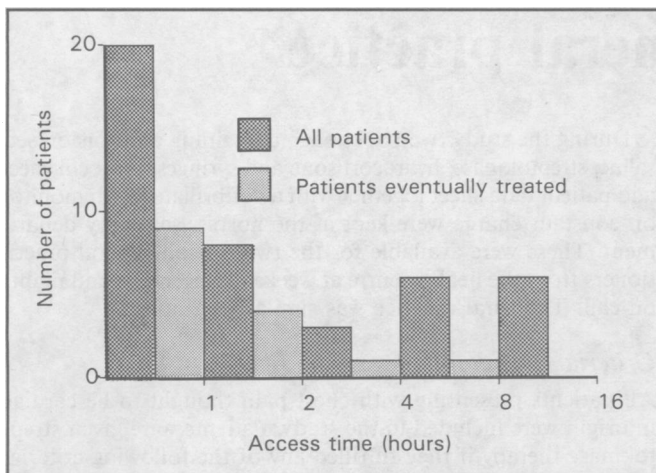


Figure 1. Time from onset of pain to arrival of general practitioner for all 43 patients and the 15 who were treated with streptokinase.

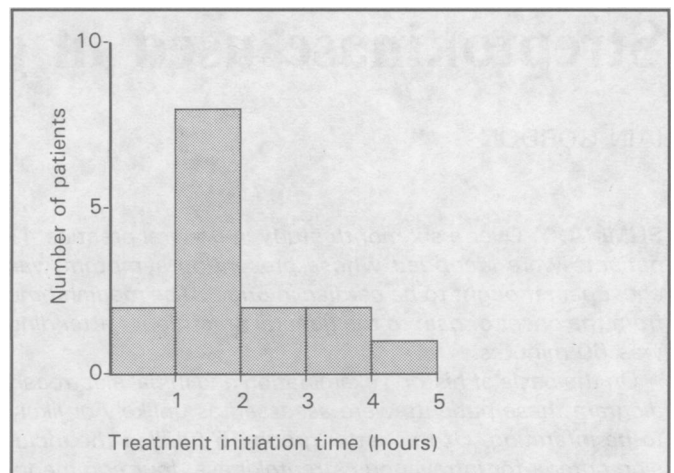


Figure 2. Time from onset of pain to initiation of treatment with streptokinase for 15 patients treated.

Table 1. Median access, admission and treatment initiation times for all patients, those with confirmed myocardial infarction and those treated with streptokinase.

	Median access time (min)	Median admission time (min)	Median treatment initiation time (min)
All patients (n = 43)	60	90	—
Confirmed infarction (n = 24)	120	140	—
Treated with streptokinase (n = 15)	60	80	120

Of the 20 patients accessed in the first hour nine were considered suitable for streptokinase; two of those commenced treatment within the first hour and six in the second hour. Of the eight accessed in the second hour four were suitable and two commenced treatment in the second hour (Figure 2).

Four patients were started on streptokinase at home and then transferred to the general practitioner medical ward. Eleven were given treatment immediately on admission.

Hypotension, haematuria and reperfusion arrhythmias were among the problems encountered in the post-treatment period. No patient gave cause for clinical concern as a result of these complications. No problems arose which did not respond to standard therapies.

Four patients died: two in the untreated group (at four hours and 20 hours) and two in the treated group (at 20 days and 35 days, the latter while still in hospital).

On initial assessment 28 patients were considered to have a myocardial infarct; 24 were confirmed. Fifteen patients were considered to have anginal pain only but three cases were confirmed as a myocardial infarction.

Discussion

Streptokinase is effective, particularly when given in the first three hours following myocardial infarction.³ It is therefore of paramount importance that patients be accessed and treatment commenced as rapidly as possible. It may be possible to educate the public to call earlier and doctors should make every effort to attend without delay but the only method immediately available to reduce the treatment time is for general practitioners to start treatment before hospital admission.

Our numbers, though small, do not reflect the findings of Rawles and colleagues;⁵ 72% of all patients were seen by the

general practitioner within four hours from the onset of pain and 70% were admitted to hospital within four hours, whereas 66% in the Aberdeen study had only sought help in that time. There may be many factors to explain this — local community health education, centralization of the population, no use of deputizing services and the relatively small practice numbers. We are also fortunate in having an excellent working relationship with the ambulance service who provide a rapid response to our requests for immediate transfer of patients to the hospital.

It is encouraging that the treated group has such a short access time and consequently treatment time; for 66% streptokinase treatment had commenced within two hours, and for 80% inside four hours. The reason for the difference in access and admission times between this group and the other patients with confirmed infarcts, but who were not treated because of various contraindications, is unclear.

It was disappointing that only four patients had treatment initiated at home. This may reflect general practitioners' initial apprehension about the use of streptokinase. Large series have shown a favourable risk-benefit profile and the complications of bleeding and allergic reactions should not deter general practitioners from using the drug.^{3,4} The incidence of bleeding complications is related more to the use of concomitant anticoagulant therapy and the presence of underlying vascular injury; in the ISSI trial the incidence of major bleeds was 0.3%.⁴ Another factor explaining the small numbers of patients treated at home is the rapid admission time in our area — 49% of patients had been admitted within two hours and 70% within four hours — and the knowledge of this may have influenced the practitioners to await admission before starting therapy.

The importance of assessing the patient accurately is a crucial factor in enabling early instigation of treatment. Of the 28 patients thought to have an infarct 24 were confirmed as having sustained myocardial damage. Two of the treated group did not show a rise in enzymes, one treated at 76 minutes and one at 240 minutes. An over-diagnosis rate of 14% exposes some patients to unnecessary treatment and its attendant risks. However, it is noteworthy that 18% of patients who fulfilled selection criteria similar to ours were found to have open vessels at angiography on initial assessment.⁶ The early and accurate clinical decision can be further complicated by intermittent coronary occlusion resulting in variable ST changes.⁷ It would appear that the risk of misdiagnosis should be accepted if the majority of patients are to gain the benefit of early treatment.

In the light of recent evidence⁸ our exclusion criteria for using streptokinase have altered. Patients irrespective of age are treated up to 24 hours after the onset of pain and receive oral

aspirin at first contact.

This study has shown that patients with chest pain presenting to general practitioners can be accessed quickly, diagnosis can be made with acceptable accuracy and treatment with streptokinase commenced early in the process of infarction without any major difficulties being encountered.

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