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INVESTIGATING THE HYPOTENSIVE EFFECTS OF INTRAVENOUS STREPTOKINASE AMONG PATIENTS WITH MYOCARDIAL INFARCTION AT GANGARAM HOSPITAL LAHORE

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Abstract:

Background/ Objective: A fall in blood pressure frequently occurs during the infusion of streptokinase in patients with myocardial infarction. Thus, hypotension is a common among the several adverse drug reactions induced by streptokinase infusion. However, there is paucity of evidences locally available to prevent and manage these reactions. The present study investigates the hypotensive effects alongside the other adverse drug reactions during streptokinase infusion in patients with myocardial infarction.

Design and subjects: This study has been conducted among the patients with MI visiting cardiac emergency of Sir Ganga Ram Hospital (SGRH), Lahore. The data have been collected retrieved from N=60 patients who were given streptokinase for thrombolytic therapy. Systolic blood pressure measurements and corresponding intervals during the occurrence of this reaction have obtained and observed.

Results: Hypotension was reported as the most common adverse drug reaction that occurred among (n=31%) followed by hemorrhagic stroke (30%), recurrent chest pain (25%), bleeding (13%), and coughing (13%). Streptokinase induced hypotension occurred at a median of 15(13) minutes after starting streptokinase infusion. Hypotensive episode recovered in a median duration of 15(10) minutes with appropriate interventions. Apart from temporarily withholding streptokinase, most patients required a combination of fluid therapy and vasopressor support to restore systolic blood pressure.

Conclusion: The risk and benefit of administering streptokinase must be assessed and effective strategies can be implemented to ensure whether streptokinase treatment is safe to all myocardial infarction patients. Moreover, the early intravenous administration of streptokinase in the hospital setting leads to a reduced rate of major cardiovascular events compared to delayed administration. However, mortality rates were not significantly affected. Secondary prevention should be targeted on modifiable demographic and psychosocial risk factors of myocardial infarction.

Keywords: Streptokinase, Myocardial Infarction, Hypotension.

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INTRODUCTION:

Cardiovascular diseases (CVD), especially ischemic heart disease, are the most common causes of death and morbidity worldwide. Among the various manifestations of ischemic heart disease, myocardial infarction continues to present a particular challenge to emergency health services. Life threatening condition occurs due to the sudden occlusion of a major coronary artery and the abrupt cessation of blood and oxygen flow to the heart muscles (Pavković and Klačar, 2018, WHO, 2022). Thus, the complete occlusion of the lumen of a major coronary artery leads to acute ST-elevation myocardial infarction (STEMI). Therefore, some complications may occur immediately following the heart attack or myocardial infarction condition that would be considered an emergency situation in order to call immediate diagnosis and treatment. In such condition, it is important that the patients presenting with features of myocardial infarction treated promptly (Redzuan et al., 2021). Thus, initial therapy should focus on stabilizing the patient's condition, relieving ischemic pain and providing thrombolytic agent to patient (Santucci et al., 2020).

Previous studies have been carried out in the past few decades in search of the best reperfusion or thrombolytic strategy (Lew et al., 1985, Herlitz et al., 1993). Correspondingly, a landmark study in Italy in 1986 established streptokinase as an effective thrombolytic agent (Lew and Ganz, 1986). Streptokinase is a bacterial protein secreted by Streptococci; the human body has ability to develop immunity to it. STK is isolated naturally from upper respiratory tract and is used to dissolve the fibrin matrix of blood clots, especially those in the arteries of the human heart and lungs (Aslanabadi et al., 2018, Khalid et al., 2021a). Moreover, streptokinase has been developed as a thrombolytic drug that was used earlier for haemothorax, pleural exudates, tuberculous meningitis treatment and then used for myocardial infarction, pulmonary embolism and empyema. Streptokinase is in the antithrombotic family of medications frequently used in developing countries due to its low cost and affordability (Capitanescu et al., 2016, Khalid et al., 2021b).

Many trials had shown that it had reduced mortality in MI patients when administered within hours of onset of symptoms like chest pain (Tatu-Chițoiu et al., 2004, Sawar et al., 2019, Elsayed, 2020, Redzuan et al., 2021). It could be administered both intravenously and intra coronary. Its over dosage should be treated promptly, otherwise it could cause fatal bleeding. The secondary prevention in myocardial infarction had its definite role in improving survival of the patients and targeting risk factors of myocardial infarction (Aslanabadi et al., 2018).

Although streptokinase is known as wonder drug; however, the side effects of streptokinase include pyrogenic reactions like malaise, headache, arthralgia and occasionally nausea and febrile responses (Afzal et al., 2015). Moreover, several theories have been proposed, including a direct vasodilative effect of streptokinase, reduction of blood viscosity (Yu et al., 2016, Aslanabadi et al., 2018), allergic reaction, etc. (Ko et al., 2019, Yusof et al., 2019). Locally, streptokinase is the thrombolytic agent commonly utilized alongside the consideration of patients' characteristics, area at risk, time to treatment, presence of contraindications as well as the risks involved before thrombolysis (Hamid et al., 2015, Babar et al., 2016, Sawar et al., 2019). However, hypotensive effects which are common adverse drug reactions related to streptokinase therapy given to patients with myocardial infarction (Sultana et al., 2010, Chau and Choi, 2013, Afzal et al., 2015) that are not fully explained and still poorly understood. Therefore, the purpose of present study is to investigate the hypotensive effects during streptokinase infusion in patients with myocardial infarction.

Aim of the Study

The aim of this study is to identify the hypotensive as well as other adverse drug reactions among myocardial infarction patients given streptokinase i.e., the degree of hypotension, when it developed and any other complications as a consequence of the hypotension or streptokinase.

Objectives of the Study

The present study has addressed the following research objective;

1. To investigate the hypotensive effects of streptokinase among the myocardial infarction patients vising cardiac emergency of Sir Ganga Ram Hospital.

2. To explore adverse drug reactions associated with streptokinase administration among myocardial infarction patients vising cardiac emergency of Sir Ganga Ram Hospital.

Research Questions

What are the adverse drug reactions such as hypotensive or others among acute myocardial infarction patients given streptokinase who are visiting cardiac emergence of Sir Ganga Ram Hospital with chest pain?

LITERATURE REVIEW

The hypotensive effect induced by streptokinase during thrombolytic therapy is a common adverse drug reaction among the patients with myocardial infarction (Aslanabadi et al., 2018). However, different studies conducted in laboratory and animal research do provide the basis for understanding, however the results of which were not immediately transferrable to humans. Studies with specific interest in the clinical outcomes of streptokinase therapy in patients with myocardial infarction are conducted with variable study designs that span from observational cohort study (Lateef and Anantharaman, 2000) to double-blind randomized controlled trial (Buckley et al., 2007, Tatu-Chiţoiu et al., 2004). Despite the continuous research that dates back to the early 1980s, the mechanism of streptokinase-induced hypotension is still poorly understood and is believed to be a rate-related phenomenon.

Retrospectively, Shiferaw et al. (2021) described that Lew et al. studied the hypotensive effect of a rapid intravenous infusion of high-dose streptokinase in 98 patients with an acute myocardial infarction (AMI) in 1985. They revealed that there were direct relationships between the rate of infusion of streptokinase and both the magnitude and the rate of fall of systolic blood pressure as well as both the magnitude and rate of fall of diastolic blood pressure. Similarly, Elsayed (2020) sates that Gemmill et al. investigated the incidence, amplitude, mechanism and relationship to prior exposure to streptococcal antigen of blood pressure changes to streptokinase-containing as thrombolytic agents among 125 patients with AMI in 1993. They indicated that the majority of patients with anterior and a smaller number of patients with inferior MI had a hypotensive response. There were no significant differences in the incidence, duration or amplitude of hypotension between the two treatment groups. Hypotension was not related to pretreatment streptokinase resistance. The blood pressure changes following treatment with streptokinase-containing thrombolytic agents in AMI were frequent but well tolerated. However, the mechanism of hypotension remained unclear, but was not related to prior exposure to streptococcal antigen.

This study detected overall insignificant low mortality rate among the patients given streptokinase. However, the hypotension was significantly higher in the patients administered streptokinase.

Another study by Sawar et al. (2019) identified the complications of Streptokinase in 297 patients with STEMI through a descriptive cross-sectional among. The study showed that the patients consisted of history of hypertension, diabetes mellitus, acute coronary syndrome, smoking and streptokinase infusion. The study revealed that during streptokinase, the complications were observed including hypotension, nausea and vomiting gums bleeding, allergic reactions, ventricular tachycardia, ventricular fibrillation, atrial fibrillation, fever, bradycardia, hemoptysis and intracranial hemorrhage. Only one patient expired due to complications.

METHODOLOGY:

Study design:

The term research design refers to the plan of organization of scientific investigations. The present study has employed prospective (cohort study) design to perform research in the cardiac emergency department of Sir Ganga Ram Hospital (SGRH) Lahore. SGRH is one of the largest public tertiary care hospitals which deals with all type of health emergencies.

In a medical cohort study, all the data are collected prospectively. The investigator defines the population that is required to be included in the cohort. Then the investigators collect a sample, classify individuals in some way, and then wait to see if the individuals develop a condition. After it, the potential exposure

of interest is measured. The participants are then classified as exposed or unexposed by the investigator (Wang and Kattan, 2020), as illustrated in Figure 1.

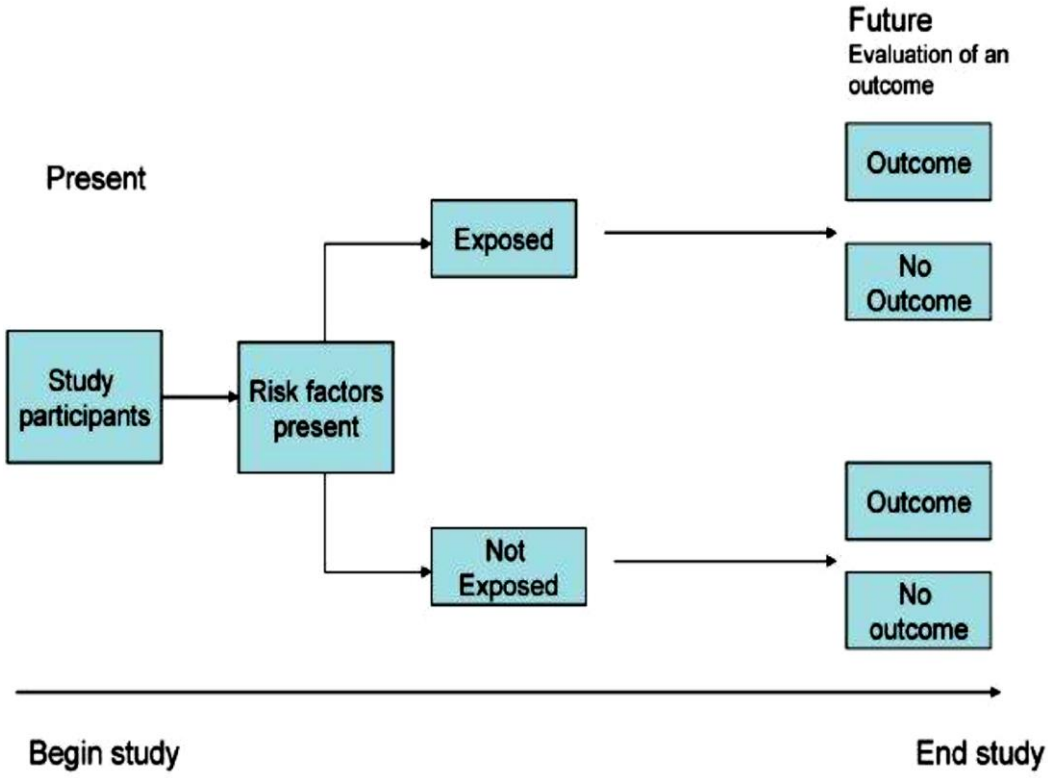


Figure 1: A schematic representation of a cohort study.

Cohort studies are considered the strongest of all observational designs. A cohort study is conceptually very straightforward. The idea is to measure and compare the incidence of disease in two or more study cohorts. In epidemiology, a cohort is a group of people who share a common experience, condition or characteristic (Kasim, 2012). Figure 1 presents a schematic representation of a typical cohort study. As the study is conducted using cohort design, outcome from participants in each cohort is measured and relationships with specific characteristics determined.

Setting

Data have been collected at cardiac emergency department of Sir Ganga Ram Hospital, Lahore. The subjects of the study are men and women who have visited cardiac emergency department with chest pain, angina or with the symptoms heart attack for the treatment of their conditions. Data collection has been completed during the months of August and September 2022 from the subjects participating voluntarily.

Duration: From June 2022 to November 2022 (6 months) after approval of project.

Target Population

The Population framework of this study consists of men, women and others who visited the tertiary care Sir Ganga Ram Hospital (SGRH), Lahore with cardiac problem.

Sample Size

The following formula for *one sample (*Pourhoseingholi et al., 2013*), continuous outcome* is used to calculate the sample size at 95% confidence level and 5% margin of error. Thus, the calculated sample size is (n=62).

$$n = \left(\frac{Z\sigma}{E}\right)^2 = \left(\frac{1.96(20)}{5}\right)^2 = 61.5$$

Where, Standard normal distribution of **Z** = 1.96 for 95% confidence level.

σ is standard deviation of the outcome variable

E is the desired margin of error which is 5% (Pourhoseingholi et al., 2013).

Sampling Technique
Due to the unavailability of complete list of population, purposive sampling technique is adopted based on inclusion criteria. Thus, a purposive sampling technique has been used to approach 62 participants visiting cardiac emergency department of SRGH, Lahore.

Inclusion Criteria
The patients' eligibility criteria were defined as:
The study included the patients of all sexes held with more than 18 years and less than 75 years of age, diagnosed with acute STEMI and receiving streptokinase as thrombolytic therapy.

Exclusion Criteria
The study excluded the patients with following characteristics;
- • Acute or chronic kidney and liver disease
- • Pregnant women
- • Patients not able to continue the study
- • Contraindications of thrombolytic therapy including recent head/facial trauma and/or ischemic stroke within last 3 months
- • Intracranial tumor
- • Prior intracranial hemorrhage
- • Suspected aortic dissection
- • Active internal bleeding, or bleeding diathesis
- • Severe uncontrolled hypertension

Administration of Streptokinase Injection
The streptokinase was administered as soon as possible after the first symptoms of STEMI (under the six hours from onset of symptoms) with the usual adult dose of AMI as1,500,000 units intravenous (IV) infusion over 60 min. In case of allergic reactions and fever, it was recommended that patients concurrently should receive corticosteroids that can be repeated during treatment. Before treatment, the patient PT and PTT were being controlled. In case of anaphylactic shock symptoms and hypotension, malaise, chills, nausea and arrhythmia, the infusion was being stopped.

Measurement Instrument
A structured performa was developed to note the basic characteristics of participants, risk factors and to detect and classify the ADRs of Streptokinase injection. Thus, data have been collected by a self-administered structured performa. All the patients receiving streptokinase have completed the informed consent form, that was used to monitor for ADRs induced by streptokinase. Detection and monitoring of ADRs have been done through completing a performa by reviewing the patients through their medical file and interviewing with the patients. The performa includes the demographic information, past medical history, comorbidity and modifiable risk factors.

Ethical Considerations
- Written approval was taken from the participants.
- Data collected from the participants was kept confidential.
- Participants were remained unspecified throughout the study.
- Participants were informed that there is no risk or harm during this study.
- Participants were be informed that they can withdraw at any time during the process of the study.

Statistical Analysis
The received responses have been fed into the statistical package for social sciences (SPSS). Then, descriptive analysis has been carried out to calculate frequencies, and percentages for qualitative variables, and means and standard deviation for quantitative variables to report results. The correlation evaluation between ADRs and the study parameters and regression analysis are performed to find out any relationships between the incidence and number of ADRs and the risk factors. Continues data are presented as mean ± standard deviation (SD). P-values less than 0.05 were considered statistically significant.

RESULTS:

This section presents the findings according to the specific objectives of the study including adverse drug reactions (ADRs) among the MI patients given streptokinase.

Demographic Characteristics of Participants
Streptokinase as thrombolytic therapy was administered among the patients who visited cardiac emergency of SRGRH with chest pain of MI symptoms during the selected period of this research. Among the MI cases (N=60) were received streptokinase within two hours after chest pain and all these cases were considered for this study. The majority of the participants were male (n = 42, 68%) aged between 41–50 years (n=21, 35%) followed by 31-40 years (n=18,30%). A total of three deaths occurred among the selected sample of the study.

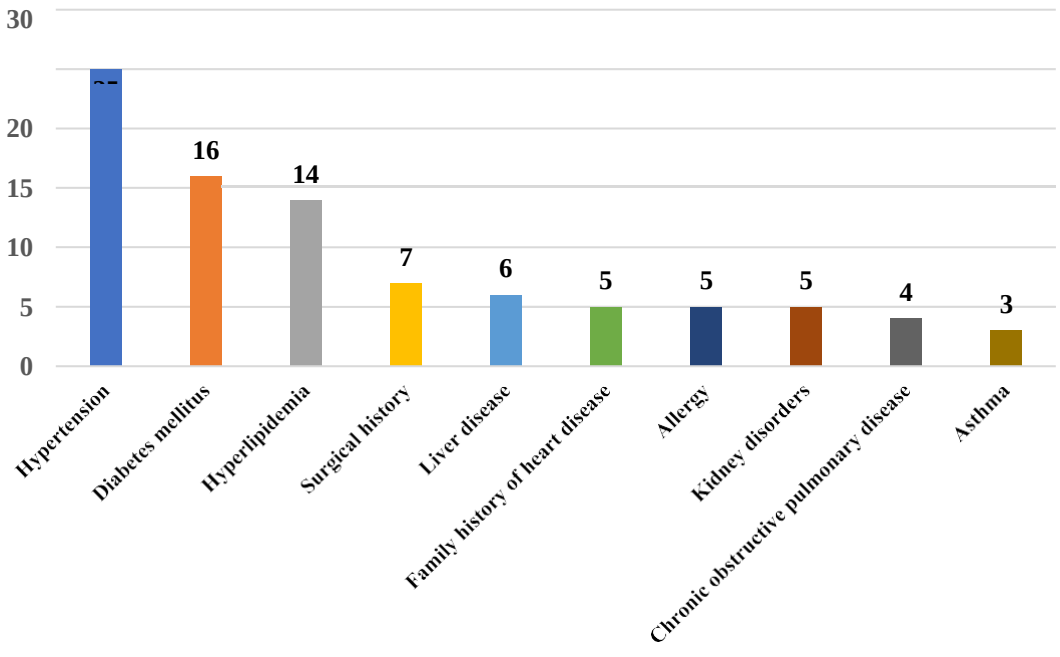
Table 1: Demographic Characteristics of Participants

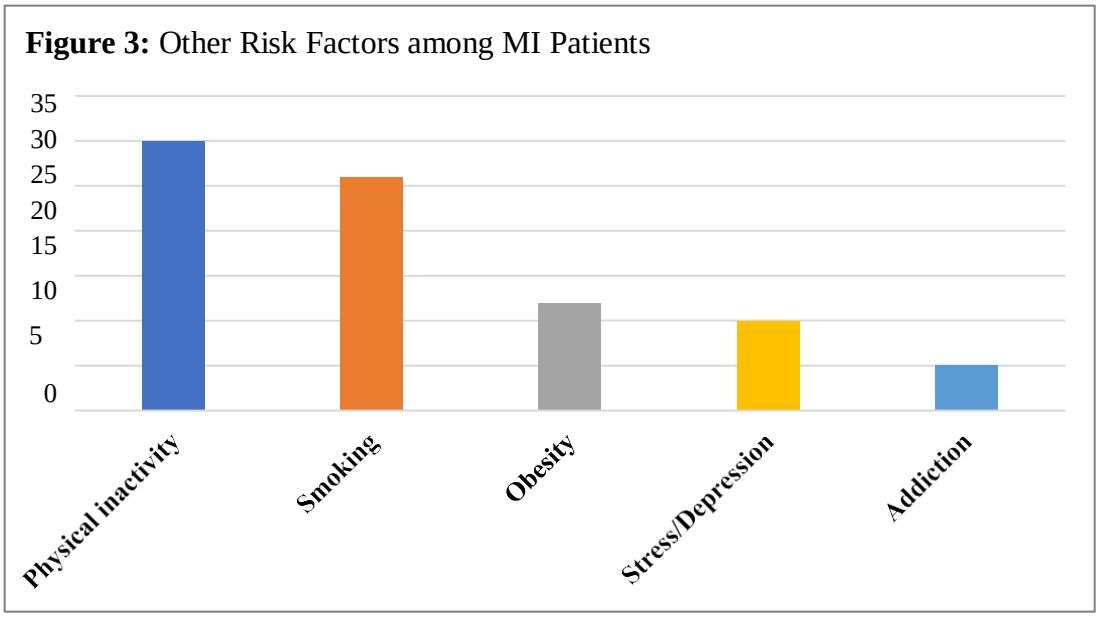
SN	Characteristics	n	%
1	Gender		
	Male	42	68
	Female	20	32
2	Age		
	<30 years	5	7
	31-40 years	18	30
	41 – 50 years	21	35
	51-60 years	11	18
	61 – 75 years	6	8
3	Education		
	Literate	42	70
	Illiterate	20	30

Status of Comorbidity and Risk Factors among MI Patients

Furthermore, Figure 2 illustrated that the majority of MI patients had comorbidity characteristics including hypertension (n=25,42%), diabetes mellitus (n=16,27%) and hyperlipidemia (n=14,23%) alongside the other risk factors includingphysical inactivity (n=30,50%) and smoking (n=26,43%) as showed in Figure 3.

Figure 2: Comorbidity Factors among MI Patients





Adverse Drug Reactions (ADRs) of Streptokinase:

The results of Table 2 revealed that the most common ADRs of streptokinase were observed including hypotension (n=18, 31%), fever (n=16, 30%), recurrent chest pain (n=15, 25%), bleeding (n=8, 13%) and coughing (n=8, 13%). Thus, the study suggested that hypotension is the most common adverse effect induced by streptokinaseamong MI patients.

Table 2. Frequency of Streptokinase Induced ADRs

Characteristics of ADRs	n	%
Hypotension	18	31
Hemorrhagic stroke	16	30
Recurrent chest pain	15	25
Bleeding	8	13
Coughing	8	13
Nausea and vomiting	6	10
Bradycardia	6	10
Sweating	6	10
Tachycardia	5	9
Fever	5	9
Arrythmias	5	8
Headache	4	6
Morality	3	6
Allergy and erythema	2	3
Diarrhea	1	1

DISCUSSION:

Streptokinase is secreted by streptococci (Zia, 2020) as the first thrombolyticdrug is used for myocardial infarction. Although more than 80% of the global burden of cardiovascular disease is contributed by low-income and middle-income countries, research and evidence of the importance of risk factors is largely derived fromdeveloped countries (Aslanabadi et al., 2018, Afzal et al., 2015). Therefore, the effect of such factors on risk of myocardial infarction in most regions of the world is unknown. Moreover, time related effects of streptokinase required investigations. This studyevaluated 62 patients with MI symptoms who received streptokinase. The major findings showed that the hypotension was one of the most occurred ADR induced by the streptokinase infusion. Moreover, in this study hemorrhagic stroke, recurrent chestpain and bleeding complications were higher than the other reports. Although, there were several other complications were documented; however, these were insignificant.

In this study Streptokinase was administered among 62 patients within 2 hours and after chest discomfort or chest pain which relieved symptoms in n=57(97%) of patients (mean 0.89 ± 0.33 SD) while in another study conducted in US showed that 30 patients presented to the hospitals in a mean time of 1.21 ± 1.08 hours and treatment commenced in a mean time of 2.77±1.3 hours after the onset of symptoms, 86.7% patients were re-perfused initially and 2 were found re-occluded within first 48 hours (Buckley et al., 2007). The study conducted on myocardial ischemia patients, showed re-occlusion in 20% of patients (Yu et al., 2016).

In our study, the incidence of ADRs by streptokinase was reported > 80% that is substantially higher than the other reports. For example, in the retrospective cohort study by (Devi et al., 2012) and prospective study by (Mohebbi et al., 2010) that were conducted in coronary care unit (CCU), the highest ADRs were seen by streptokinase in about 60%. However, this rate is similar to our recent study on reteplase with the incidence rate of 85% (Aslanabadi et al., 2018).

One of the most occurred ADR was hypotension that may linked with the rapid injection of the drug. According to the previous studies, hypotension during streptokinase injection is a vasodilatory effect that is occurred by activation of plasmin and producing bradykinin (Afzal et al., 2015, Aslanabadi et al., 2018, Chau and Choi, 2013). The rate of hypotension during streptokinase therapy was reported between 1- 10% that is relatively lower than our study finding (more than 50%) which can reflect the rapid injection of streptokinase (Bunker et al., 2003). In the recent review of Iranian literature, hypotension and arrhythmia were identified as the most frequent ADRs induced by streptokinase that is in agreement with our findings (Albus, 2010).

A couple of study involving patients of acute myocardial infarction who received streptokinase 1.5 million units within 12 hours of onset of chest pain had successful reperfusion in 47% patients. The adverse effects reported were bleeding, hypotension and allergic reactions. In our study similar adverse effects were found however streptokinase was administered within 6 hours after chest pain and relieve of symptoms were found in 87% patients (Afzal et al., 2015, Aslanabadi et al., 2018).

In another study the researchers concluded that shock, recurrent chest pain and ischemia occurred more often in patients of STEMI, which supported our research findings that recurrent chest pain was found statistically significant and more frequency in late administration of streptokinase than early administration (Sultana et al., 2010).

Hemorrhagic stroke was the most severe side effect that occurred duringhospitalization after the injection of streptokinase by documenting in 16 cases (30%). However, the incidence of hemorrhagic stroke in these patients substantially was higher than the other reports. In a prospective and spontaneous reporting-based pharmacovigilance program in Cuba among 792 patients who received streptokinase, the hemorrhagic stroke was reported only in 3 cases (0.3%) (Betancourt et al., 2005). In GISI-1 and ISIS-2 trials the incidence of major bleeding such as hemorrhagic stroke was reported between 0.3- 0.5% (4, 5). Moreover, in the study by (Maggioni et al., 1992), the incidence of various forms of stroke in patients treated with streptokinase was 0.94 %. Many factors including drug related factors such as bleeding complications as well as host related factors such as older age, female gender, anterior MI, history of smoking and hypertension are the main participating factors in occurring stroke (Aslanabadi et al., 2018). Mortality rate in this study was 5.7%, while in another study conducted in Pakistan, mortality rate was 3.4% recorded. It was also seen that only one mortality occurred after 2 months of hospital stay and 51 out of 55 patients of MI in Pakistan were back to work after treatment (Afzal et al., 2015).

Smoking was found risk factor in 36% and obesity in 20% of Myocardial infarction or STEMI (Symons et al., 2016). Lack of exercise was the risk factor in 7-12% of cases of Myocardial infarction. Other risk factors included psychological stresssuch as job stress

in 3% of cases, and chronic high psychological stress levels (Ek et al., 2019).

In other research studies tobacco smoking, including secondhand smoke, lack of physical status or poverty, social isolation and negative emotions were found to increase the risk of myocardial infarction and its complications. Socioeconomic factors such as an illiteracy and lower income were correlated with a higher risk of myocardial infarction.22 Similar risk factors were found in present study (Ek et al., 2019, Symonset al., 2016).

CONCLUSION

Early intravenous administration of streptokinase in the hospital setting reduced the rate of major cardiovascular events compared to delayed administration beyond 2 hours. Secondary prevention should be targeted on modifiable demographic, and psychosocial risk factors of STEMI including psychological stress (87%), lack of sleep (69%), smoking (66%), sedentary life style (51%), poverty (46%) and illiteracy (31%), depression (28%), and generalized anxiety disorder (36%) in the study population. Thetargeted approach to the psychosocial risk factors through health awareness can help in reducing disease burden in future.

Limitations

This study included a limited sample that might be a major limitation of the study. There was no control group so that no comparison of adverse effects and risk factors in quantitative data and qualitative data could be made. Government had provided streptokinase free of cost to most of the patients in public sector hospitals thus streptokinase was the preferred therapy for thrombolysis in MI patients. The patients were not administered other thrombolytic agents (e.g., Alteplase) and accepted procedures in public sector hospitals due to high cost and high financial burden. Thus,comparison between different thrombolytic agents could not be made. Thus, present research showed that reduced complications were significantly associated with timely administration of streptokinase (within 2 hours). Moreover, the current study was conducted at a single hospital among a small sample undertaking prospect approach; thus, the findings might not be generalized to the general population. The findings might not be generalized to a larger population on account of limited data sources. An important aspect not considered in this manuscript is the duration of hypotension. Thus, we did not know whether a prolonged episode of hypotension during infusion of streptokinase might be associated with an increased risk of death. Furthermore, we had no information regarding the efficacy of streptokinase as assessed by creatine kinase curves, catheterization data or other means.

Recommendation

The present study recommends that healthcare providers and medical staff should made efforts to promote awareness, education and provide necessary information to behavioral change among MI patients modifiable risk factors. Media related sources for information should be devised to propagate messages among the community. Health specialists should improve knowledge, attitude and practices of nursing staff and health care providers towards administering thrombolytic agents among MI patients through interventional and educational programs.

REFERENCES:

1. AFZAL, S., KHAN, M. A., MUHAMMAD, H., ASHRAF, A. & AFZAL, M. 2015.
2. Psychosocial risk factors of myocardial infarction and adverse effects of streptokinase in public sector hospitals. Pak J Med Sci, 31, 821-6.
3. ALBUS, C. 2010. Psychological and social factors in coronary heart disease. Ann Med, 42, 487-94.
4. ASLANABADI, N., SAFAIE, N., TALEBI, F., DOUSTI, S. & ENTEZARI-
5. MALEKI, T. 2018. The Streptokinase Therapy Complications and its Associated Risk Factors in Patients with Acute ST Elevation Myocardial Infarction. Iran J Pharm Res, 17, 53-63.
6. BABAR, M. Z. M., MAJID, A. & IQBAL, J. 2016. Acute myocardial infarction; effects of thrombolysis on TIMI flow rate in infarct related artery (IRA) in patients of ST elevated acute myocardial infarction. Prof Med J, 23, 1412-1416.
7. BETANCOURT, B. Y., MARRERO-MIRAGAYA, M. A., JIMÉNEZ-LÓPEZ, G., VALENZUELA-SILVA, C., GARCÍA-IGLESIAS, E., HERNÁNDEZ- BERNAL, F., DEBESA-GARCÍA, F., GONZÁLEZ-LÓPEZ, T., ALVAREZ-
8. FALCÓN, L. & LÓPEZ-SAURA, P. A. 2005. Pharmacovigilance program to monitor adverse reactions of recombinant streptokinase in acute myocardial infarction. BMC Clin Pharmacol, 5, 5.
9. BUCKLEY, T., MCKINLEY, S., GALLAGHER, R., DRACUP, K., MOSER, D. K.

10. & AITKEN, L. M. 2007. The Effect of Education and Counselling on Knowledge, Attitudes and Beliefs about Responses to Acute Myocardial Infarction Symptoms. Eur J Cardiovasc Nurs, 6, 105-111.
11. BUNKER, S. J., COLQUHOUN, D. M., ESLER, M. D., HICKIE, I. B., HUNT, D.,
12. JELINEK, V. M., OLDENBURG, B. F., PEACH, H. G., RUTH, D.,
13. TENNANT, C. C. & TONKIN, A. M. 2003. "Stress" and coronary heart disease: psychosocial risk factors. Med J Aust, 178, 272-6.
14. CAPITANESCU, C., MACOVEI OPRESCU, A. M., IONITA, D., DINCA, G. V., TURCULET, C., MANOLE, G. & MACOVEI, R. A. 2016. Molecular processes in the streptokinase thrombolytic therapy. J Enzyme Inhib Med Chem, 31, 1411-1414.
15. CHAU, H. & CHOI, K. 2013. Efficacy and Safety of Tenectaplase versus Streptokinase in Treating ST-Elevation Myocardial Infarction Patients in Hong Kong: A Four-Year Retrospective Review in Queen Elizabeth Hospital. Hong Kong J Emerg Med, 20, 359-363.
16. DEVI, P., KAMATH, D. Y., ANTHONY, N., SANTOSH, S. & DIAS, B. 2012.
17. Patterns, predictors and preventability of adverse drug reactions in the coronary care unit of a tertiary care hospital. Eur J Clin Pharmacol, 68, 427- 33.
18. EDWARDS, I. R. & ARONSON, J. K. 2000. Adverse drug reactions: definitions, diagnosis, and management. The Lancet, 356, 1255-1259.
19. EK, A., EKBLOM, Ö., HAMBRAEUS, K., CIDER, Å., KALLINGS, L. V. &
20. BÖRJESSON, M. 2019. Physical inactivity and smoking after myocardial infarction as predictors for readmission and survival: results from the SWEDEHEART-registry. Clin Res Cardiol, 108, 324-332.
21. ELSAYED, Y. M. H. 2020. Streptokinase-inducing hypotension in acute myocardial infarction but blood pressure normalizing in acute massive pulmonary embolism; Why? Thromb Haemost Res 4, 1046.
22. GEMMILL, J. D., HOGG, K. J., DOUGLAS, J. T., DUNN, F. G., LOWE, G. D. O.,
23. RAE, A. P. & HILLIS, W. S. 1993. The incidence and mechanism of hypotension following thrombolytic therapy for acute myocardixal infarction with streptokinase-containing agents — lack of relationship to pretreatment streptokinase resistance. Eur Heart J, 14, 819-825.
24. HAMID, S., KUNDAL, V., MAHAJAN, N. & SINGH, P. 2015. Failure of
25. thrombolysis with streptokinase in acute myocardial infarction using ECG criteria: An observational study. JK Science, 17, 123.
26. HERLITZ, J., HARTFORD, M., AUNE, S. & KARLSSON, T. 1993. Occurrence of
27. hypotension during streptokinase infusion in suspected acute myocardial infarction, and its relation to prognosis and metoprolol therapy. Am J Cardiol, 71, 1021-1024.
28. KASIM, K. 2012. Basic concepts of modern epidemiology: Epidemiology and research, Saarbrucken, Germany, LAP LAMBERT Academic Publishing
29. KHALID, K., AHMAD, R., LUI, S. & ABIDIN, I. 2021a. Killip classification and baseline heart rate can be used to predict streptokinase-induced hypotension in acute myocardial infarction. World Acad Sci J, 3(4), 1-7.
30. KHALID, K., ELINA AHMAD, R., Y.H. TONG, A., YEE LUI, S. & ZAINOL
31. ABIDIN, I. Z. 2021b. Pathophysiology of streptokinase-induced hypotension in acute myocardial infarction: a systematic review of clinical evidence. Arch Med Sci Atheroscler Dis, 6, 85-94.
32. KO, A. T. Y., TEO, Y., TEO, H. G. & CHAM, Y. L. 2019. Factors and outcomes associated with streptokinase-related hypotension in patients with ST Segment Elevation Myocardial Infarction (STEMI) in A secondary care hospital in Malaysia. Int J Cardiol, 297, 16-17.
33. LATEEF, F. & ANANTHARAMAN, V. 2000. Hypotension in acute myocardial infarction patients given streptokinase. Singapore medical journal, 41, 172- 176.
34. LEW, A. & GANZ, W. 1986. Streptokinase thrombolytic therapy in acute myocardial infarction. Pathophysiol Haemos Thromb, 16, 113-121.
35. LEW, A., LARAMEE, P., CERCEK, B., SHAH, P. & GANZ, W. 1985. The
36. hypotensive effect of intravenous streptokinase in patients with acute myocardial infarction. Circulation, 72, 1321-1326.
37. MAGGIONI, A. P., FRANZOSI, M. G., SANTORO, E., WHITE, H., VAN DE
38. WERF, F. & TOGNONI, G. 1992. The risk of stroke in patients with acute myocardial infarction after thrombolytic and antithrombotic treatment. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico II (GISSI-2), and The International Study Group. N Engl J Med, 327, 1-6.

39. MOHEBBI, N., SHALVIRI, G., SALARIFAR, M., SALAMZADEH, J. &
40. GHOLAMI, K. 2010. Adverse drug reactions induced by cardiovascular drugs in cardiovascular care unit patients. Pharmacoepidemiol Drug Saf, 19, 889-94.
41. PAVKOVIĆ, B. & KLAČAR, M. 2018. Acute myocardial infarction in a patient with coronary artery aneurysm. Timočki medicinski glasnik, 43(4),183-187.
42. PERNAT, A., POHAR, B. & HORVAT, M. 1997. Effect of hydrocortisone on streptokinase-induced hypotension in patients with acute myocardial infarction. Fibrinolysis and Proteolysis, 11, 103-107.
43. REDZUAN, A. M., MOHAN, K. & NAGARAJAH, J. 2021. Risk factors associated with the occurrence of streptokinase induced hypotension among ST-elevation myocardial patients (STEMI). J Cardiovasc Dis Res, 12, 1301-1309.
44. SANTUCCI, A., RICCINI, C. & CAVALLINI, C. 2020. Treatment of stable
45. ischaemic heart disease: the old and the new. Eur Heart J Suppl, 22, E54-e59.
46. SAWAR, S., KHAN, B., KHAN, A. T., NOOR, N., RAHMAN, F. & REHMAN, N.
47. 2019. Complications of streptokinase in patients with acute st segment elevation myocardial infarction: No reason to withhold this effective therapy. JPMI: J Postgrad Med Insti, 33(4), 293-298.
48. SHIFERAW, M. B., SINISHAW, M. A., AMARE, D., ALEM, G., ASEFA, D. &
49. KLINKENBERG, E. 2021. Prevalence of active tuberculosis disease among healthcare workers and support staff in healthcare settings of the Amhara region, Ethiopia. PLOS ONE, 16, e0253177.
50. SULTANA, R., SULTANA, N., RASHEED, A., RASHEED, Z., AHMED, M.,
51. ISHAQ, M. & SAMAD, A. 2010. Door to needle time of streptokinase and ST segment resolution assessing the efficacy of reperfusion therapy at Karachi Institute of Heart Diseases. J Ayub Med Coll, 22(1), 150-3.
52. SYMONS, R., MASCI, P. G., FRANCONE, M., CLAUS, P., BARISON, A., CARBONE, I., AGATI, L., GALEA, N., JANSSENS, S. & BOGAERT, J.
53. 2016. Impact of active smoking on myocardial infarction severity in reperfused ST-segment elevation myocardial infarction patients: the smoker's paradox revisited. Europ Heart J, 37, 2756-2764.
54. TATU-CHIŢOIU, G., TEODORESCU, C., DAN, M., GURAN, M., CĂPRARU, P., ISTRĂŢESCU, O., TATU-CHIŢOIU, A., BUMBU, A., CHIONCEL, V.,
55. ARVANITOPOL, S. & DOROBANŢU, M. 2004. Streptokinase-induced hypotension has no detrimental effect on patients with thrombolytic treatment for acute myocardial infarction. A substudy of the Romanian Study for Accelerated Streptokinase in Acute Myocardial Infarction (ASK-ROMANIA). Rom J Intern Med, 42, 557-73.
56. WANG, X. & KATTAN, M. W. 2020. Cohort Studies. Chest, 158, S72-S78.
57. WHO. 2022. Cardiovascular diseases (CVDs): Key facts [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases- (cvds) [Accessed 10 Semptember 2022].
58. YU, S.-H., LI, L. & ZHANG, S. 2016. Clinical effect of intravenous thrombolysis combined with nicorandil therapy in patients with acute ST-segment elevation myocardial infarction. Trop J Pharm Res, 15, 1335-1339.
59. YUSOF, T. T., LIU, K. & KASIM, S. 2019. Impact of a regional STEMI network on patient outcomes in Malaysia. Int J Cardiol, 297, 16-30.
60. ZIA, M. A. 2020. Streptokinase: an efficient enzyme in cardiac medicine. Protein Pept Lett, 27, 111-119.