A Survey of the Side Effects of Intravenous Streptokinase in Iranian Patients with Acute Myocardial Infarction: A systematic review and meta-analysis

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Abstract

Introduction :
Myocardial infarction is one of the most common heart diseases and is often caused by a sudden decrease in coronary blood flow after the thrombotic occlusion of one of the coronary arteries previously narrowed by atherosclerosis. Thrombolyticdrugs such as streptokinase, by converting plasminogen to plasmin and thrombosis resolution, reduce the size of the myocardial infarct area, decrease myocardial infarction complications such as cardiogenic shock, malignant dysrhythmias, and so on and maintain myocardial function.The aim of this study was asurvey of the side effects of intravenous streptokinase in Iranian patients with acute myocardial infarction.

Methods:
The methods used in this systematic review were based on the Checklist (PRISMA) Guidelines.In this research, cross-sectional, case-control, and cohort studies were included and case studies, letters to editors, case reports, clinical trials, study protocols, systematic reviews and narrative reviews were excluded. The searches were conducted by two independent researchers and the aim was to find the relevant studies published from 1/1/2000 to 30/5/2019.

Results:
According to the random effect model, the total prevalence of allergic complication in 588 patients with Acute Myocardial Infarction was 14% (11%-17% at a 95% confidence interval, $I^2 = 99.5\%$) , the total prevalence of hematologic complication in 588 patients with Acute Myocardial Infarction was 12% (10%-14% at a 95% confidence interval, $I^2 = 93.5\%$) and the total prevalence of cardiac complication was 20% (17%-23% at a 95% confidence interval, $I^2 = 96\%$).

Conclusion:
The use of thrombolytic therapy in elderly patients is associated with risks and complications, given the low prevalence of its side effects compared to its beneficial effects, this treatment should be considered for elderly patients with acute myocardial infarction, especially in centersthat do not have emergency angioplasty facilities.

Keywords: Streptokinase complications, Myocardial infarction, Cardiac intensive care unit

Introduction

Myocardial infarction is one of the most common heart diseases and is often caused by a sudden decrease in coronary blood flow after the thrombotic occlusion of one of the coronary arteries previously narrowed by atherosclerosis (1-3). In the United States, every 20 seconds, one person develops myocardial infarction, and in spite of the decline in mortality caused by it in the

last three decades, it still accounts for one third of deaths (4 and 5). Myocardial infarction occurs in more than 90% of cases due to complete coronary artery occlusion by thrombosis, and in only less than 5% of cases in normal coronary artery (6). In the absence of reperfusion, appropriate and timely, the rate of heart damage after myocardial infarction becomes 2 to 6 times more (7 and 8). One of the therapeutic measures for reperfusion is the use of thrombolyticdrugs, especially streptokinase (9-11). Thrombolyticdrugs such as streptokinase, by converting plasminogen to plasmin and thrombosis resolution, reduce the size of the myocardial infarct area, decrease myocardial infarction complications such as cardiogenic shock, malignant dysrhythmias, and so on and maintain myocardial function (12).

Methods

Inclusion Criteria (Eligibility Criteria):

The methods used in this systematic review were based on the Checklist (PRISMA) Guidelines.In this research, cross-sectional, case-control, and cohort studies were included and case studies, letters to editors, case reports, clinical trials, study protocols, systematic reviews and narrative reviews were excluded.

Participants: All studies of Survey of the Side Effects of Intravenous Streptokinase in Iranian Patients with Acute Myocardial Infarction .

Findings: The main purpose of this study was to determine Survey of the Side Effects of Intravenous Streptokinase in Iranian Patients with Acute Myocardial Infarction and the findings were reported.

Sampling Methods and Sample Size: All observational studies were included in the systematic review regardless of their design. The minimum sample size was 25 patients or more.

Search Strategy:

The searches were conducted by two independent researchers and the aim was to find the relevant studies published from 1/1/2000 to 30/5/2019. The researchers searched for published studies in the English language in MEDLINE via PubMed, EMBASETM via Ovid, the Cochrane Library and Trip database. To select studies published in other languages, National Database (Magiran and SID, KoreaMed and LILACS), and for unpublished studies, OpenGrey (www.opengrey.eu/), World Health Organization Clinical Trials Registry (who.int/ictrp), and ongoing studies were searched. To ensure that the studies are adequate, the reference lists of the retrieved studies were also searched and studied. Specific search strategies were performed using the Health Science Librarian website, which searches systematic review articles using MESH and open terms in accordance with publication standards. After the MEDLINE strategy was finalized, the results were compared in order to search for other databases, as well as PROSPERO was searched for recent or ongoing systematic reviews. The keywords used in the search strategy are: Streptokinase complications, Myocardial infarction, Cardiac intensive care unit

Study Selection and Data Extraction

The two researchers independently analyzed the titles and abstracts of the articles according to the eligibility criteria. After excluding additional studies, the full text of each study was evaluated on the basis of the eligibility criteria and the information about the authors was collected as needed. The general information (the first author, country in which the study was conducted and year of publication), study information (the sampling technique, diagnostic criteria, data collection method, research conditions, the sample size, and risk of bias) and output scale (the prevalence of complication) were collected.

Quality Assessment

The extended scale of Hoy et al. was used to evaluate the quality of method and the risk of bias in each observational study. This 10-item scale assesses the quality of studies according to their external validity (items 1 to 4 evaluate the target population, sampling frame, and minimum selection bias) and internal validity (items 5 to 9 evaluate the data collection, problem statement, research scale and data collection tool, while item 10 evaluates the data analysis bias). The risk of bias was measured by two researchers independently and disagreements were resolved by consensus.

Data Collection

All eligible studies were included in the data collection after a systematic review and the data were integrated using the cumulative chart. The random effect model was evaluated based on the overall prevalence of the disease among the participants. The heterogeneity of the initial studies was assessed using the I^2 test. In addition, subgroups were analyzed to determine the heterogeneity by participants' age, year of publication, and country. Finally, a meta-analysis was performed using STATA14 statistical software.

Results

Study Selection

A total of 564 articles were extracted through preliminary searches in various databases. Of the 564 essential studies identified by the analysis of titles and abstracts, 421ones were eliminated because of irrelevant titles. Of the 43 existing studies, 37ones were excluded. Of the 37 excluded studies, 21 had no full-text articles, 5 were review articles, 2 were a letter to the editor, and 9 did not meet the study inclusion criteria. Of the remaining studies, 6 met the study inclusion criteria. (Fig. 1)
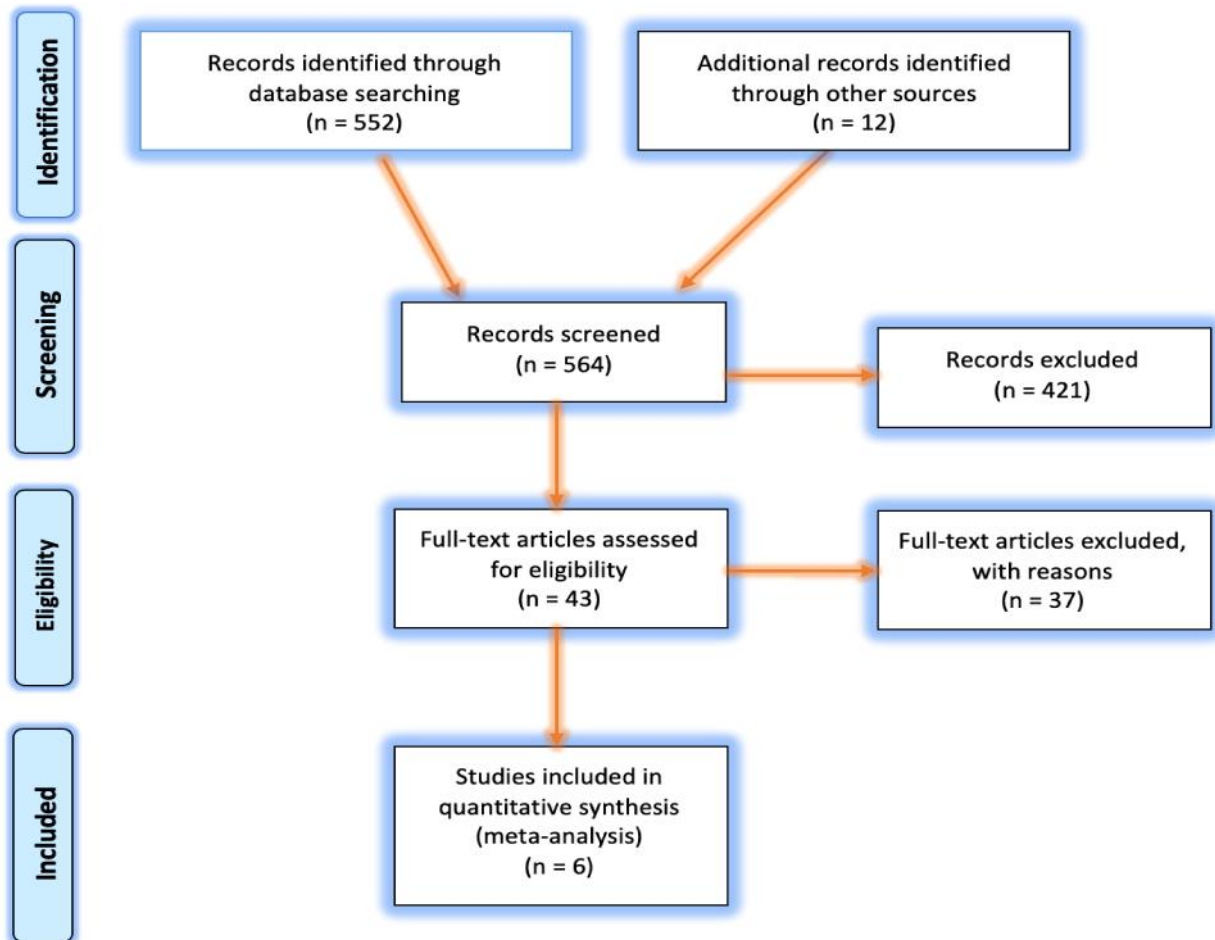
PRISMA 2009 Flow Diagram

Fig 1: PRISMA flow diagram

Research Properties

A total of 588 patients who had acute myocardial infarction and a total of 6 studies from 6 province that met the inclusion criteria were evaluated. Simple sampling was used to select the sample (n = 6). All of studies, were retrospective. studies from the Jahrom, Ahvaz, Ghazvin, Ardabil, Boushehr and Ramsar. In most studies the risk of bias was low. Data were originally collected from medical records. The main study sites were intensive care units (n = 6). (Table 1)

Table 1.Demographic characteristics for the included studies

ID	Frist author	Publication year	City or province	Participants	Male to Female	Age mean ± SD	Risk of bias
1	Shojaei	2009	Jahrom	100	82/18	61.7	Low
2	Fayazi	2012	Ahvaz	120	78/42	--	Low
3	Behnam moghaddam	2013	Ghazvin	100	76/24	61.24	Low
4	Zamani	2014	Ardabil	100	62/38	--	Low
5	Iranpour	2014	Boushehr	108	--	---	Low
6	Nasiri	2010	Ramsar	60	---	---	Low

The meta-analysis of the Side Effects of Intravenous Streptokinase in Iranian Patients with Acute Myocardial Infarction:

According to the random effect model, the total prevalence of allergic complication in 588 patients with Acute Myocardial Infarction was 14% (11%-17% at a 95% confidence interval, I^2 = 99.5%) , the total prevalence of hematologic complication in 588 patients with Acute Myocardial Infarction was 12% (10%-14% at a 95% confidence interval, I^2 = 93.5%) and the total prevalence of cardiac complication was 20% (17%-23% at a 95% confidence interval, I^2 = 96%). (Fig. 2, 3 and 4, Table 2)

Table 2. The meta-analysis of the Side Effects of Intravenous Streptokinase in Iranian Patients with Acute Myocardial Infarction

Firs Author	95% conf. interval (Allergic)				95% conf. interval(Hematologic)				95% conf. interval(Cardiac)				Publication year	Participants
	Down	Up	ES	Weight	Down	UP	ES	Weight	Down	UP	ES	Weight	------	-------
Shojaei[17]	0.15	0.31	0.23	9.81	0.17	0.35	0.26	6.13	-	-	-	-	2009	100
Fayazi[18]	0.16	0.32	0.24	11.44	0.25	0.41	0.33	6.39	0.25	0.41	0.33	13.72	2012	120
Behnam moghaddam[19]	0.21	0.39	0.30	8.25	0.06	0.20	0.13	10.42	-	-	-	-	2013	100
Zamani[20]	0.23	0.41	0.32	7.97	0.23	0.41	0.32	5.42	0.22	0.38	0.30	13.79	2014	100
Iranpour[21]	0.00	0.08	0.04	48.96	0.08	0.16	0.12	30.94	0.08	0.16	0.12	66.42	2014	108
Nasiri[22]	0.08	0.22	0.15	13.58	0.00	0.06	0.03	40.70	0.37	0.63	0.50	6.07	2010	60
All	0.11	0.17	0.14	100	0.10	0.14	0.12	100	0.17	0.23	0.20	100	2009	100

Meta Regression Results

Meta-regression between the year of publication and the prevalence of allergic complication:

The meta-regression of the studies was evaluated according to the relationship between the prevalence of allergic complication and the year of publication and the overall rate of complication. There was no significant linear trend in the univariate meta-regression to explain the effect size of the year of publication. (Fig.5).
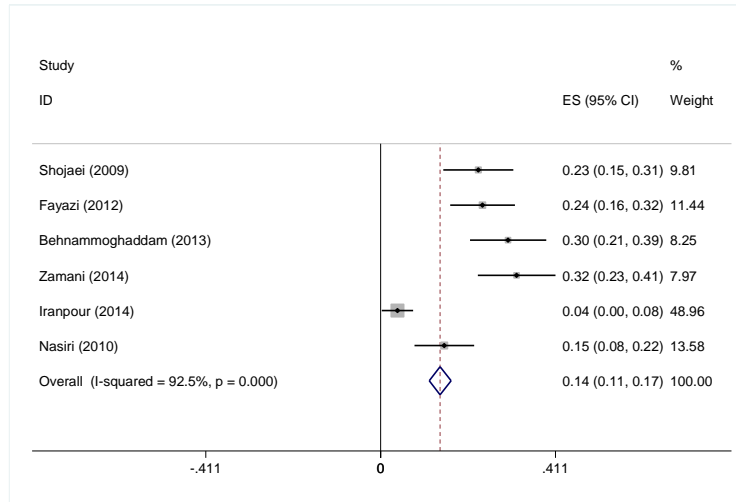
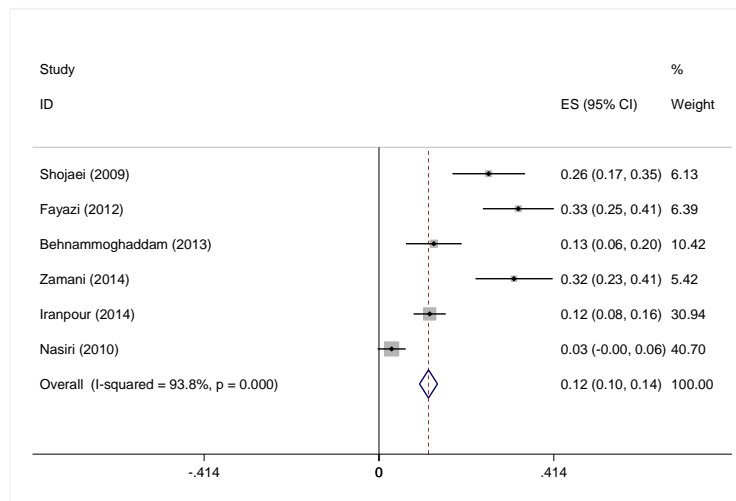Fig 2:The total prevalence of allergic complicationin Iranian Patients with Acute Myocardial Infarction

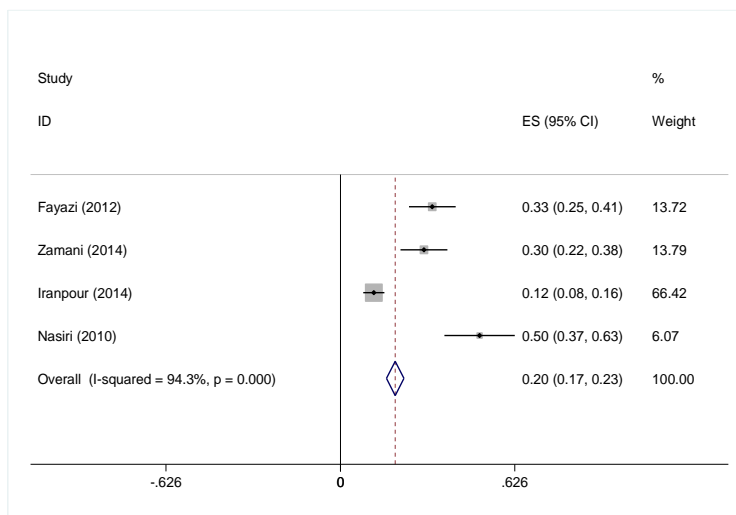Fig 3:The total prevalence of hematologic complicationin Iranian Patients with Acute Myocardial Infarction

Fig 4:The total prevalence of cardiac complicationin Iranian Patients with Acute Myocardial Infarction

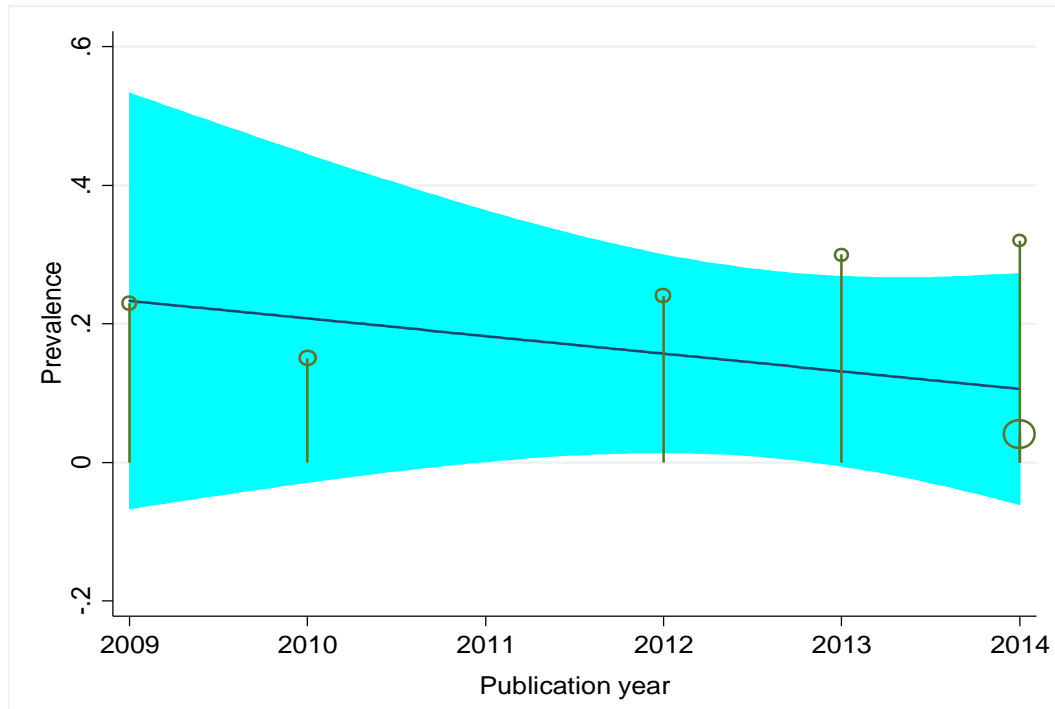Fig 5:Meta-regression between publication year of study and prevalence of allergic complication

Discussion

Use of streptokinase, despite the beneficial therapeutic effects, can pose serious risks such as intracerebral hemorrhage, gastrointestinal and internal bleeding, bleeding from mouth and nose, anaphylactic shock, coagulation disorders, drop in blood pressure, and conduction disorders (13 and 14). According to the random effect model, the total prevalence of allergic complication in 588 patients with Acute Myocardial Infarction was 14% (11%-17% at a 95% confidence interval, $I^2 = 99.5\%$) , the total prevalence of hematologic complication in 588 patients with Acute Myocardial Infarction was 12% (10%-14% at a 95% confidence interval, $I^2 = 93.5\%$) and the total prevalence of cardiac complication was 20% (17%-23% at a 95% confidence interval, $I^2 = 96\%$).The use of thrombolytic drugs in patients with myocardial infarction, who have not felt pain for more than 4 hours and whose age is less than 75 years, is preferred and of greater benefit. The therapeutic effect of thrombolytic drugs in reducing the mortality of patients under 75 has been proved by extensive studies and without any ambiguity. In western societies, 30% of patients are over 75 years of age, and the efficacy of thrombolytic therapy for this group is not completely clear (15). Hemorrhage is the most serious and common complication of streptokinase, which will increase mortality, especially in the elderly. Intracerebral hemorrhage is the most dangerous type of bleeding, which is about 0.5-0.9%.This rate in patients older than 70 years is twice than that of younger patients. Although the benefits of using thrombolytic drugs have been proved in patients younger than 75 years of age, the value of using them in the treatment of myocardial infarction with ST-segment elevation myocardial infarction (STEMI) in patients aged 75 years and over is controversial and there are still many questions about their safety and their impact on this patient group. Despite the efficacy of thrombolytic drugs in reducing mortality from acute myocardial infarction, a small number of elderly patients are using these drugs so that, today, between 10 and 27 percent of elderly patients are deprived of receiving thrombolytic drugs. Numerous studies have been performed on thrombolytic drugs, but in most preliminary studies, individuals over the age of 75 have been excluded, and the study of complications of venous thrombolytic drugs has been associated with contradictory results (16). The reason for less use of this type of treatment in the elderly is due to the physicians' fear of dangerous hemorrhages including intracerebral hemorrhage in the patients.

Conclusion

Although, in this study, the use of thrombolytic therapy in elderly patients is associated with risks and complications, given the low prevalence of its side effects compared to its beneficial effects, this treatment should be considered for elderly patients with acute myocardial infarction, especially in centersthat do not have emergency angioplasty facilities.

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