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[Intervention Review]

Thrombolysis for acute deep vein thrombosis

Lorna Watson[1], Cathryn Broderick[2], Matthew P Armon[3]

[1]Cameron House, Leven, UK. [2]Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK. [3]Department of General Surgery, Norfolk and Norwich University Hospital, Norwich, UK

Contact address: Lorna Watson, Cameron House, Cameron Bridge, Windygates, Leven, KY8 5RG, UK. lwatson@nhs.net.

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ABSTRACT

Background

Standard treatment for deep vein thrombosis aims to reduce immediate complications. Use of thrombolysis or clot dissolving drugs could reduce the long-term complications of post-thrombotic syndrome (PTS) including pain, swelling, skin discolouration, or venous ulceration in the affected leg. This is the third update of a review first published in 2004.

Objectives

To assess the effects of thrombolytic therapy and anticoagulation compared to anticoagulation alone for the management of people with acute deep vein thrombosis (DVT) of the lower limb as determined by the effects on pulmonary embolism, recurrent venous thromboembolism, major bleeding, post-thrombotic complications, venous patency and venous function.

Search methods

For this update the Cochrane Vascular Information Specialist (CIS) searched the Specialised Register (February 2016). In addition the CIS searched the Cochrane Register of Studies (CENTRAL (2016, Issue 1)). Trial registries were searched for details of ongoing or unpublished studies.

Selection criteria

Randomised controlled trials (RCTs) examining thrombolysis and anticoagulation versus anticoagulation for acute DVT were considered.

Data collection and analysis

For this update (2016), LW and CB selected trials, extracted data independently, and sought advice from MPA where necessary. We assessed study quality with the Cochrane risk of bias tool. For dichotomous outcomes, we calculated the risk ratio (RR) and corresponding 95% confidence interval (CI). Data were pooled using a fixed-effect model unless significant heterogeneity was identified in which case a random-effects model was used. GRADE was used to assess the overall quality of the evidence supporting the outcomes assessed in this review.

Main results

Seventeen RCTs with 1103 participants were included. These studies differed in the both thrombolytic agent used and in the technique used to deliver it. Systemic, loco-regional and catheter-directed thrombolysis (CDT) were all included. Fourteen studies were rated as low risk of bias and three studies were rated as high risk of bias. We combined the results as any (all) thrombolysis compared to standard anticoagulation. Complete clot lysis occurred significantly more often in the treatment group at early follow-up (RR 4.91; 95% CI 1.66

to 14.53, P = 0.004) and at intermediate follow-up (RR 2.44; 95% CI 1.40 to 4.27, P = 0.002; moderate quality evidence). A similar effect was seen for any degree of improvement in venous patency. Up to five years after treatment significantly less PTS occurred in those receiving thrombolysis (RR 0.66, 95% CI 0.53 to 0.81; P < 0.0001; moderate quality evidence). This reduction in PTS was still observed at late follow-up (beyond five years), in two studies (RR 0.58, 95% CI 0.45 to 0.77; P < 0.0001; moderate quality evidence). Leg ulceration was reduced although the data were limited by small numbers (RR 0.87; 95% CI 0.16 to 4.73, P = 0.87). Those receiving thrombolysis had increased bleeding complications (RR 2.23; 95% CI 1.41 to 3.52, P = 0.0006; moderate quality evidence). Three strokes occurred in the treatment group, all in trials conducted pre-1990, and none in the control group. There was no significant effect on mortality detected at either early or intermediate follow-up. Data on the occurrence of pulmonary embolism (PE) and recurrent DVT were inconclusive. Systemic thrombolysis and CDT had similar levels of effectiveness. Studies of CDT included two trials in femoral and iliofemoral DVT, and results from these are consistent with those from trials of systemic thrombolysis in DVT at other levels of occlusion.

Authors' conclusions

Thrombolysis increases the patency of veins and reduces the incidence of PTS following proximal DVT by a third. Evidence suggests that systemic administration and CDT have similar effectiveness. Strict eligibility criteria appears to improve safety in recent studies and may be necessary to reduce the risk of bleeding complications. This may limit the applicability of this treatment. In those who are treated there is a small increased risk of bleeding. Using GRADE assessment, the evidence was judged to be of moderate quality due to many trials having low numbers of participants. However, the results across studies were consistent and we have reasonable confidence in these results.

PLAIN LANGUAGE SUMMARY

Thrombolysis for treatment of acute deep vein thrombosis

Background

Deep vein thrombosis (DVT) occurs when a blood clot forms in a leg vein. The clot can break up and move to the lungs, leading to a potentially serious blockage in blood flow (pulmonary embolism or PE). Because of the damage to the leg vein, post-thrombotic syndrome (PTS) may develop any time over the next couple of years. Symptoms include leg pain, swelling, skin pigmentation and leg ulcers, leading to loss of mobility. Anticoagulants are the standard treatment for DVT or a clot in a calf vein. These thin the blood to reduce further clots from forming and prevent PE; yet PTS can still develop. Thrombolysis breaks down the blood clot. For DVT, drugs such as streptokinase, urokinase and tissue plasminogen activator are infused into a vein in the arm or foot or, in some cases, directly at the site of the clot using a catheter and X-ray control. Bleeding complications, stroke or intracerebral haemorrhage are potential harmful events for both treatments.

Study characteristics and key results

The review results are based on 17 controlled trials that randomised a total of 1103 people with acute DVT (within 21 days of onset of symptoms) to receive thrombolysis or anticoagulant treatment. Trials were carried out principally in the USA, Scandinavia, Germany and the UK. All trials included men and women ranging in age from 18 to 75 years with a preponderance of older adults.

The present review (current until February 2016) showed that thrombolysis may have advantages over standard anticoagulation treatment. Thrombolysis effectively dissolved the clot so that complete clot breakdown occurred more often with thrombolysis than with standard anticoagulant therapy. Blood flow in the affected vein (venous patency) was also better maintained. Three trials (306 participants) continued for over six months and found that fewer people developed PTS when treated with thrombolysis, 45% compared with 66% in the standard anticoagulation treatment group. Two trials (211 participants) which continued for over five years also showed that fewer people developed PTS when treated with thrombolysis.

Those receiving thrombolysis had more bleeding complications than with standard anticoagulation (10% versus 8%). Most bleeding episodes and deaths occurred in the older studies. Use of strict eligibility criteria appears to have improved the safety of this treatment, which is effective delivered directly to the clot by catheter or via bloodstream from another vein.

Qualitity of the evidence

Using GRADE assessment, the evidence was judged to be of moderate quality due to many trials having low numbers of participants. However, the results across studies were consistent and we have reasonable confidence in these results.