FIBRINOLYTICS

(THROMBOLYTICS)

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Fibrinolytics

- Also known as **Thrombolytics**
- **Used to dissolve blood clot / thrombi**
- Used to recanalize occluded blood vessels
- **Used for treatment (curative), not for prophylaxis**
- **Promotes conversion of plasminogen to plasmin à Degrades fibrin into fibrin degraded products à which rapidly dissolves blood clot.**

Fibrinoltyics

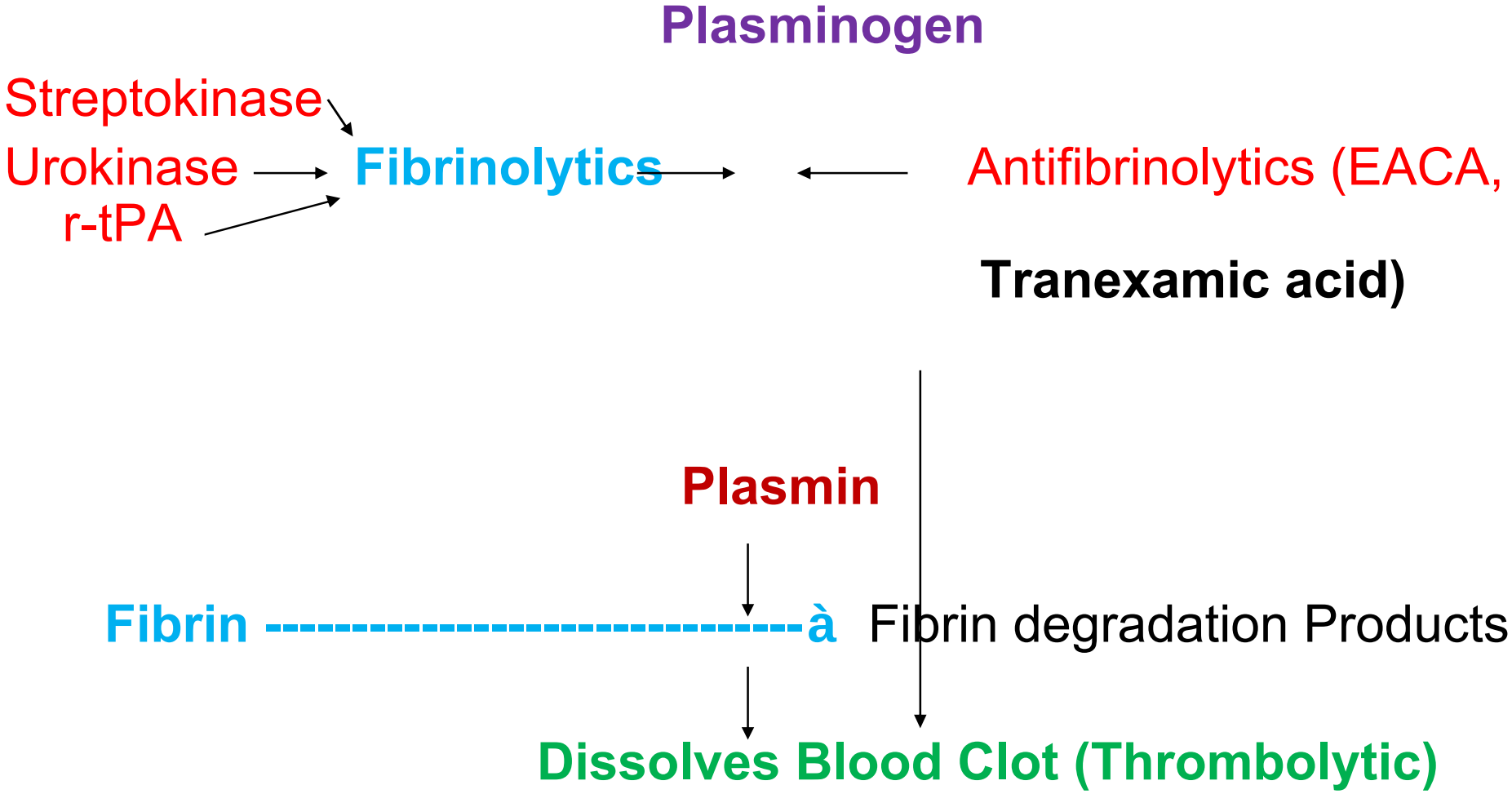
- **Classification :-**

I) **Streptokinase – Protein derived from bacteria**

II) **Urokinase – Enzyme derived from human foetal kidney –cell culture**

III) **R-TPA (Alteplase) :- Derived from recombinant DNA technology**

Mechanism of Action (Fibrinolytics)



Comparison of Fibrinolytics

	Streptokinase	Urokinase	Alteplase (r-tPA)
1.	Protein	An Enzyme	An Enzyme
2.	Derived from B-hemolytic Streptococci	Derived from human foetal kidney cell culture	Derived from recombinant DNA technology
3.	Binds with circulating Plasminogen	Directly activates Plasminogen to Plasmin	Selectively activates fibrin– bound Plasminogen
4.	* Antigenic * Pyogenic * Destroyed by Antistreptococcal antibodies	* Non- antigenic * Non- pyogenic * Not destroyed by antibodies	* Non-antigenic * Non- pyogenic * Not destroyed by antibodies

Comparison of Fibrinolytics

Streptokinase	Urokinase	Alteplase (r-tPA)
5. Moderately	Fast acting	Rapidly acting
Less potent	More Potent	More Potent
Less expensive	Costly	More Expensive
6. Administered by	Initially I.V. bolus	Initially I.V. bolus
I.V. infusion	then, I.V. infusion	then, I.V. Infusion
7. M.I. : 7.5 – 15	2.5 Lac IU i.v.	15 mg i.v. bolus, then
lac IU infused i.v.	over 10 min, then	50 mg over 30 min, then
over 1 hr.	5 lac IU over next	35 mg over next 1 hr.
8. DVT/PE :		
2.5 lac IU Loading	4400 IU/Kg over 10 min,	100mg infused i.v.
dose over 1 hr.	4400 IU/Kg/hr for 12 hrs.	over 2 hrs.

Comparison of Fibrinolytics

• Streptokinase	**Urokinase**	Alteplase (r-tPA)
9. Adverse Effects		
-Hypotension	- Hypotension (Rare)	-No Hypotension
- Bleeding	- Bleeding	- Less Bleeding
- **Allergic reaction**	**- Less**	**- Less**
- **Fever**	**- No Fever**	**- No fever**

USES OF FIBRINOLYTICS

1) Acute Myocardial Infarction (AMI) :-

* Alternative to emergency Percutaneous Coronary intervention (PCI) with stent replacement.

Advantages :-

- 90 % success rate in dissolving clot if given within 1st four hrs
- Produces recanalization of occluded blood vessels
- Reduces area of infarct size & area of necrosis
- Preserves ventricular functions
- Prevents Ventricular arrhythmias and sudden death
- Reduces mortality rates
- Aspirin with or without Heparin prevents re-occlusion.

USES OF FIBRINOLYTICS

2) Deep Vein Thrombosis (DVT) :- (Leg, Pelvis, Shoulder)

- **Advantages :-**
- **Treats 60 % of the patients successfully**
- **Relieves subscequent pain and swelling**
- **Preserves functions of the venous valves**
- **Reduces the risk of Pulmonary embolism (PE).**

3) Pulmonary Embolism (PE) :-

- **Indicated in Large, Life- threatening PE**
- **Retains or Preserves Lung functions better**
- **No decrease in mortality**

USES OF FIBRINOLYTICS

4) Peripheral Arterial Occlusion :-

Advantages :-

- **Recanalizes 40 % limb artery occlusion if treated within 72 hrs**
- **Indicated only, when surgical Thrombectomy not possible**
- **Regional intra-arterial fibrinolytics used for limb arteries**
- **Peripheral arterial thrombolysis is followed by short-term and long-term asprin therapy**

Disadvantages :-

- **No role in chronic peripheral vascular diseases (PVD)**

USES OF FIBRINOLYTICS

6) Stroke :-

Advantages :-

- **Thrombolytic therapy in ishcaemic stroke is controversial**
- **Only r-tPA (Alteplase) approved for :-**

i) **Used in ischaemic stroke in carefully selected patients if administered i.v. within 3 hrs**

ii) **Used in whom intracanial haemorrhage is ruled out along with all risk factors for bleeding**

- **Improves Neurological outcomes**

Disadvantages :-

* **No change in mortality rates.**

ADVERSE EFFECTS OF THROMBOLYICS

1) Bleeding
2) Hypotension
3) Allergic reacrion
4) Anaphylactoid shock
5) Skin rashes
6) Fever
7) Chills

CONTRAINDICATIONS OF THROMBOLYTICS

1) Recent Trauma, Head injury
2) Recent surgery, Biopsies
3) Haemorrhagic stroke
4) Peptic ulcer
5) Severe hypertension
6) Pregnancy
7) Acute pancreatitis
8) Bleeding disorders
9) Haemophilia
10) Aneurysms

ANTI-FIBRINOLTYICS

- **Inhibits Plasminogen activation**
- **Inhibits Dissolution of blood clot**
- **Example :-**
- 1) **Epsilon Amino-Caproic Acid (EACA)**
- **2) Tranexamic acid**

EACA

- Is analogue of Amino-acid Lysine
- Is administered orally or parenterally
- Acts by :-
- Binds with the lysine binding sites of Plasminogen & Plasminà prevents conversion of plasminogen to plasminà No binding of plasmin to fibrin à does not dissolve the clot

USES of EACA

1) Used as an antidote to fibrinolytics
2) Used in many Hyper-Plasminaemic states associated with excessive Intravascular fibrinolysis resulting in bleeding :-

i) Overdose of streptokinase/urokinase/r-tPA

ii) To prevent recurrence of subarachnoid haemorrhage & GI bleeding

iii) Traumatic and surgical bleedings :- Prostatectomy, Tooth extraction in Haemophilics

iv) Menorrhaegia, PPH

Adverse Effects of EACA

1) In Haematuriaà can cause ureteric obstruction by unlysed clots
2) Rapid I.V. administration à
   - Hypotension
   - Bradycardia
   - Arrhythmias
3) Myopathy

Dose :- 5 Gm oral ‘i.v , then 1 Gm till bleeding stops. (500 mg Tabs; 5 g/20 ml inj.).

TRANEXAEMIC ACID

- Anti-fibrinolytic – orally & parenterally
- 7 times more potent than EACA
- Binds to lysine binding site on plasminogen and prevents its combination with fibrin.
- Useful in prevention of excessive bleeding in :-

i) Overdose of fibrinolytics

ii) After cardio-pulmonary bypass surgery

iii) After tonsillectomy, prostatic surgery, tooth extraction in haemophilics

iv) Menorrhaegia due to IUCD

v) Recurrent epistaxis, ocular trauma, bleeding peptic ulcers. (Side effects : Diarrhoea, Headache)