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[Intervention Review]

Haemostatic therapies for acute spontaneous intracerebral haemorrhage

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ABSTRACT

Background

Outcome after spontaneous (non-traumatic) intracerebral haemorrhage (ICH) is influenced by haematoma volume; up to one-third of ICHs enlarge within 24 hours of onset. Early haemostatic therapy might improve outcome by limiting haematoma growth. This is an update of a Cochrane Review first published in 2006, and last updated in 2009.

Objectives

To examine 1) the effectiveness and safety of individual classes of haemostatic therapies, compared against placebo or open control, in adults with acute spontaneous intracerebral haemorrhage, and 2) the effects of each class of haemostatic therapy according to the type of antithrombotic drug taken immediately before ICH onset (i.e. anticoagulant, antiplatelet, or none).

Search methods

We searched the Cochrane Stroke Trials Register, CENTRAL; 2017, Issue 11, MEDLINE Ovid, and Embase Ovid on 27 November 2017. In an effort to identify further published, ongoing, and unpublished randomised controlled trials (RCT), we scanned bibliographies of relevant articles and searched international registers of RCTs in November 2017.

Selection criteria

We sought randomised controlled trials (RCTs) of any haemostatic intervention (i.e. pro-coagulant treatments such as coagulation factors, antifibrinolytic drugs, or platelet transfusion) for acute spontaneous ICH, compared with placebo, open control, or an active comparator, reporting relevant clinical outcome measures.

Data collection and analysis

Two authors independently extracted data, assessed risk of bias, and contacted corresponding authors of eligible RCTs for specific data if they were not provided in the published report of an RCT.

Main results

We included 12 RCTs involving 1732 participants. There were seven RCTs of blood clotting factors versus placebo or open control involving 1480 participants, three RCTs of antifibrinolytic drugs versus placebo or open control involving 57 participants, one RCT of platelet transfusion versus open control involving 190 participants, and one RCT of blood clotting factors versus fresh frozen plasma involving five

participants. We were unable to include two eligible RCTs because they presented aggregate data for adults with ICH and other types of intracranial haemorrhage. We identified 10 ongoing RCTs. Across all seven criteria in the 12 included RCTs, the risk of bias was unclear in 37 (44%), high in 16 (19%), and low in 31 (37%). Only one RCT was at low risk of bias in all criteria.

In one RCT of platelet transfusion versus open control for acute spontaneous ICH associated with antiplatelet drug use, there was a significant increase in death or dependence (modified Rankin Scale score 4 to 6) at day 90 (70/97 versus 52/93; risk ratio (RR) 1.29, 95% confidence interval (CI) 1.04 to 1.61, one trial, 190 participants, moderate-quality evidence). All findings were non-significant for blood clotting factors versus placebo or open control for acute spontaneous ICH with or without surgery (moderate-quality evidence), for antifibrinolytic drugs versus placebo (moderate-quality evidence) or open control for acute spontaneous ICH (moderate-quality evidence), and for clotting factors versus fresh frozen plasma for acute spontaneous ICH associated with anticoagulant drug use (no evidence).

Authors' conclusions

Based on moderate-quality evidence from one trial, platelet transfusion seems hazardous in comparison to standard care for adults with antiplatelet-associated ICH.

We were unable to draw firm conclusions about the efficacy and safety of blood clotting factors for acute spontaneous ICH with or without surgery, antifibrinolytic drugs for acute spontaneous ICH, and clotting factors versus fresh frozen plasma for acute spontaneous ICH associated with anticoagulant drug use.

Further RCTs are warranted, and we await the results of the 10 ongoing RCTs with interest.

PLAIN LANGUAGE SUMMARY

Treatments to help blood clotting to improve the recovery of adults with stroke due to bleeding in the brain

Review question

Do treatments to help blood clot reduce the risk of death and disability for adults with stroke due to bleeding in the brain?

Background

More than one-tenth of all strokes are caused by bleeding in the brain (known as brain haemorrhage). The bigger the haemorrhage, the more likely it is to be fatal. Roughly one-third of brain haemorrhages enlarge significantly within the first 24 hours. Therefore, treatments that promote blood clotting might reduce the risk of death or being disabled after brain haemorrhage by limiting its growth, if given soon after the bleeding starts. However, haemostatic drugs might cause unwanted clotting, leading to unwanted side effects, such as heart attacks and clots in leg veins.

Study characteristics

We found 12 randomised controlled trials, including 1732 participants, up to November 2017.

Key results

We found moderate-quality evidence of harm from platelet transfusion for people who had used antiplatelet drugs until they had a brain haemorrhage. We found no evidence of either benefit or harm from other haemostatic therapies for people with brain haemorrhage.

Quality of the evidence

Overall, the quality of the evidence was moderate to low.

More information will become available from the 10 trials that are ongoing.