Effect of antihypertensive agents on cerebral blood flow and flow velocity in acute ischaemic stroke: systematic review of controlled studies
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CRD summary
This review assessed the effect of antihypertensive agents on cerebral blood flow or cerebral blood flow velocity in patients with acute or recent ischaemic stroke and found no effect for any agent. Results were consistent across all studies, but should be viewed cautiously due to the small size and number and variable quality of studies and weaknesses in review methods.

Authors' objectives
To assess the effect of antihypertensive agents on cerebral blood flow (CBF) or cerebral blood flow velocity (CBFv) in patients with acute or recent ischaemic stroke.

Searching
PubMed, EMBASE, Web of Science and The Cochrane Library were searched; search terms, but not dates, were reported. Bibliographies of retrieved studies and reviews were screened for additional studies.

Study selection
Controlled clinical trials that assessed the effect of antihypertensive agents on CBF or CBFv in patients with acute or recent (less than seven days from index event) ischaemic stroke were eligible for inclusion. Trials in which CBF was assessed only qualitatively were excluded.

Most of the included studies were of angiotensin-converting enzyme inhibitors (ACE-I) or calcium channel blockers (CCB); other antihypertensives assessed were nitrate, a diuretic and an angiotensin-receptor antagonist (ARA). Time from stroke to randomisation ranged from acute stroke to eight days. Three patients in one study were recruited beyond seven days post-stroke and two patients in another study had primary intracerebral haemorrhage. The methods used to measure CBF were single photon emission computed tomography (SPECT), transcranial Doppler (TCD), xenon computed tomography (CT) and positron emission tomography (PET).

The authors did not state how many reviewers assessed studies for inclusion.

Assessment of study quality
The authors stated that methodological quality of included studies was assessed according to the QUORUM statement (no further details were reported). Study quality was reported as a score out of 5.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Mean and standard deviation CBF and CBFv were extracted for treatment and control groups. Data for CBF were extracted, related to the hemispheric and penumbral measurements as available, on the ipsilateral side to the stroke. Data for CBFv were obtained for the ipsilateral artery. Where studies assessed more than one treatment dose, data were extracted separately for all doses. If more than one post-treatment assessment was reported, the earliest measurement was used. Blood pressure data for corresponding times were extracted, where possible. Missing data were imputed from graphs or obtained from authors, where possible.

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Random-effects models weighted by inverse variance were used to estimate standardised mean difference (SMD) with 95% confidence interval (CI) for CBF and weighted mean difference (WMD) in metres per second with 95% CI for CBFv. Statistical heterogeneity was assessed using the $\chi^2$ test.

**Results of the review**

Eleven studies (12 in results table) (n=307) were included in the review. Studies were RCTs and before-and-after studies; some studies appeared to have been classified as both study designs. Quality score ranged from zero to 4.

Overall, antihypertensive agents did not significantly effect CBF (SMD 0.02, 95% CI -0.34 to 0.39; eight studies) or CBFv, (WMD 1.96m/s, 95% CI -1.99 to 5.90; five studies).

Stratification by antihypertensive class showed no significant treatment effects for ACE-I, CCB, ARR, diuretics or nitrate. Stratification by study design (RCTs and before-and-after studies) produced similar results.

No significant heterogeneity was identified in any analysis.

**Authors’ conclusions**

There were few quality studies that assessed the effect of antihypertensive agents on cerebral blood flow and flow velocity. There was little existing evidence that antihypertensives reduced cerebral blood flow, in spite of their effects on lowering blood pressure. Analysis of randomised controlled trials revealed no alteration in cerebral blood flow for any antihypertensive agent.

**CRD commentary**

The review addressed a clearly stated research question defined by appropriate inclusion criteria. A number of sources were searched for relevant studies and no restrictions were reported. The review process was poorly reported and it was unclear whether measures were taken to minimise error and bias in study selection, data extraction and quality assessment. The results of quality assessment were recorded as overall scores only. The meta-analyses reported were appropriate for the data presented and the lack of effect of antihypertensives on CBF was consistent across all studies.

Some caution should be applied when considering these results, due to the small size and number and variable quality of the included studies and weaknesses in the review process.

**Implications of the review for practice and research**

**Practice:** The authors made no recommendations for practice.

**Research:** The authors stated that future studies should use a randomised design and consistent approaches to measuring and analysing CBF. They further stated that studies should assess whether vasodepressant drugs induced cerebral steal, which would require an assessment of CBF in the unaffected hemisphere.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.