PREvention of Complications to Improve OUtcome in elderly patients with acute Stroke

Inclusion procedure:

1. Check in- and exclusion criteria (see overleaf)
2. Ask for Informed Consent
   a Remember resistance sub-study.
3. Randomise via www.precious-trial.eu
   a Press on the yellow randomization button
   b Log in with your own 'Username' and 'Password'
   c Press 'Add new subject' in left top corner
   d Select correct study 'site' and press 'Save'
   e Fill in the inclusion form
   f Press 'Randomise'
   g The randomisation result appears in the screen
   (NB: write the randomisation result in the electronic patient file)
   h Press "Close" on the randomisation screen
   i Press "Submit" at the bottom right corner of the inclusion form
4. If allocated to treatment, **start treatment as soon as possible, but within 24 hours after symptom onset**

Medications:

prescribe use of medication of for 96 hours

- Ceftriaxone once daily 2000mg. Administration: intravenous.
- Paracetamol 4 times daily 1000mg. Administration: oral, rectal, or intravenous.
- Metoclopramide thrice daily 10mg. Administration: oral, rectal, or intravenous.

For metoclopramide, adjust the dosage to renal or hepatic function:

- End-stage renal disease (creatinine clearance ≤ 15 ml/min): 3 times 2.5mg daily
- Moderate to severe renal impairment (15-60 ml/min) or severe hepatic impairment (liver cirrhosis): 3 times 5mg daily

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Inclusion criteria:

1. A clinical diagnosis of acute ischaemic stroke or intracerebral haemorrhage, confirmed with CT or MRI scan. A normal CT scan is considered compatible with ischaemic stroke;
2. A score on the National Institutes of Health Stroke Scale (NIHSS) ≥ 6, indicating moderately severe to severe stroke;
3. Age 66 years or older;
4. The possibility to start treatment within 24 hours of symptom onset
5. Written informed consent.

Exclusion criteria:

1. Active infection requiring antibiotic treatment, as judged by the treating physician;
2. Pre-stroke score on the mRS ≥4;
3. Death appearing imminent at the time of assessment.

For the ceftriaxone stratum:

1. Known hypersensitivity to beta-lactam antibiotics;
2. Clinical indication for antibiotic treatment. The use of an antibiotic before screening is not an exclusion criterion.

For the paracetamol stratum:

1. Known hypersensitivity to paracetamol or any of the excipients
2. Known severe hepatic insufficiency;
3. Chronic alcoholism.
4. Clinical indication for the use of paracetamol. Incidental use of paracetamol before screening is not an exclusion criterion.

For the metoclopramide stratum:

1. Hypersensitivity to metoclopramide or to any of the excipients;
2. Gastrointestinal haemorrhage, mechanical obstruction or gastro-intestinal perforation for which the stimulation of gastrointestinal motility constitutes a risk;
3. Confirmed or suspected pheochromocytoma;
4. History of neuroleptic or metoclopramide-induced tardive dyskinesia;
5. Epilepsy;
6. Parkinson's disease;
7. Use of levodopa or dopaminergic agonists;
8. Known history of methaemoglobinaemia with metoclopramide or of NADH cytochrome-b5 deficiency.
9. Clinical indication for the use of metoclopramide. Incidental use of metoclopramide before screening is not an exclusion criterion.