The ABCs of cardioprotection in dialysis patients: a systematic review

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CRD summary
This review found that it unclear whether cardioprotective medication such as angiotensin-converting enzyme (ACE) inhibitors, adrenergic beta antagonists (beta-blockers) and calcium channel blockers (CCBs) had beneficial effects in dialysis patients. The review suffered from some limitations, but the authors' conclusions were sufficiently cautious and likely to be reliable.

Authors' objectives
To determine the effects of angiotensin-converting enzyme inhibitors, adrenergic beta antagonists (beta-blockers) and calcium channel blockers in kidney dialysis patients.

Searching
MEDLINE via PubMed and CINAHL were searched from 1988 to October 2007. Search terms were reported. Reference lists of all studies (including review articles, editorials and invited commentaries) were screened to identify additional studies. The review was restricted to English-language studies.

Study selection
Randomised controlled trials (RCTs) and observational studies that assessed angiotensin-converting enzyme inhibitors, beta-blockers and calcium channel blockers in incidence and prevalent dialysis patients were eligible for inclusion. Studies had to assess at least one of the following outcomes: mortality, morbidity or cardiovascular events.

Mean age of included patients ranged from 52 to 75 years. Duration of follow-up ranged from 30 days to nine years.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors stated that they did not assess study quality.

Data extraction
Two reviewers independently extracted data using a standardised form.

Methods of synthesis
A narrative synthesis was presented, stratified according to intervention and study design.

Results of the review
Seventeen studies (n=32,636) were included in the review: two RCTs and one pseudo RCT (n=661); seven observational studies (n=28,698) that were analyses of the Dialysis Morbidity and Mortality Studies (DMMS) conducted by the US Renal Data System; and seven other observational studies (n=3,277).

Beta blockers: One RCT reported that carvedilol was associated with decreased rates of all-cause mortality compared to standard treatment (odds ratio 0.51, 95% CI: 0.32 to 0.82) and decreased cardiovascular deaths (odds ratio 0.32, 95% CI: 0.18 to 0.57) in dialysis patients with class II or III congestive heart failure at two years. The largest DMMS study reported decreased all-cause mortality among dialysis patients treated with beta-blockers (adjusted hazard ratio 0.84, 95% CI: 0.75 to 0.93). Most other studies did not show a benefit of treatment.

Calcium channel blockers: One pseudo RCT randomised dialysis patients who remained hypertensive despite various interventions to receive an angiotensin-converting enzyme inhibitor or a calcium channel blockers, but the study was considered unreliable. The largest DMMS study reported a modest unadjusted association of calcium channel blockers with reduced all-cause mortality (p=0.04), but this finding was no longer significant in the adjusted analysis. Other
studies also reported beneficial effects of calcium channel blockers on all-cause mortality and cardiovascular related morbidity and mortality.

**Angiotensin-converting enzyme inhibitors:** One placebo-controlled RCT showed that fosinopril did not decrease the rate of cardiovascular events (relative risk 0.93, 95% CI: 0.68 to 1.26). A second RCT found that angiotensin-converting enzyme inhibitor use was associated with an 81% decrease in all-cause mortality (p<0.0003). None of the seven DMMS studies and only one of the other cohort studies reported beneficial effects of angiotensin-converting enzyme inhibitors on morbidity or mortality outcomes.

**Authors’ conclusions**
It was unclear whether cardioprotective medication offered a survival advantage to dialysis populations as a whole or even to patients with specific indications, such as those with congestive heart failure.

**CRD commentary**
The review addressed a broad objective supported by defined inclusion criteria. The literature search was adequate, but did not include specific attempts to locate unpublished studies and the review was limited to English-language studies, so there was a possibility of language and publication biases. Study quality was not assessed formally, although aspects of methodological quality were discussed and more emphasis was placed on findings from RCTs. Appropriate steps were taken to minimise bias and error in the extraction of data, but it was unclear whether such steps were also taken for the selection of studies. Very limited details were reported on the included studies, which made it difficult to determine the generalisability of the review findings. A narrative synthesis was appropriate given the differences between studies. However, the narrative was somewhat difficult to follow and tables that summarised the results across studies would have been helpful. Despite suffering from some methodological limitations, the authors’ conclusions were sufficiently cautious and likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that there was a need for RCTs and well-designed observational studies adjusted for non-random treatment assignment and longitudinal drug exposure.

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