ORIGINAL ARTICLE

STREPTOKINASE FOR ACUTE MYOCARDIAL INFARCTION IN THE ELDERLY

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Background: Acute myocardial infarction is one of the leading causes of death in the elderly, however clinical data reveals a disproportionately lower use of thrombolytics because of fear of complications especially intracranial haemorrhage. Our objective was to evaluate the safety of most commonly used thrombolytic streptokinase in elderly patients presenting with acute myocardial infarction. **Methods:** This descriptive case series was conducted at Punjab Institute of Cardiology, Lahore from September to December 2012 (4 months). One hundred elderly patients presenting with acute myocardial infarction were randomly selected for the study keeping in view the inclusion and exclusion criteria. All patients were thrombolysed with streptokinase within 12 hours of onset of symptoms and were monitored and investigated for electrical, mechanical and biochemical complications. **Results:** Out of one hundred patients 77 (77%) were males and 23 (23%) were females. Mean age was 73.39±5.29 years. The two most common complications of streptokinase were hypotension (33%) and bleeding (19%). Major bleed occurred only in 3 (3%) patients. No patient developed intracranial haemorrhage. Other complications included arrhythmias (6%), allergic reactions (4%), raised LFTs (6%) and raised RFTs (7%). No patient died of streptokinase related complications. **Conclusions:** Use of streptokinase for acute myocardial infarction should not be discouraged in the elderly.

Keywords: Acute myocardial infarction, Streptokinase, Thrombolytics

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INTRODUCTION

Streptokinase (SK) is an extensively used thrombolytic agent for the management of acute myocardial infarction (AMI) worldwide[1] and is the most commonly used thrombolytic in Pakistan because of its lower cost and ready availability[2]. It is a 1st generation fibrin non-specific thrombolytic and biochemically is a serine protease enzyme derived from certain strains of beta haemolytic streptococci.[3] It consists of a single polypeptide chain containing 414 amino acids.[4] It was first used in acute myocardial infarction in 1958 and since then it has revolutionized the management of acute myocardial infarction.[4] However its efficacy was first proven without any doubt in the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-1) trial published in 1986. Apart from acute myocardial infarction it is also administered for pulmonary thromboembolism, acute arterial occlusion and deep venous thrombosis.[1] Its efficacy and safety has been studied in various large scale multi-centre trials.[5,6]

Early parenteral SK therapy improves survival in patients with ST-elevation myocardial infarction (STEMI).[7] Most benefit is achieved if it is infused within 2 hours of onset of symptoms[8] however, Late Assessment of Thrombolytic Efficacy (LATE)[9] and Estudio Multicéntrico Estreptoquinasa Repúblicas de América del Sur (EMERAS)[10] trial have proved its significance in lowering mortality rate and Post-MI complications even if given up to 12 hours after onset of the symptoms. This benefit of SK in reduction of mortality and complications goes beyond years.[11,12]

Most common complication of SK is bleeding and most dreadful and feared complication is intracranial haemorrhage (ICH).[13] Predisposing risk factors for intracranial haemorrhage include age >70 years, body weight <70 kg, uncontrolled hypertension, recent stroke, head injury, intracranial tumour, wide pulse pressure, bleeding disorder and female sex.[14] Primary percutaneous coronary intervention (PCI) is undoubtedly the treatment of first choice in elderly patients with acute myocardial infarction.[15–18] However, most of the centres even in the developed countries do not have this facility.

Acute Myocardial infarction accounts for 1/3rd of deaths in the elderly population[20] and they should not be denied appropriate treatment just because of fear of very rare complication, i.e., intracranial haemorrhage. There is no documented evidence so far that the risk benefit ratio of thrombolysis substantially differ in elderly than in young.[19] Recent studies suggest that chronological age is less important than the assessment of general health status, functional status and risk related to myocardial infarction and a one-size-fits-to-all approach of care in the old is not feasible.[21] Our Objective was to assess the safety of SK in the elderly acute myocardial infarction patients.

MATERIAL AND METHODS

This descriptive case series was conducted at Punjab institute of cardiology Lahore from September to December 2012. One hundred patients presenting with acute myocardial infarction were selected by Non-probability convenient sampling for the study keeping in view the inclusion and exclusion criteria. Complete history was taken including risk factor evaluation. Clinical examination was done with full protocol. Informed consent was taken from every patient and the study was approved by ethical review committee. Blood and urine samples were taken for various haematological and biochemical tests on arrival of patient in the emergency. Every patient was given chewable Aspirin (300 mg), clopidogrel (300 mg) and adequate sedation and analgesia. Injection streptokinase was administered 1.5 MU in 100 ml normal saline in microburette in 1 hour through peripheral venous line with half dose going in 1st 20 minutes. Patient was continuously monitored for occurrence of any mechanical, electrical, fibrinolytic complications during infusion. Patients were not given heparin in any form pre or post- SK. ECG was repeated at 90 minutes post- SK for assessing success of thrombolysis. Patients were kept admitted in hospital for 48-72 hours with repeated evaluation and monitoring for any complications of thrombolysis. Cardiac enzymes, renal function tests, liver function tests, blood counts, serum electrolytes and urine routine examinations were repeated 12 hours post-SK. Patients with deranged lab tests underwent repeat investigation one week later on follow up in OPD of Punjab Institute of Cardiology Lahore.

Patients of acute myocardial infarction with age 70 years or above and presenting within 12 hours of onset of symptoms

Patients taking anticoagulants, any prior intracranial haemorrhage, known structural cerebral vascular lesion (e.g., arterio-venous malformation), Known malignant intracranial neoplasm (primary or metastatic), ischemic stroke within 3 months, closed head injury within 3 months, active bleeding (excluding menses), bleeding diathesis, suspected aortic dissection, prior exposure to streptokinase within 2 years, active peptic ulcer disease, recent surgery (within 4 weeks), internal bleed (2–4 weeks), decompensated or active liver or kidney disease.

All statistical analyses were performed using SPSS-16 for windows. Quantitative variables like age were expressed as Mean±Standard deviation. Qualitative variables like gender and risk factors for ischemic heart disease (Diabetes, hypertension, smoking, hyperlipidemia and positive family history) were presented by calculating frequency and percentage. Complications of streptokinase were also expressed as frequency and percentages.

RESULTS

Out of one hundred patients 77 (77%) were males and 23 (23%) were females. Mean age was 73.39±5.29 years. Oldest patient was 94 years of age while the youngest was 70. Baseline characteristics are shown in Table-2. Mean door to needle time was 5.43±2.5 hours. Thrombolysis was successful in 63 (63%) patients.

Bleeding occurred in 19 (19%) patients. Sixteen patients had minor bleed only while 3 had major bleed, one of them had lower GI bleed (cause was haemorrhoids which were banded on the next day and patient recovered uneventfully), one had upper GI bleed (endoscopy revealed pan- gastritis-was managed with blood transfusions and intravenous omeprazole-recovered well) while one had haemoptysis (Chest X-ray revealed bronchiectatic cavitations. Bleeding settled within 24 hours, managed with blood transfusion and pulmonology consultation referral). Most common sites of bleeding were vascular puncture sites and oropharyngeal bleeds (gum bleed)-Table-4. No patient developed ICH. Mean age of patients that developed bleeding was 72.58±5.86 years.

Most common complication was hypotension that occurred in 33 (33%) patients. All of them developed this during SK infusion. No patient had a major allergic reaction. Minor reactions occurred in 4 (4%) patients. Sustained arrhythmia developed in 6 patients with two having sustained ventricular tachycardia and had to be electrically cardioverted while one developed atrial fibrillation and responded to IV amiodarone. Two patients developed complete heart block and were paced with temporary pacemaker (TPM).

Three patients died during hospital stay from ischemia related complications. All three were males. None of the patients died due to Streptokinase related complications.

Table-1: Age of patients

Age group (Years)	Number of patients
70–80	93 (93%)
81–90	5 (5%)
>90	2 (2%)
Total	100 (100%)
Mean age	73.39±5.29

Table-2: Baseline characteristics

Risk factors	Number of patients
Diabetic	26 (26%)
Hypertensive	31 (31%)
Smoker	39 (39%)
Positive Family History	9 (9%)
Hyperlipidemia	17 (17%)

Table-3: Complications of streptokinase

Complication	Number of patients
Bleeding	19 (19%)
Intracranial Haemorrhage	0
Hypotension	33 (33%)
Allergic Reactions	4 (4%)
Thrombocytopenia	1 (1%)
Raised LFTS	6 (6%)
Deranged RFTS	7 (7%)
Proteinuria	Zero
Fever	3 (03%)
Arrythmias	6 (06%)
ARDS	0
Peripheral Neuropathy	0
Cholesterol Embolization	0
Death directly due to SK	0

Table-4: Sites of bleeding

Sites of bleeding	Number of patients
Vascular Puncture Sites	6
Oropharyngeal	6
GI Bleed	3
Respiratory Tract	1
Urinary Tract	2
Muscle And Skin	1
Intracranial	0
Total	19

DISCUSSION

Streptokinase is a drug with significant mortality benefit in acute myocardial infarction but even in developed countries like USA elderly have been denied this treatment because of the fear of complications especially intracranial haemorrhage (ICH). A study conducted by Weaver *et al*[22] revealed that as compared to the 50.7% patients having age less than 65 years only 19% of patients aged between 65–75 years and 7.04% of patients aged greater than 75 years received thrombolysis for acute myocardial infarction.[22]

This fear is not imaginary as studies have proved that complications of thrombolytic therapy tend to occur more in the elderly group.[23–27] Elderly have more haemorrhagic strokes, hypotension, cardiogenic shock, and heart failure.[22]

In our study minor bleeding occurred in 16% patients while major bleed occurred in only 3% patients. No patient developed life threatening haemorrhage like intracranial haemorrhage. These results are not different from studies involving young adults. An incidence of 3.6% for minor bleeding and 0.4% for major haemorrhage is derived from the combined results of the GISSI[6] and ISIS-2[28] trials. Results of GUSTO-I[29] trial showed 1.2% patients suffered severe bleeding and 11.4% experienced moderate haemorrhage at a variety of sites. Risk of ICH with streptokinase in a study conducted by Goreet *et al*[30] was 1.19% irrespective of age. ICH may be related to the long lasting fibrinolytic state of bolus thrombolytic therapy which is more pronounced in the elderly.[31] ICH with AMI has significant mortality.[28,29,32]

Hypotension occurred in 33% patients while in a study conducted by Haroon *et al*[2] it occurred in 24% of the patients. No case of anaphylaxis occurred in our study. This result is comparable to ISIS-2 trial in which out of 8592 patients none had anaphylaxis.[5]

Recent data reflects that Thrombolysis saves 30 lives per 1000 patients.[29] In FTT trial[16] involving 3300 patients over 75 years of age, 18 lives were saved per 1000. Also in another study there was 13% reduction in mortality after 1 year with the use of streptokinase.[33] There is 3.9% absolute reduction in mortality in those aged above 75.[34] Available thrombolytic regimen differ in their rates of causing ICH with SK having the lowest rate.[35,36] This important clinical data should be kept in mind while deciding for thrombolysis in the elderly.

All this data suggest that in carefully selected elderly patients benefit of streptokinase overweighs the risk. It is for the same reasons that guidelines of thrombolysis have changed dramatically in last 20 years. Previously thrombolysis in 70–75 years of age was a class II a indication and in patients >75 years it was a class II b indication; it changed to II a in 1999.[7] Currently age as a relative contraindication does not feature in thrombolysis guidelines.[7] So what is needed is a careful assessment of a net benefit to risk ratio that results in selection of appropriate patients.

The limitations of the study were a small study population, inclusion of acute myocardial infarction patients only and there was no control group to compare the results.

CONCLUSION

In conclusion, thrombolysis should not be denied to the elderly patients with acute myocardial infarction on the basis of age. Its benefits overweigh the risks associated with it even in the elderly

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