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Peripheral arterial thromboembolism. Thrombolytics including streptokinase may be used in the management of peripheral arterial thromboembolism (p.1178). Streptokinase has been injected intravenously or intra-arterially directly into the clot as an alternative to surgical treatment of the occlusion. It has also been infused intra-arterially to remove distal clots during surgery. The *intravenous* dose generally used is 250 000 units over 30 minutes followed by 100 000 units/hour. A lower dose of 5000 units/hour has been used *intra-arterially* directly into the clot[1] and for removal of distal clots during surgery streptokinase has been given intra-arterially in a dose of 100 000 units over 30 minutes or as five bolus doses of 20 000 units at 5-minute intervals.[2]

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Stroke. Stroke (p.1185) is normally considered a contra-indication to the use of thrombolytics, and clearly they would be inappropriate in acute haemorrhagic stroke. However, when stroke is associated with thrombotic occlusion there is evidence, as with myocardial infarction, that a degree of neuronal recovery is possible if the occlusion is reversed sufficiently quickly, and thrombolytics may therefore have a role in some patients with acute ischaemic stroke.

Early studies with intravenous thrombolytics in acute *ischaemic stroke* suggested a reduction in early death, although subsequent randomised trials produced disappointing results, with the exception of one with alteplase given within 3 hours of the onset of stroke (NINDS—National Institute of Neurological Disorders and Stroke rt-PA Stroke Trial).[1] The studies using streptokinase—MAST-E (Multicentre Acute Stroke Trial-Europe),[2] ASK (Australian Streptokinase Trial),[3] and MAST-I (Multicentre Acute Stroke Trial-Italy)[4,5]—were terminated before completion because of adverse outcomes (intracranial bleeding and increased mortality) in the treatment groups, particularly in those receiving therapy more than 3 hours after stroke onset.[3] The study investigating alteplase given within 6 hours of the onset of symptoms (ECASS I—European Cooperative Acute Stroke Study)[6] reported that, although some patients might benefit, overall alteplase was associated with higher mortality rates and an increase in some intracranial bleeding (parenchymal haemorrhage). In the NINDS randomised study,[1] alteplase given within 3 hours of the onset of ischaemic stroke appeared to improve clinical outcome despite an increased incidence of symptomatic intracerebral haemorrhage. Patients treated with alteplase were more likely to have minimal or no disability 3 months after stroke,[1] and this benefit was maintained at 12 months.[7] However, there was no difference in mortality or rate of recurrence of stroke. A second ECASS study (ECASS II)[8] that hoped to confirm the early findings of the NINDS study failed to confirm a statistical benefit for alteplase over placebo and found no significant differences between patients who received alteplase within 3 hours or between 3 and 6 hours. A review[9] of several studies confirmed that alteplase needed to be given early, and preferably within 90 minutes, if it was to be effective.

On the basis of the NINDS study, alteplase given within 3 hours of the onset of ischaemic stroke is now recommended for selected patients in most guidelines on stroke management.[10-14] Despite their own disappointing results, the ECASS II investigators reached a similar conclusion. However, these recommendations have been criticised.[15,16] It has been pointed out[17,18] that very few patients will be eligible for treatment with alteplase, since the time of onset of symptoms is often uncertain and in many patients more than 3 hours elapses before a definite diagnosis of ischaemic stroke is made. In addition, the NINDS study[1] excluded patients with severe stroke and those taking anticoagulants. The rationale for exclusion of patients with severe stroke is that haemorrhagic transformation is more likely to occur with large areas of infarction.[17] However, size of infarct is difficult to identify by CT scanning.[17] Anticoagulants or antiplatelets are also contra-indicated in the first 24 hours after use of alteplase. The poor results obtained in studies using streptokinase have led to recommendations that streptokinase should be avoided in ischaemic stroke,[13] although an overview of thrombolytic studies[18] suggested that it may not be worse than alteplase and that the apparent hazards of streptokinase may be accounted for by differences in trial design (for example use with anticoagulants) and in patient population. Thus, while alteplase can be considered for those few patients meeting the entry criteria for the NINDS study, a systematic review[19] concluded that further large studies are required to establish more clearly the overall role of thrombolytics in acute ischaemic stroke. Studies of the use of alteplase outside the setting of a clinical trial have had mixed results.[20-22] However, an observational study[23] found that alteplase was safe and effective when used in accordance with guidelines, while another study[24] found that it could be used in elderly patients (80 years-of-age and older), a group normally excluded from clinical trials.

Intra-arterial thrombolytics may have advantages over intravenous use and may be used in selected patients.[12-14] Studies with nasaruplase[25] and urokinase[26] have suggested benefit up to 6 hours after stroke due to middle cerebral artery occlusion, and use of intra-arterial thrombolytics may therefore be considered in such patients.[12-14] Intra-arterial thrombolytics are also used in basilar artery occlusion, although evidence to support this is limited;[12,13,27] intravenous alteplase may be an alternative.[28] Combined use of intravenous and intra-arterial alteplase,[29] as well as use of adjunctive therapies such as therapeutic ultrasound[30] or antithrombotics, are under investigation but do not yet have an established role.[13]

Intravenous thrombolytics have no role in the management of acute *haemorrhagic stroke*, but they have been given locally to facilitate the aspiration of haematomas in both intracerebral[31] and subarachnoid haemorrhage. Small studies with urokinase have shown benefit in patients with intraventricular haemorrhage.

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Preparations

BP 2008: Streptokinase Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Streptase; ***Austral.:*** Streptase; ***Austria:*** Streptase; ***Belg.:*** Streptase; ***Braz.:*** Kabikinase†; Solustrep; Streptase; Streptokin; Streptonase; Unitinase†; ***Canad.:*** Streptase; ***Chile:*** Streptase†; ***Cz.:*** Kabikinase†; Streptase; ***Denm.:*** Streptase; ***Fin.:*** Streptase; ***Fr.:*** Streptase; ***Ger.:*** Streptase; ***Gr.:*** Streptase; ***Hong Kong:*** Streptase; ***Hung.:*** Streptase; ***India:*** Fibrokinase; STpase; Streptase; Zykinase; ***Indon.:*** Streptase; ***Irl.:*** Streptase†; ***Israel:*** Kabikinase; Streptase; ***Ital.:*** Streptase†; ***Malaysia:*** Streptase†; ***Mex.:*** Streptase; ***Neth.:*** Streptase; ***Norw.:*** Kabikinase†; Streptase; ***NZ:*** Streptase; ***Pol.:*** Streptase; ***Port.:*** Streptase; ***S.Afr.:*** Streptase; ***Spain:*** Kabikinase†; Streptase; ***Swed.:*** Streptase; ***Switz.:*** Streptase; ***Thai.:*** Streptase; ***UK:*** Streptase; ***USA:*** Streptase; ***Venez.:*** Streptase.

Multi-ingredient: ***Arg.:*** Varidasa†; ***Austral.:*** Varidase†; ***Austria:*** Varidase; ***Denm.:*** Varidase; ***Fin.:*** Varidase; ***Ger.:*** Varidase; ***Irl.:*** Varidase†; ***Ital.:*** Varidase†; ***Mex.:*** Varidasa; ***Norw.:*** Varidase; ***Pol.:*** Distreptaza; ***Port.:*** Varidasa†; ***Spain:*** Ernodasa; Varidasa; ***Swed.:*** Varidase; ***UK:*** Varidase†.

Strophanthin-K

Estrofantina; Kombé Strophanthin; Strophanthin; Strophanthoside-K.

CAS — 11005-63-3.

NOTE. Do not confuse with K-strophanthin-α which is Cymarin.

Pharmacopoeias. In *Chin.*

Profile

Strophanthin-K is a cardiac glycoside or a mixture of cardiac glycosides from strophanthus, the seeds of *Strophanthus kombe* (Apocynaceae) or other spp., adjusted by admixture with a suitable diluent such as lactose so as generally to possess 40% of the activity of anhydrous ouabain.

Strophanthin-K is a positive inotrope with general properties similar to those of digoxin (p.1259). It is poorly absorbed from the gastrointestinal tract but may be given intravenously in maintenance doses of 125 to 250 micrograms daily in the management of heart failure (p.1165).

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Kombetin.

Suleparoid *(rINNM)*

Heparan Sulfate; Heparan Sulphate; Heparitin Sulfate; Suléparoïde; Suleparoide; Suleparoidum.

Сулепароид

CAS — 9050-30-0.

Suleparoid Sodium *(rINN)*

Heparan Sulfate Sodium; Sodium Heparitin Sulphate; Suleparoide sódico; Suléparoïde Sodique; Suleparoidum Natricum.

Сулепароид Натрий

CAS — 57459-72-0.

Profile

Suleparoid is a naturally occurring glycosaminoglycan given orally in the management of thromboembolic disorders; it is also used topically. Suleparoid sodium is a component of danaparoid sodium (p.1255).

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Aremin; Arteven; Clarema; Hemovasal; Leparan†; Spatix†; Tavidan; Vas; Vasorema†.

Multi-ingredient: ***Ital.:*** Osmogel.

Sulodexide *(rINN)*

KRX-101; Sulodexida; Sulodexidum. Glucurono-2-amino-2-deoxyglucoglucan sulfate.

Сулодексид

CAS — 57821-29-1.
ATC — B01AB11.
ATC Vet — QB01AB11.