Role of Streptokinase in Treatment of STEMI Patients in Afghanistan

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Key works: streptokinase -myocardial infarction- treatment

Background

Streptokinase is a protein (not an enzyme itself), obtained from culture filtrates of certain strains of streptococcus hemolytic group C, that converts the inactive plasminogen to active plasmin. In fact, plasmin itself can't be used because naturally inhibitors in plasma prevent its effects. However, the absence of inhibitors for Urokinase and the Streptokinase –proactivator complex permit their use clinically. Streptokinase is a powder that is soluble in water, has a Ph of 6.8 to 7.5.

Streptokinase is rapidly cleared from circulation following IV administration. Clearance is biphasic with the initial and more rapid

phase being due to specific Ab. Half life of streptokinase – activator complex is 23 minutes.

Among all Fibrinolytic agents, streptokinase is the only agent of this family that came to the markets of Afghanistan in 2006 for the treatment of STEMI and any other related required diseases. As long ago there was no possibility, availability or interests for the medicine companies to import such vital medical agent to recur the required patients in spite of frequent orders of physicians for its requirement in the clinic.

As it has come to the literature that streptokinase is not commonly used in the USA because of its less effectiveness at opening occulted arteries and less effective at reducing mortality.

Indications**:** in spite of its use for Myocardial Infarction in the clinic; this drug has also been indicated for Multiple Systemic Emboli**,** Deep Vein Thrombosis**,** Unstable angina and ischemic stroke, but the last two cases are less well-established.

Obsolete Contraindication:

- Previous hemorrhagic stroke
- CVA within the past 1 year
- Known intracranial neoplasm
- Recent head trauma (including minor trauma)
- Active internal bleeding(excluding menstruation)
- Suspected Aortic Dissection

Relative Contraindications:

- BP more than 180/110 mm-Hg at presentation
- Known bleeding diathesis
- Trauma including minor ones with the past 2-4 weeks
- Major surgery within 3 weeks prolonged more than 10

minutes

- Recent CPR 2-4weeks
- Internal bleeding
- Non compressible vascular puncture
- Active diabetic neuropathy
- Pregnancy (particular at first 18 weeks)
- Active Peptic Ulcer Diseases
- History of severe hypertension
- Current use of anticoagulant INR> 2.0-3.0
- Any allergic condition for the giving streptokinase to the patients
- Age more than 70 years

Adjunctive drugs (in different trials):

- Morphine: to decrease pain
- Beta blockers: decreases MI size, prevent arrhythmias, decreases reinfarction, and improves survivals.
- Antiplatelets: Aspirin and Clopidogrel alone or with streptokinase decreases mortality, but increases the risk of hemorrhage.
- Oral anticoagulants: are best used with depressed left ventricular function or systemic emboli, heparin was necessary for adjunct for tPA but was less useful in streptokinase plus aspirin because increased the risk of bleeding.
- ACE inhibitors: decrease the infarct expansion and arrhythmias and improves survivals.
- Direct thrombin Inhibitors: are like Hirudin and Bivalirudin, are undergoing clinical trial with thrombolytic therapy.

- Nitrates: this is given at the beginning of MI.

Methods

Streptokinase can be administered in two methods to MI patients depended to the tolerance of patients which is explaining in beneath;

1. The total dose of streptokinase -1.500.000 IU dilutes with 100 cc of physiologic serum to be infused within 60 minutes IV.
2. Streptokinase 1.500.000 IU dilutes with 100 cc serums physiologic and administers in two divided steps – 50 cc of saline that contains 750.000 IU can be infused within first 20 minutes and the next ratio- the left 50 cc saline of containing 750.000 IU is given to the patients within the next 40 minutes IV.

The most effective time to administer streptokinase for the STEMI patients is in its golden time- the first three hours (the most useful and the most effective time is the first 60 minutes).

This agent can also be given to the patients even if it is required up to the first 12- 24 hours of chest pain onset. So, I have given the beneath term for its importance and effectiveness of time administration.

- Diamond Minutes: the first 30 minutes (door to needle)
- Golden Hours: the first three hours of MI
- Silver Hours: the first six hours of MI
- Bronze Hours: the 12 to 24 hour of MI established

By administering of this drug some changes such as; chest pain reduction, reduction in infarct size, limitation in left ventricular dysfunction ,reduction in hospital mortality up to 50%, reduction in incidence of serious complications like LV dysfunction, septum rupture, cardiogenic shock, malignant ventricular arrhythmias may occur.

Results

As a matter of fact, there is no certain data or a well-equipped center to pursue the patients after being streptokinase administered in our hospitals to view whether this agent could successfully work or not? As this agent has been administered in some patients, we can deduce thus; I along with my colleagues in hospital have given streptokinase to around 70 STEMI patients in a standard way; however the outcome of its effects were not as it had been expected.

Therefore; here are some factors I could find in my practice mentioning beneath;

1. Due to low education level among the people in the third world countries in particular Afghanistan, the patients may come much later than golden period of streptokinase required.
2. Streptokinase which is currently available at the markets of Herat city is the patent name of Myokinase from Biocon Co. limited, costs 60$. (As in CMDT 2010 the cost of streptokinase indicated $562.50) this matter shows the big difference in the price of literature mentioned rather than streptokinase which is available in our regions, it itself directly goes to the quality and effect of the agent.

3. As it was mentioned in the streptokinase administration part, in the US the utility of this agent would be very less due to not getting good response from administration in compare with the other agents of Fibrinolytic, so in here we should not focus too much on streptokinase for more potency or getting the result of TIMI 2 or 3 aftermath. On the other hand this agent would not be given as bolus. So it is a non-specific –fibrin.
4. There is another important factor in quality of that how it should be saved and stored in a standard way. Strepto-kinase should be store in a temperature of +2 to +8 and should be fully protected from light as well. There might be some problem in its transport or storing by the time it can be store in a well- equipped center in a hospital or in a drugstore till it is utilized.
5. Selection of MI patients for streptokinase administration is a significant matter to be careful about it.
6. This is obvious for all that streptokinase does not have the potency to open occlusion more than 50%, relying on this agent or expecting further outcome than its effects would be over trust.
7. As this matter is not common, sometimes the mistake of medical team can also cause that the total time of strepto-kinase management disrupts by some mistakes of nurses not to follow up their patients completely.

In here, among all those patients who have been given strepto-kinase I only mentioned for three cases as briefing in Herat Re-gional Hospital- Internal Medicine Ward.

Name	Mohammad
Age	70 years
Sex	Male
Education	Lawyer
Risk Factors	Male, Old age
Co- morbid Diseases	Rheumatoid Arthritis
Clinical Manifestations	Chest pain, diaphoresis, weakness, BP= 95/65
Drug therapy at presentation	NTG, Aspirin, Morphine, streptokinase
ECG findings	ST Elevation in about 1mm at the beginning
Time of admission	Within the 45 minutes of chest pain onset
Time of streptokinase administered	An hour after chest pain onset
Streptokinase administration aftermath	STEMI + Q wave establishment (Extensive STEMI)
Effect of streptokinase	Chest pain relief, limited LV dysfunction, no arrhythmias

Name	Omar
Age	32 years
Sex	Male
Education	MD
Risk factor	Family
Co-morbid Diseases	None, may be Dyslipidemia
Clinical Manifestations	Chest pain, weakness, BP=120/80
Drug therapy at presentation	NTG, Antiplatelets, Morphine, streptokinase
ECG findings	Inferior MI plus AV block
Time of admission	The first hour of chest pain onset
Time of streptokinase administered	An hour after chest pain onset
Streptokinase administrated aftermath	Dissolved ST segment by 50%, AVB corrected

Name	Fatimah
Age	60 years
Sex	Female
Education	No education
Risk factor	Dyslipidemia, Hypertension
Co-morbid Diseases:	Dyspepsia, Hypertension
Clinical Manifestations	Chest pain, vomiting, BP: 170/100 mm-Hg
Drug therapy at presentation	Morphine, NTG, Antiplatelets, anti HTN
ECG findings	Inferior MI
Time of admission	4 hours after chest pain onset
Time of streptokinase administered	after five hours
Streptokinase impacts:	Pain reduction, VF and bleeding established, no change

Adverse Effects

Back Pain: Streptokinase infusion has been associated with the development of very severe low back pain from 1 to 10 days.

Allergic reaction: happens only 2% of cases.

Effects on Blood: hemolytic anemia

Effects on Eyes: Acute Uveitis and Iritis

Effects on Kidneys: transient proteinuria and acute oliguric renal failure.

Effects on the Liver: raised ALT and in some cases raised AST. a concomitant raised in gama glutamyl trasferase activity and bilirubin concentration suggested an hepatic source. hepatic rupture during the administration of streptokinase may occur.

Effects of Nervous System: Guillian Barre Syndrome following treatment with streptokinase.

Effects on Reparatory System: Fatal ARDS

Effects on Skin: Skin rashes may occur. In some report skin necrosis possibly associated with cholesterol embolism.

Embolism: Streptokinase causes the breakage of the clot from the thrombus , so it may cause the spread of it in any parts fatal pulmonary emboli ,7 patients out of 475 who were treated with streptokinase for MI the site of emboli were the legs (in 4) and brain (in 3).

Hemorrhage: 0.5 to 0.9% is a common adverse effect of thrombolytic therapy, hemospermia has been reported following thrombolysis in patient with mild prostatic symptoms, diabetic patient are at risk of retinal hemorrhage if they have diabetic retinopathy. More than 70% of bleeding episodes happen at the puncture site so invasive procedure should be avoided if possible.

In some studies, ruptures of follicle in menstruating women have been reported in thrombolytic therapy. Rupture of the heart with fatal consequences has been reported. Randomized studies did not suggest that thrombolysis therapy following MI increases the overall risk of cardiac rupture, although women may be at increased risk for early rupture.

In our practice, the physician were not witness for any significant reaction due to administration of streptokinase, only a few cases of GI upset and bleeding were seen.

Conclusion

Streptokinase is not the only miracle agent to have potency at opening occlusions

The best quality of streptokinase is not available in our region as the physicians expect.

Both the government and drug agencies should be convinced to provide the other derivatives of Fibrinolytic to have an open hand in management of concerned patients.

The exact impact of this agent would be cleared whenever we have a well-equipped center to pursue the cases practically.

Allergic or contraindicated patients should be identified at prior.

The knowledge of the patients regarding cardiovascular diseases should be increased.

For the diseases like MI and other life-threatening conditions, all the businessmen and medicine companies should think for the best quality medicine to import.

For more investigation after streptokinase administration a

Cath Lab should be instituted to monitor the patients after streptokinase or indication of any PCI maneuvers.

A professional research and data system should be established at the level of Afghanistan

hospitals to pursue not only the cardiovascular diseases but also the other disease.

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