IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

"Breaking Clots, Mending Hearts : Exploring The Dynamics Of Thrombolysis In Myocardial Infarction"(STREPTOKINASE AND RETEPLASE)

Omkar N Swami, Sahil G Shaikh, Shahu V Dhutmal, Deval K Patil, Mrs. Vidya Kapse.

Shivlingeshwar Collage Of Pharmacy (Pharm-D) Almala. Tq. Ausa Dist. Latur, Maharashtra.

Abstract

In the present era, thrombolytic therapy and primary percutaneous coronary intervention (PPCI) has revolutionized the way patients with AMI are managed resulting in significant reduction in cardiovascular mortality In the intricate landscape of myocardial infarction, thrombolysis emerges as a key intervention, wielding the power to dissolve the obstructive blood clots and restore the vital flow of circulation. Often referred to as Fibrinolysis, thrombolysis represents a beacon of hope in critical scenarios such as Myocardial Infarction. In this we will see Thrombolysis treatment with reteplase and streptokinase.

Keywords

Acute myocardial infarction, Reteplase Streptokinase, plasminogen , plasmin

Introduction

Acute myocardial infarction (AMI) is one of the leading causes of death in the developed world. The prevalence of the disease approaches 3 million people worldwide, with more than 1 million deaths in the United States annually. Nearly a century ago, in 1912, Herrick described "complete obliteration of the proximal segment of the left anterior descending artery with a red thrombus" as the cause of AMI in a 55-year old man during an autopsy examination. In 1958, Fletcher first reported the use of thrombolytic therapy for the management of MI. Subsequently several small trials reported the benefit of streptokinase (SK) in the management of patients with MI. streptokinase (SK) in the management of patients with AMI. Newer agents including tissue plasminogen activators (TPA) such as alteplase, reteplase, tenecteplase (TNK) were developed subsequently.(1,2)

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History of Thrombolytic Agents

In 1933, Dr. William Tillett discovered SK through sheer chance when he observed that streptococci agglutinated plasma but not serum. He inferred that fibrinogen contained in the plasma and not in the serum resulted in the agglutination of streptococci as fibrinogen gets absorbed onto the surface of streptococci. He furthers concluded that any plasma containing streptococci would not clot and this laid the foundation for thrombolysis in various settings.

Christensen and MacLeod coined the term "streptokinase" in 1945 [17]. SK was originally utilized in the treatment of patients with tuberculous haemorrhagic pleural effusions and tuberculosis meningitis. In the setting of AMI, SK produced by various species of streptococci can bind and activate human plasminogen into plasmin that results in fibrinolysis.(3–5)

Mechanism of Thrombolysis

The mechanism of thrombolysis involves the usage of drugs which dissolves the blood clots a process also knows as Fibrinolysis. The goal is to restore the normal flow of circulation by breaking down the fibrin meshwork that constitutes the clot. Following are the step by step mechanism of Thrombolysis.(6–8)

1. **Introduction of Thrombolytic Agents**
   Thrombolytic Agents such as streptokinase or reteplase are introduced in the blood stream. These agents play a vital role in initiation of fibrinolysis process.
2. **Conversion of Plasminogen to Plasmin**
   Thrombolytic Agents react with the plasminogen, an inactive precursor in the clot. The interaction initiates a conformational change in plasminogen, converting it into the active form called plasmin.
3. **Plasmin Activity**
   Plasmin is a proteolytic enzyme that function to break down fibrin.
4. **Fibrinolysis and clot Dissolution**
   The activates Plasmin initiates a cascade of reaction which results in the breakdown of fibrin strands with clot.
5. **Release of Degradation Product**
   As fibrin in broken down the soluble fibrin in released in blood stream.
6. **Restoration of Blood Flow**
   with the dissolution of clot blood flows in a normal way through the affected blood vessels.(6–10)

Comparison of Streptokinase with Tissue Plasminogen Activators

Newer thrombolytic agents have been developed in order to provide longer half-life to enable bolus administration, fibrin specificity, and to be resistant to natural inhibitors such as plasminogen activator inhibitor-1 (PAI-1). Newer agents and their properties are displayed in Table 1. Following the breakthrough discovery of SK in the treatment of patients with AMI and the emergence of novel agents, the attention shifted to determine which thrombolytic agent was the best. The GUSTO (Global Use of Strategies to Open Occluded Coronary Arteries), GISSI-2, and ISIS-3. investigators compared intravenous SK and TPA in the treatment of MI.(9–11)

Agent	Molecular weight (D)	Plasma half life (min)	Fibrin specificity	Plasminogen activation	Antigenicity	Dose
Streptokinase	47 000	23–29	–	Indirect	+	1.5 MIU/60 min
Mutants of native tissue plasminogen activator						
Tenecteplase	70 000	20	+++	Direct	–	0.5 mg/kg bolus
Alteplase	70 000	4–8	++	Direct	–	100 mg/90 min
Reteplase	39 000	15	+	Direct	–	2 × 10 IU boluses 30 min apart
Lanoteplase	53 500	23	+	Direct	–	120 IU/kg bolus
Recombinant single-chain urokinase plasminogen activator						
Saruplase	46 500	9	±	Direct	–	80 mg/60 min
Staphylokinase	16 500	6	++++	Indirect	+	20–30 mg/30 min

TABLE:-1

Reteplase

Reteplase is a recombinant peptide which consists of the cringle 2 and protease domains of human tissue-type plasminogen activator. It has been developed as a thrombolytic treatment for acute myocardial infarction (AMI). The half-life of reteplase allows administration as a double-bolus injection (second injection given 30 minutes after the first) rather than by the prolonged and, in some cases, more complex intravenous infusion regimens that are required for most other thrombolytic agents.

Reteplase is a drug that belongs to a class of fibrinolytics. Which are designed to dissolve blood clots and repair the damaged Arteries. Here are some important key points for reteplase in treatment of myocardial.(1,9–11)

1. **Mechanism of Action**
   Reteplase works by activating body natural clot dissolving system. It is a recombinant form of tissue Plasminogen activator. Specially designed to enhance its clot dissolving properties. Reteplase works by converting plasminogen to plasmin.(7,8,12)
2. **Administration**
   Reteplase is administered intravenously in hospital setting.
3. **Indications**
   Reteplase is indicated for the ST segment elevation myocardial infarction.
4. **Considerations and Contraindications**
   Reteplaee, is like other thrombolytics which is not suitable for all patients. It is contraindicated in certain conditions, for example recent major surgery, bleeding disorders and a history of stroke.(3,4,6,11)

CHARACTERISTIC	THROMBOLYTIC THERAPY (N = 2095)	PRIMARY ANGIOPLASTY (N = 1050)	P VALUE
Age (yr)	59.8±11.9	59.9±11.9	0.89
Female sex (%)	23.9	23.4	0.76
Prior infarct (%)	13.0	14.8	0.16
Prior heart failure (%)	3.7	3.3	0.62
Prior bypass surgery (%)	5.5	7.8	0.01
History of stroke (%)	4.2	6.5	0.16
History of gastrointestinal bleeding (%)	0.8	2.8	0.007
Systolic blood pressure >180 mm Hg (%)	5.9	7.8	0.1
Heart rate >100 beats/min (%)	10.0	11.6	0.19
Systolic blood pressure <100 mm Hg (%)	10.3	11.7	0.32
Anterior location of infarct (%)	37.3	34.2	0.08
High risk (%)†	54.6	57.0	0.28
Time to treatment (hr)	1.0±1.0	1.7±1.2	<0.001

TABLE 2

Limitations Of Thrombolysis

1. Contraindications to Thrombolysis
2. Timing Of Thrombolytic Treatment
3. Cerebrovascular Events
4. Potency of Infarct Arteries
5. Reinfarction and recurrent ischemia
6. Age
7. Infarct shape and size(3–6,13)

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