

Use

Alteplase is a fibrinolytic drug used to dissolve intravascular thrombi. Streptokinase (q.v.) is cheaper.

Pharmacology

All fibrinolytic drugs work by activating plasminogen to plasmin, which then degrades fibrin, causing the break up of intravascular thrombi. Treatment should always be started as soon as possible after any clot has formed. Streptokinase and alteplase both have an established role in the management of myocardial infarction, but controlled trials show that benefit is limited if treatment is delayed for more than twelve hours. Alteplase, a human tissue plasminogen activator first manufactured by a recombinant DNA process in 1983, is a glycoprotein which directly activates the conversion of plasminogen to plasmin. It became commercially available in 1988. When given IV it remains relatively inactive in the circulation until it binds to fibrin, for which it has a high affinity. It is, however, rapidly destroyed by the liver, with a plasma half life of only five minutes. As a result, adverse effects (including excess bleeding) are uncommon in adults and usually controlled without difficulty by stopping treatment. There is little experience of use during pregnancy. The high molecular weight makes placental transfer unlikely. There is no evidence of teratogenicity, but placental bleeding is a theoretical possibility. Use during lactation seems unlikely to pose any serious problem.

There have been many reports of the use of alteplase to lyse arterial and intracardiac thrombi in the neonatal period, but it is not clear whether it any safer or more effective than streptokinase and the drug is considerably more expensive. There is, however, probably rather less risk of an adverse effect, and less theoretical risk of an allergic reaction. Visualise the clot and take advice from a vascular surgeon before starting treatment, remembering that ultrasound review has shown that the great majority of catheter-related thrombi never give rise to symptoms. Use can certainly speed the resolution of infective endocarditis. However there is a risk of bleeding, especially if the platelet count is below $100 \times 10^9/l$, or the fibrinogen level falls below 1 g/l. Intracranial bleeding was a common complication with sustained use in one recent neonatal case series, so risk assessment is important before starting treatment. Combined use with heparin (q.v.) optimises outcome in adults with myocardial infarction, but the value of such dual treatment in babies has not been properly studied. Try and avoid venepuncture and IM injections during treatment. See the web site for a commentary on the slim evidence base that currently underpins the management of clots and emboli in early infancy.

Alteplase (0.5 mg/kg) has been instilled experimentally into the cerebral ventricles of babies with severe intraventricular bleeding in an attempt to reduce post-haemorrhagic hydrocephalus, but neither of the first two trials of this strategy showed any real evidence of benefit and such treatment may provoke further bleeding.

Prophylaxis

A 1 mg/ml solution of alteplase is better (if more expensive) than heparin at keeping 'stopped-off' long lines patent. Slightly overfill the line, and aspirate before reuse to stop small emboli being shed into the lung.

Treatment

Blocked catheters: Instil a volume of alteplase (1 mg/ml) slightly greater than the catheter dead space. Other strategies, as outlined in the monograph on urokinase, may sometimes work better in lines that have been used to infuse parenteral nutrition.

Thrombi: Give 500 micrograms/kg over 30 minutes. If Doppler ultrasound shows inadequate resolution consider a second similar dose followed by a continuous infusion of 200 micrograms/kg per hour.

Monitoring

Monitor the fibrinogen level regularly during sustained treatment, and adjust the dose if the level falls below 1 g/l. Give cryoprecipitate or fresh frozen plasma (q.v.) at once if a bleeding tendency develops.

Supply and administration

10 mg (5.8 mega unit) vials of powder suitable for reconstitution using 10 ml of water for injection (as provided) cost £135. The resultant solution (containing 1 mg of alteplase per ml) must be used within 24 hours, even if stored at 4°C, but small pre-prepared syringes can be kept for 3 months at -20°C. To give 200 micrograms/kg per hour dilute the reconstituted solution with an equal volume of 0.9% sodium chloride and infuse at a rate of 0.4 ml/kg per hour. Do not dilute the reconstituted solution with anything except 0.9% sodium chloride.

References

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