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ROLE OF EMERGENCY TISSUE PLASMINOGEN ACTIVATOR IN ISCHEMIC STROKE

Tissue plasminogen activator efficiency in ischemic stroke.

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Abstract:

Background:

Intravenous tissue plasminogen activator (t-PA) was recognized and approved as the thrombolytic agent for acute ischemic stroke that can improve patients' outcome and resolve their neurological deficits. The main reason for the difficulty of stroke treatment is the narrow time window. The cost-effectiveness and feasibility of intravenous t-PA for treatment of acute stroke in 3 - 4.5 hour time window, after symptom onset, have been confirmed in previous studies.

Aim: *To determine the role of emergency tissue plasminogen activator in ischemic stroke.Also, to study its risk factors, complications, regulatory approvals and its efficiency with time.*

Methods: *The data were obtained after searching the available studies published in English language using several key words (tissue plasminogen activator, ischemic stroke, efficiency and role) on the scientific websites as Pubmed, ResearchGate, and Google scholar.*

Results: *This study included 27 randomized and non randomized trials as well as systemic reviews. The data were extracted according to the inclusion and exclusion criteria, the time of treatment, the dosage, follow up and the history of the patients. The included articles were published between the years 2000 to 2018.*

Conclusion: *The results of this study indicated that the administration of intravenous rt-PA among stroke patients could reduce the unfavorable outcome and increase the quality of life as well the neurological activity. After acute ischemic stroke, the guidelines suggest using rt-PA within 3 -4.5 h after the initiation of the stroke to achieve the best outcomes and decrease the risk of hemorrhage.*

Keywords: *Emergency, tissue plasminogen activator, ischemic stroke, safety, side effects.*

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INTRODUCTION:

Stroke is a chiefbasis of mortality in the United States and about 800,000 new strokes are reported each year(1, 2). It is associated with high rates of disability among elder stroke patients (1).

During the treatment of acute ischemic stroke, the administration of intravenous tissue-type plasminogen activator (IV tPA) is the only approved treatment for lysis of the thrombus(3). Since the approval of t-PA in 1996, the number of ischemic stroke patients treated with t-PA has been increased but still low than the proper number as only rate 3.4% to 5.2% of all American AIS patients were treated with t-PA (4). The rate of using rt-PA is associated with the delay of emergency medical services, the process and time of treatment initiation, and the time window for each treatment (5). Current efforts are done to rise the treatment rate for IV tPA to all patients with stroke who are eligible and present within 2 hours from the onset of the symptoms (6). Some studies proved that the usage and enlargement oftelestroke networks arerelated toenhancing the usage of IV tPA treatment (7, 8).

Also, in order to increase the treatment rates, the therapeutic time window must be expanded as the US Food and Drug Administration (FDA) approved the usage of IV tPAtreatment patients suffering from AIS within 3 hours of the onset of stroke symptoms. On the other hand, some other studies showed that efficacy and safety of using rt-PA with extending the time window more than 3 hours then treatment time window was expanded to<4.5 hours in Europe and other countries(9-11).

One of the most common complications resulting in high mortality and morbidity rates is intracerebral hemorrhagethus adherence to the clinical guidelines during rt-PA treatment among stroke patients could be associated with decreasing the risk of hemorrhage and increase the efficiency of other stroke medications (12, 13). In this review, we aimed at determining the role of emergency tissue plasminogen activator in ischemic stroke. Also, to study its risk factors, complications, regulatory approvals and its efficiency with time.

MATERIALS AND METHODS:

The data were obtained after searching the available studies published in English language using several key words (tissue plasminogen activator, ischemic stroke, efficiency and role) on the scientific websites as Pubmed, ResearchGate, Google scholar, ….etc. After the first search, 30 studies were available then 3 studies were excluded. This study included 27 randomized and non randomized trials as well as systemic reviews. The data were extracted according to the inclusion and exclusion criteria, the time of treatment, the dosage, follow up and the history of the patients. The included articles were published between the years 2000 to 2018.

Discussion:

Tissue Plasminogen Activator in Stroke: Dosage and Time Window

Intravenous t-PA was documented as the appropriate thrombolytic factorthat can improve the neurological deficits and outcomes among acute ischemic stroke patients. Stroke treatment is mainly difficult due to the narrow time window resulting in decreasing the suitability of using t-PA among stroke patients (14). Large studies were conducted to study the efficiency and safety margins of t-PA among patients suffering from acute ischemic stroke. These studies suggested that the proper dosage of t-PA is 0.9 mg/kg up during the first 4 hours of the onset of stroke(3, 10, 15-21).

Interestingly, the earlier treatment is favorable resulting in decreasing the complications of stroke patients within 3 h of the onset of stroke and its efficiency is decreased with time, age and the timing of initiation of treatment and those treated between 3-6 h showed higher incidence of death rates among the patients (22-27).

The profits of t-PA among stroke patients

The treatment of stroke patients using t-PA within the time window (3-4.5 h) would give favorable outcomes among most of included patients and increase the quality of life (18, 20, 21, 28-31). A study showed that the quality of life was adjusted and the health benefits were increased when compared to those who didn't receive t-PA treatment within the time window (29). Also, other studies proved that the t-PA usage could be associated with better outcomes and less adverse effects but associated with age, sex, and duration of stroke (32, 33).

The complications of t-PA among stroke patients

Some clinical trials studied the adverse effects of the t-PA showed that the rates of death were slightly larger if treated with t-PA after 3 hours till 6 hours(9, 27, 34, 35).The most common reported and serious complication of rt-PA therapy during stroke is intracranial hemorrhage (ICH) (14, 34, 36). Also, a clinical trials showed that the incidence of ICH after rt-PA is affected by the ethnicity, differences in coagulation and fibrinolytic factors (37). However, other trials showed no significant difference in the incidence of symptomatic intracranial

haemorrhageamong stroke patients treated with rt-PA within 3 h when compared to those who received them after 3-6 hours(22, 27, 34).

CONCLUSION:

The results of this study indicated that the administration of intravenous rt-PA among stroke patients could reduce the unfavorable outcome and increase the quality of life as well the neurological activity. After acute ischemic stroke, the guidelines suggest using rt-PA within 3 -4.5 h after the initiation of the stroke to achieve the best outcomes and decrease the risk of hemorrhage.Large population clinical trials must be conducted to investigate the adverse effects and the dosage as well as identifying the high risk intracranial hemorrhage patients after treating with rt-PA.

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