Pressor Therapy in Acute Ischemic Stroke
Systematic Review

Amit K. Mistri, MRCP; Thompson G. Robinson, FRCP; John F. Potter, FRCP

Background and Purpose—Systolic blood pressure (SBP) levels below 140 mm Hg after acute stroke occur in 18% to 25% of patients, and may be associated with adverse outcome, in terms of death and disability. It has thus been proposed that BP elevation in acute ischemic stroke may be beneficial by increasing perfusion to the peri-infarct penumbra, though not only in those with low BP levels.

Methods—All articles studying BP elevation in the context of acute stroke were identified using a structured search strategy.

Results—Two reviewers independently searched the databases, and 12 relevant publications were identified. All identified publications related to acute ischemic stroke and no articles on pressor therapy in primary hemorrhagic stroke were found. The review included 319 subjects (age: 42 to 88 years, 46% male), with phenylephrine being the most commonly used pressor agent, though 8 studies incorporated volume expansion. Because of small numbers, and varying entry/outcome criteria, no meta-analysis of outcome measures was possible. Overall, in these few studies undertaken, pressor therapy in acute stroke appears feasible and well-tolerated. The benefit and risks in terms of clinical outcomes remains unknown, but intensive monitoring is advised if such therapy is undertaken.

Conclusions—Theoretical arguments exist for inducing BP elevation in acute ischemic stroke to increase blood flow to the ischemic penumbra across patients with a broad BP range. To date, there have only been a few small trials with inconclusive results. Many questions are still unanswered about the safety and potential benefits of pressor therapy in acute stroke. Hopefully, ongoing trials will answer some of these important questions. (Stroke. 2006;37:1565-1571.)

Key Words: blood pressure ■ stroke, acute
stroke. Cerebral autoregulation is impaired after acute ischemic stroke,10 ie, cerebral blood flow (CBF) is passively dependent on the mean arterial pressure (MAP). Olsen et al11 demonstrated the existence of pressure-passive noninfarcted low-flow areas in 48 patients with ischemic stroke, where an induced BP-rise resulted in an increase in CBF (as assessed by scintigraphy after an intracarotid injection of Xenon-133). Indeed, animal studies have shown that induced hypertension can reduce focal cerebral injury, by increasing intraluminal hydrostatic pressure, which opens collateral channels and improves perfusion to the penumbra.12 Also, induced hypertension is recommended for prevention and treatment of cerebral ischemic complications in patients with vasospasm after subarachnoid hemorrhage.13

Hence, in patients with a recent stroke, an argument can be made to elevate BP levels, and thereby CBF, thus optimizing perfusion and minimizing ischemic brain injury. The actual therapeutic window for benefit is uncertain, though earlier intervention is likely to be more beneficial.

Volume expansion/hemodilution is commonly incorporated as part of the treatment regime. Hemodilution increases CBF, which may be beneficial in recovery from acute cerebral infarction. However, the Cochrane Review on Hemodilution in Acute Stroke14 (3119 patients, 18 trials) reported no improvement in 4-week mortality, 3- to 6-month mortality and 3- to 6-month death/dependency rates with the use of hemodilution alone.

Current guidelines about the management of poststroke hypotension provide no objective clarification as to the appropriate treatment, which is a reflection of the paucity of evidence in this field, and an indicator of the practical difficulties of carrying out research in the setting of acute stroke. The European Stroke Initiative Recommendations for Stroke Management15 mentions that “low cardiac output states may need inotropic support.” They imply that potential causes for low BP must be looked for and dealt with, and due consideration be given to pressor therapy. The Guidelines for the Early Management of Patients With Ischemic Stroke16 states that “at present, drug-induced hypertension cannot be recommended for the treatment of most patients with ischemic stroke (grade A).” The Cochrane Analysis, by the Blood Pressure in Acute Stroke Collaboration17 found insufficient data to draw any conclusions about deliberate alteration of BP within 2 weeks of a stroke. Thus, it is difficult to define a set BP level at which pressor therapy should be considered; it could be argued that only a stroke patient with a significant SBP fall (eg, >20 mm Hg) could benefit from pressor therapy, irrespective of absolute BP levels.

The current evidence regarding the use of pressor therapy in patients with acute stroke will now be considered.

Search Strategy
We systematically identified and reviewed all articles studying interventions to specifically elevate BP in the setting of acute stroke, to assess the effect on neurological outcomes and complication rates. A.K.M. and T.G.R. searched for articles in MEDLINE from 1951 and EMBASE from 1974, using the MeSH headings Stroke and Cerebrovascular Accident, and the keywords Stroke, induced ADJ (adjacent) hypertension, elevation NEAR BP OR elevation NEAR blood ADJ pressure, and pressor ADJ therapy. Articles were also identified from the Cochrane Database (2005-Issue 1). Of the resultant 451 articles, relevant articles were handpicked by literature review. Reference lists from published reviews were also searched for relevant articles. Inclusion criteria were as follows: all studies looking at BP elevation in the setting of neuroradiologically confirmed, acute ischemic stroke in humans. An independent observer (J.F.P.) resolved any differences between reviewers.

Results
Twelve publications fitting the criteria were identified, all relating to acute ischemic stroke, including 1 randomized controlled trial (RCT), 1 randomized trial (with conventional management as comparator), 1 case-control study, 1 observational study, 3 case series, 2 retrospective reviews and 3 case reports. No articles on pressor therapy in primary hemorrhagic stroke were found. Four articles were excluded: 3 because there was no classification and confirmation (neuroradiological or other) of stroke type, and 1 study of amphetamine use because BP elevation was neither the aim of the trial nor the proposed mechanism of action.

The review included 319 subjects (age 42 to 88 years, 46% male). The pressor agents used were phenylephrine, norepinephrine, epinephrine, dobutamine, dopamine and diaspirin cross-linked hemoglobin (DCLHb). Phenylephrine was the most commonly used agent in 62 of 194 patients receiving pressor therapy, with 8 studies also incorporating volume expansion. However, because of the small numbers, and varying entry and outcome criteria, a meta-analysis of outcome variables was not possible.

The study design and BP characteristics of the identified studies are summarized in Tables 1 and 2, respectively. Tables 3 and 4 depict the relative pressor effect of different agents according to their method of action. The individual pressor agents and studies are outlined below.

Phenylephrine18
Phenylephrine (PE; a selective α1-agonist) increases BP by peripheral vasoconstriction, without substantial direct cerebral vasoconstriction, attributable to a low density of α1-receptors in cerebral vessels.19 It is less likely to cause tachyarrhythmias, having negligible β-agonist action, compared with other pressor agents.

In an unblinded, retrospective case–control analysis of 63 patients with acute ischemic stroke PE, Rordorf et al20 evaluated the effects of pressor therapy with phenylephrine within 24 hours of onset, given as part of routine clinical practice. A threshold SBP for neurological deficit (defined as the SBP below which a sustained, consistent, neurological decline occurred at least twice, and above which the decline was rapidly reversed after induced BP elevation) was identified in 10 of the 33 PE-treated patients. Pressor therapy was continued in only these patients up to 24 days. Three of 33 patients receiving PE developed creatinine phosphokinase elevation, (but no ECG abnormalities). One patient had a paroxysm of atrial fibrillation, but none discontinued treatment because of complications. There were no significant differences in clinical complications, morbidity and mortality, between the 2 groups.

Subsequently, in a prospective case series of 13 patients with acute ischemic stroke, Rordorf et al21 successfully used
PE to elevate BP, achieving target SBP (≥160 mm Hg or 20% above admission value, to a maximum of 200 mm Hg) within the first hour. NIH improved by ≥2 points in 7 of the 13 patients and a BP threshold was found in 6 of these 7 patients. There were no systemic or neurological complications. Patients with a BP threshold (threshold SBP 174 (+/−15) mm Hg) had their infusion continued for 1 to 6 days, and maintained their improved NIHSS until discharge. Patients benefiting seemed to be patients with large extracranial/intracerebral vessel stenosis/occlusion.

Hillis et al22 reported marked and immediate improvement in naming when MAP was increased (values not reported) in a case series of 6 patients, with stroke onset within 1 week. No adverse effects of treatment were mentioned.

The group further published the case of a 55-year old man, who presented with paraphasias and clumsy right hand move-

### TABLE 1. Published Studies of Pressor Therapy in Acute Ischemic Stroke: Study Design

<table>
<thead>
<tr>
<th>Authors</th>
<th>Treated/Placebo or Untreated</th>
<th>Design</th>
<th>Onset to Treatment Time</th>
<th>Duration of Pressor Stimulus</th>
<th>Outcomes</th>
<th>Volume Expansion/ Hemodilution</th>
<th>Cardiac Effects</th>
<th>ICH/Cerebral Edema (%)</th>
<th>Death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE Rordorf et al21 1997</td>
<td>33/30</td>
<td>Retrospective case note review</td>
<td>&lt;24 h</td>
<td>7–576 h</td>
<td>Morbidity (complications, CXR, Brain scan) Mortality</td>
<td>Normal saline or Albumin</td>
<td>1 (PAF)</td>
<td>0</td>
<td>4/9 no significant difference</td>
</tr>
<tr>
<td>Rordorf et al22 2001</td>
<td>13</td>
<td>Pilot study/ case series</td>
<td>7–10 h</td>
<td>1–6 d</td>
<td>NIHSS</td>
<td>None</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hills et al23 2001</td>
<td>6 (4 PE &amp; 2 IV fluids)</td>
<td>Case series</td>
<td>&lt;7 d</td>
<td>Until function improved or MAP ≥130</td>
<td>Lexical semantics (oral, auditory and picture naming)</td>
<td>IV Normal saline in 2 patients not receiving PE</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hills et al24 2001</td>
<td>1</td>
<td>Case</td>
<td>24 h</td>
<td>12 h</td>
<td>Language</td>
<td>None</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hills et al25 2003</td>
<td>9/6</td>
<td>RT (2 treated: 1 untreated)</td>
<td>&lt;7 d</td>
<td>24–72 h</td>
<td>NIHSS cognitive score volume of hypoperfused tissue</td>
<td>Normal saline (as per clinical indication)</td>
<td>0</td>
<td>0</td>
<td>0/1</td>
</tr>
<tr>
<td>Hills et al26 2004</td>
<td>10/5 (8 PE + 2 IV fluids)</td>
<td>Case series</td>
<td>&lt;7 d</td>
<td>24–72 h</td>
<td>NIHSS cognitive score volume of hypoperfused tissue</td>
<td>Normal saline (as per clinical indication)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>NE Schwarz et al27 2002</td>
<td>19</td>
<td>Observational</td>
<td>6–143 h</td>
<td>5-min sessions</td>
<td>CPP &amp; CBF VmMCA</td>
<td>Crystalloids and hydroxyethyl starch</td>
<td>0</td>
<td>0</td>
<td>4 (ICH)</td>
</tr>
<tr>
<td>Marzan et al28 2004</td>
<td>34</td>
<td>Retrospective</td>
<td>4–26 h (13+/−5)</td>
<td>14–96 h</td>
<td>NIHSS</td>
<td>None</td>
<td>1 (AFib)</td>
<td>1 (3)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Epinephrine Meier F et al29 1991</td>
<td>30/44</td>
<td>RT</td>
<td>&lt;6 h</td>
<td>3×1h sessions</td>
<td>3 week survival</td>
<td>Low molecular dextans</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Dobutamine Duke et al30 1998</td>
<td>1</td>
<td>Case</td>
<td>?</td>
<td>~48 h</td>
<td>NIHSS</td>
<td>Volume, not specified</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Dopamine Oliviera-Filho et al31 2002</td>
<td>1</td>
<td>Case</td>
<td>?</td>
<td>NIHSS</td>
<td>Volume, not specified</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>DCLHb Saxena et al32 1998</td>
<td>40/45</td>
<td>RCT</td>
<td>&lt;18 h (6 hourly infusions)</td>
<td>72 h</td>
<td>NIHSS, Rankin, Barthel</td>
<td>No significant difference</td>
<td>4 edema, 2/6 hemorrhagic transformation</td>
<td>Higher Rx arm</td>
<td>—</td>
</tr>
</tbody>
</table>

PAF indicates paroxysmal atrial fibrillation; RT, randomized trial; ICH, intracranial hypertension; NIHSS, National Institute of Health Stroke Scale; SSS, Scandinavian Stroke Scale; —, not mentioned; CPP, cerebral perfusion pressure; CBF VmMCA, peak mean flow velocity of the middle cerebral artery.

Mistri et al  
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1567
ments, MRI showing an acute infarct in the left frontal lobe, insula and putamen, with an additional larger area of hypoperfused tissue, which included Wernicke area. MAP drop (107 to 87 mm Hg) was associated with development of global aphasia, but all language tasks improved again in parallel with the increase in MAP. Repeat MRI on treatment revealed improved perfusion of Wernicke area. Language improvement appeared to be dependent on maintaining a MAP > 100 mm Hg.

In a randomized trial including 15 patients with ischemic stroke (within a week of onset) and >20% diffusion-

<table>
<thead>
<tr>
<th>Authors</th>
<th>Treated/Placebo or Untreated</th>
<th>Design</th>
<th>Baseline BP</th>
<th>Target BP</th>
<th>Change in BP With Pressor Stimulus</th>
<th>% Attained Target BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rordorf et al21</td>
<td>33/30</td>
<td>Retrospective case note review</td>
<td>152 (±34.5)</td>
<td>&gt;-threshold SBP mean 161 (±20)</td>
<td>100% by definition (ie threshold BP)</td>
<td></td>
</tr>
<tr>
<td>Rordorf et al22</td>
<td>13</td>
<td>Pilot study/case series</td>
<td>141 (±30)</td>
<td>SBP &gt;160 or Rise of 20% (max 200)</td>
<td>100% within 60 minutes</td>
<td></td>
</tr>
<tr>
<td>Hills et al23</td>
<td>6 (4 PE &amp; 2 IV fluids)</td>
<td>Case series</td>
<td>—</td>
<td>Increments of 10% MAP (max 130)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hills et al24</td>
<td>1 Case</td>
<td>—</td>
<td>87</td>
<td>MAP 90–100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hills et al25</td>
<td>10/5 (8 PE + 2 IV fluids)</td>
<td>RT</td>
<td>—</td>
<td>10% increments in MAP until functional improvement (max 130)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hills et al26</td>
<td>9/6</td>
<td>Case series (2 treated: 1 untreated)</td>
<td>97.9 (±15)</td>
<td>10–20% increase in MAP (within 8 hours), further 10% increments if no functional improvement (max 130–140)</td>
<td></td>
<td>100% (by 12 h)</td>
</tr>
<tr>
<td>NE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schwarz et al27</td>
<td>19 Observational</td>
<td>—</td>
<td>83.6 (±1.6)</td>
<td>MAP increase of 10% (max 130)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marzan et al28</td>
<td>34 Retrospective</td>
<td>—</td>
<td>127 (±20)</td>
<td>10–20% increase in SBP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meier F et al29</td>
<td>30/44</td>
<td>RT</td>
<td>—</td>
<td>SBP 210–220</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dobutamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duke et al30</td>
<td>1 Case</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oliviera-Filho et al31</td>
<td>1 Case</td>
<td>—</td>
<td>—</td>
<td>SBP &gt;160</td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>DCLHb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saxena et al32</td>
<td>40/45</td>
<td>RCT</td>
<td>—</td>
<td>MAP 134 (±20), (Control SBP 109 ±16)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DBP indicates diastolic blood pressure; —, not mentioned.
perfusion mismatch on MRI, Hillis et al\textsuperscript{24} reported significant improvement of NIHSS, cognitive score and volume of hypoperfused tissue (132 to 58 mL) on perfusion-weighted imaging, in the treatment group with no adverse treatment effects (cardiac ischemia or hemorrhagic conversion of infarct). In a subsequent case series (including an overlap of some patients from the previous study), looking at the role of MRI in patient selection for pressor therapy,\textsuperscript{25} they reported a significantly larger reduction in hypoperfused tissue (identified by perfusion-weighted MRI) in those showing functional improvement (NIH increase \( \geq 3 \)). Mean NIHSS improved from 9.3 at baseline to 4.8 on day 3, in the treated group (untreated group—no difference 12 to 11.8), \( P < 0.001 \). No adverse events were reported.

**Conclusion**

PE appears to be a suitable candidate agent for studying the effect of BP elevation on outcome after acute stroke.

**Norepinephrine\textsuperscript{18}**

The pressor effect of norepinephrine (NE) is attributable to a combination of its \( \beta_1 \)-agonist (inotropic, chronotropic) and \( \alpha \)-agonist (vasoconstrictive) properties, the \( \beta_1 \)-effects being potentially detrimental by causing increased myocardial oxygen demand and a propensity to tachyarrhythmias.

Schwarz et al\textsuperscript{26} studied 19 patients with large hemispheric stroke (>2/3 of middle cerebral artery territory), receiving NE in an open, unblinded study, with intensive monitoring of intracranial pressure and middle cerebral artery blood flow (transcranial Doppler via temporal windows). Cerebral perfusion pressure and peak\textsuperscript{27} mean flow velocity of the middle cerebral arteries improved with no significant increase in intracranial pressure or adverse side effects. No evidence of hemorrhagic transformation was reported on follow-up CT scans, but 4 patients died of uncontrollable intracranial hypertension, 28 to 84 hours after the last pressor infusion.

In a retrospective case-note evaluation of 34 patients with acute ischemic stroke and SBP \( \leq 140 \) mm Hg, receiving intravenous NE within 26 hours of ictus, Marzan et al\textsuperscript{27} reported a single recurrence of paroxysmal atrial fibrillation, with accompanying ventricular tachycardia necessitating treatment discontinuation. Overall, 4 (12\%) patients died from massive space occupying hemorrhagic transformation, uncontrollable intracranial hypertension, pneumonia and acute cardiac insufficiency, locked-in syndrome. Early (within 8 hours) neurological improvement (NIH rise \( \geq 2 \)) occurred in 9 (27\%) patients, and no deaths were reported during treatment. It should be noted that all patients in this study received heparin, and antiplatelet therapy (aspirin or clopidogrel) and thrombolysis were also allowed if appropriate.

**Conclusion**

NE may not be the ideal agent because of its potential for cardiac side effects.

**Epinephrine (Adrenaline)\textsuperscript{18}**

Epinephrine has mixed \( \beta \)-receptor stimulation with some added \( \alpha \)-mediated effects.
In the study by Meier et al, using short-term pressor therapy with repeated bolus intravenous epinephrine, significantly more patients in the intervention group survived to 21 days (62.2% versus 36.4%; *P* = 0.02). There were no significant improvements in level of consciousness or severity of paresis.

**Conclusion**

Because of its indiscriminate stimulation of all sympathetic receptor subtypes, epinephrine theoretically has a higher risk of side effects than phenylephrine.

**Dobutamine**

Dobutamine is primarily a β₁-agonist, having positive inotropic and chronotropic effects similar to norepinephrine, with additional effects on α₁ and β₂-receptors. Its peripheral vascular effects are minimal, the vasoconstrictive effects of α₁-stimulation being counterbalanced by the vasodilatory effects of β₂-stimulation. Tolerance can develop if used for >24 to 72 hours.

Duke et al used dobutamine in a patient who developed an ischemic stroke 8 hours after carotid endarterectomy, demonstrating reperfusion on angiography, alongside BP elevation and associated clinical improvement.

**Dopamine**

The pressor effects of dopamine are attributable to its β-receptor property (inotropic effect) and at higher levels, α-receptor activity (vasoconstriction). Oliveira-Filho et al reported a case of an 81-year-old woman with multiple infaracts in the posterior circulation, who had worsening neurological deficits coincident with fall of BP, where induced hypertension with dopamine was followed by rapid clinical improvement, within 30 minutes. The infusion was weaned off over a period of 2 days, the patient remaining stable. At 6 months, the patient was independently mobile, with no recurrent cerebrovascular events.

**Conclusion**

The pressor effects of dobutamine and dopamine are primarily attributable to cardiac stimulation, and this may not be ideal for the population being studied, with a high coexistence of ischemic heart disease.

**DCLHb**

DCLHb is a cell-free, hemoglobin-based oxygen-carrying solution, which offers the potential advantage of hemodilution without a decrease in oxygen delivery. In animal models, it induces a hypertensive response, with significant reductions in extent of brain injury, and in healthy human volunteers, it causes a dose-dependent increase in MAP. It may also be a nitric oxide scavenger, and its effects are not simply related to BP changes.

In a placebo-controlled safety study, DCLHb resulted in a rapid rise in BP, with the duration of the pressor effect being dose-dependent. Outcome at 3 months was significantly worse in the treatment group (unfavourable outcome (Rankin score 3 to 6 at 3 months): 85% in treated patients, and 51% in untreated patients; *P* = 0.002), and more serious adverse events and deaths occurred. However, effects other than elevating BP, including a dose-dependent increase in endothelin-1 levels and baseline stroke severity, may have contributed to the negative outcome.

**Discussion**

There has been only 1 small structured randomized trial to date studying pressor therapy in acute stroke. PE was the pressor agent, and no systemic or neurological complications were reported. The DCLHb study is difficult to interpret in view of the nonpressor effects of the agent.

Atrial fibrillation has been reported secondary to both PE and NE use. However, mortality in the case-note review by Rordorf et al was not significantly different in the treated and untreated groups. Importantly, adverse events were not reported consistently in all the studies reviewed.

We would suggest that PE is perhaps the best candidate pressor agent in acute stroke populations, in view of the following:

1. It is the agent that has been studied the most.
2. Because of its selective action on α₁-receptors, it is less likely to cause:
   a. significant direct cerebral vasoconstriction, and
   b. β-receptor mediated tachyarrhythmias, and increased myocardial oxygen demand.

It is proposed that those acute ischemic stroke patients most likely to benefit from induced BP elevation would have the following characteristics:

1. Patients with sustained SBP <130 to 150 mm Hg (the prognosis in these patients is worse than for those with higher BP levels), or those with good evidence of a symptomatic BP decrease (>20 mm Hg) immediately postischemic stroke, but with levels still below those where guidelines advise antihypertensive therapy.
2. Severe ipsilateral large extracranial or intracerebral vessel stenosis or occlusion.
3. Presenting within 12 hours or perhaps 24 hours after symptom onset, those presenting earlier after onset being more likely to have salvageable ischemic penubra, and therefore more likely to benefit.
4. Patients without obvious exclusion criteria to pressor therapy, ie, cardiac function (ejection fraction <25%), recent congestive heart failure, myocardial infarction or unstable angina, bradycardia, uncontrolled angina, past medical history of arrhythmias or significant occlusive vascular disease, coexisting treatment with digoxin, quinidine or tricyclic antidepressants, and current use of monoamine oxidase inhibitors or use within the previous 14 days (unpublished CHHIPS Study Protocol).

Obstacles to clinical application of pressor therapy are much the same as those for thrombolysis in acute stroke, mainly relating to the narrow time window, need for urgent neuroradiology input and manpower issues with monitoring.

**Conclusions**

Though small studies have shown that BP elevation can be carried out safely in acute stroke (with close monitoring), no large-scale trial has been carried out to-date. Interpretation of the results of published studies reviewed here is complicated by differences in trial methodology. The small size of what are mostly pilot trials limits reliable conclusion as to the effects on outcomes, both benefits and harms. The balance of benefit versus harm with induced hypertension in acute stroke needs to be demonstrated in a well-structured RCT. We suggest that PE...
(with volume replacement) would appear the most suitable (with volume replacement) would appear the most suitable.

To our knowledge, there are 2 ongoing trials studying induced BP elevation in acute ischemic stroke:

1. The first, based in John Hopkins Hospital, Massachusetts General Hospital, and University of Maryland, aims to determine whether MRI before intervention with PE is useful in selecting patients who are likely to benefit (personal communication. Hillis AE, Wityk RJ).

2. We are coordinating a UK-based RCT studying BP manipulation in acute stroke (CHHIPS33), which has a pressor arm, where PE is used to induce BP elevation until 24 hours from symptom onset (www.le.ac.uk/CHHIPS/HomePage.html).

Acknowledgments

Jane Tatlow (Clinical Librarian) advised on the search strategy for identification of articles. Professor R. Panerai kindly translated the Portuguese article. Dr Mistri and the CHHIPS trial are funded by a Health Technology Assessment Programme.

References


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