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## Controlling Hypertension and Hypotension Immediately Post-Stroke (CHHIPS) Trial

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**Purpose:** Blood pressure (BP) changes are common following acute stroke with up to 60% of patients being hypertensive (SBP  $\geq$  160mmHg) and 20% hypotensive (SBP  $\leq$  140mmHg), and may be associated with adverse prognosis. There is preliminary evidence to support use of drugs inhibiting renin-angiotensin system: ACE inhibition reduces BP without adverse effects on cerebral blood flow, and angiotensin II blockade reduces mortality when commenced within 72 hrs of stroke onset in severely hypertensive patients. Also, hypertensive patients treated with labetalol (LAB) in placebo arm of NINDS Trial had lower mortality. Use of pressor therapy in hypotensive patients may reduce focal cerebral injury by improving perfusion to penumbral ischaemic tissue. However, at present the acute management of post-stroke BP changes is a matter of debate. **Design:** Prospective, multi-centre, randomized, double-blind, placebo-controlled, titrated-dose trial. **Sample size:** 2000 patients. **Population studied:** 3 groups will be studied - (1) Hypotensive (SBP  $\leq$  140mmHg) non-haemorrhagic, neuroradiologically-confirmed stroke patients treated within 12 hrs of stroke onset; (2) Hypertensive (SBP  $\geq$  160mmHg), non-dysphagic ischaemic and haemorrhagic stroke patients within 24 hrs of stroke onset; (3) Hypertensive, dysphagic ischaemic and haemorrhagic stroke patients within 24 hrs of stroke onset. **Interventions:** All routine aspects of management of patients will be continued as standard local practice. The following specific interventions will be given to individual groups: (1) intravenous (iv) phenylephrine at 80 $\mu$ g/min or matching placebo (PLA), titrated to target SBP 150mmHg (range 145 to 155) or 15mmHg increase above baseline, and continued until maximum period 24 hrs after stroke onset; (2) oral lisinopril (LIS) 5mg or LAB 50mg or matching PLA, repeated if necessary at 4 and 8 hrs after initial dosing to target SBP 150mmHg (145 to 155) or 15mmHg reduction from baseline, and continued at dose of LIS 5 to 15mg daily or LAB 50 to 150mg twice daily or matching PLA until 2 wks after stroke onset; (3) sublingual (sl) LIS 5mg and iv PLA or sl PLA and iv LAB 15mg/ hour or sl and iv PLA, adjusted if necessary at 4 and 8 hours after initial dosing to target SBP 150mmHg (145 to 155) or 15mmHg reduction from baseline, and continued at dose of LIS 5 to 15 mg daily or LAB 15 to 45mg/ hour or PLA until 72 hours after stroke onset, thereafter as LIS, LAB or PLA suspension by nasogastric tube (in patients remaining non-dysphagic) or orally (in patients regaining swallow) until 2 weeks after stroke onset. **Outcomes:** Primary outcome will be proportion of patients dead or dependent (mRS  $>$ 2) at 14 days following stroke onset. Secondary outcomes will include early ( $<$ 72 hours) neurological deterioration, stroke recurrence over 2 weeks, treatment discontinuations, trial withdrawals, BP changes at 24 hrs and 2 wks, and health-related quality of life at 3 months. **Statistical Analysis:** 400 patients recruited to pressor arm (group 1) would have an 80% power at 5% significance level to detect relative reduction of 25% in death and dependency between treatment and placebo groups. 1650 patients recruited to the depressor arms (groups 2 and 3) would have an 80% power at 5% significance level to detect relative reduction of 15% in death and dependency between either treatment group and placebo. **Trial status:** Planning (Funded). **Web site:** www.le.ac.uk/medther/