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Desmopressin for reversal of Antiplatelet drugs in Stroke due to Haemorrhage (DASH): rationale and design of a phase II double blind randomised controlled trial

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Abstract Content: **Abstract Content: Rationale**

Intracerebral haemorrhage caused ~3 million deaths worldwide in 2015. Two-thirds of survivors are left dependent on others. Roughly one third of patients are taking antiplatelet drugs at the time of intracerebral haemorrhage in high-income countries, and this proportion has been increasing over time. Pre-stroke antiplatelet drug use is associated with a 27% relative increase in one-month case fatality compared to patients not using antithrombotic drugs. Platelet transfusion, tranexamic acid, and recombinant activated factor VII do not seem to improve outcome after antiplatelet-associated intracerebral haemorrhage, but desmopressin has seemed promising in non-randomised pilot studies.

Objectives

We aim to assess the feasibility of screening, checking the eligibility, approaching, randomising, administering desmopressin or placebo, and completing follow-up for patients with antiplatelet-associated intracerebral haemorrhage.

Design

We aim to include 50 patients within 12 hours of spontaneous intracerebral haemorrhage onset, associated with oral antiplatelet drug(s) use in the preceding seven days. Exclusion criteria are: known secondary cause for intracerebral haemorrhage; risk of fluid retention associated with desmopressin; significant hypotension (SBP<90mmHg); known drug-eluting coronary artery stent in previous three months; allergy to desmopressin; pre-stroke dependency; Glasgow coma scale <5; pre-morbid life expectancy <3 months; and pregnant or breastfeeding at randomisation. Patients will be randomised (1:1) to receive intravenous desmopressin 20μg in 50 mls Sodium Chloride 0.9% infused over 20 minutes or matching placebo. We will mask participants, relatives, researchers and outcome assessors to treatment allocation. Feasibility outcomes include proportion of patients approached being randomised, number of patients receiving allocated treatment, rate of recruitment, and adherence to treatment and follow up. Secondary outcomes include change in intracerebral haemorrhage volume at 24 hours; hyponatraemia at 24 hours, length of hospital stay, discharge destination, early mortality <28 days, death or dependency at day 90, mortality up to day 90, serious adverse events (including thromboembolic events) up to day 90; disability (Barthel index, day 90), quality of life (EuroQol, day 90), cognition (telephone MMSE day 90), and health economic assessment (EQ-5D). Baseline platelet dysfunction will be measured and correlated with response to desmopressin; and change in factor VIII, VWF antigen and VWF activity will be assessed one hour after administration of desmopressin.

Conclusion

This is a feasibility trial, which will inform the design of a definitive trial.

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