Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch™ Rapid Update 2 – January 2018

Chronic kidney disease: benefits from intensive blood pressure control?

A meta-analysis of randomised controlled trials (RCTs) found that people with chronic kidney disease (CKD) who were treated with more intensive blood pressure (BP) lowering therapy had a 14% lower relative risk of all-cause mortality compared with people treated with less intensive therapy at around 4 years. The more intensive group achieved a systolic blood pressure (SBP) of 132 mmHg, compared with 140 mmHg in the less intensive group.

This review supports the NICE guideline on CKD, which recommends people with CKD try to maintain a SBP between **120 and 139 mmHg**. The review did not report on adverse events associated with more intensive BP lowering; other studies on intensive BP lowering have reported an increase in hypotension and acute kidney injury.

Reference: Malhotra R, Nguyen HA, Benavente O *et al*. (2017) Association Between More Intensive vs Less Intensive Blood Pressure Lowering and Risk of Mortality in Chronic Kidney Disease Stages 3 to 5 - A Systematic Review and Meta-analysis. JAMA Intern Med. 177(10):1498-1505.

What do we know already?

- The NICE guideline on CKD in adults recommends that people with CKD have a SBP below 140 mmHg (target range 120 to 139 mmHg). The guideline recommends a lower BP target for people with CKD and diabetes, and also in people with an albumin-to-creatinine ratio (ACR) of 70 mg/mmol or more. For these people, the goal should be to keep SBP below 130 mmHg (target range 120 to 129 mmHg) and diastolic blood pressure (DBP) below 80 mmHg.
- A number of major studies have investigated more intensive BP lowering, but not exclusively in a population with CKD. An open-label RCT (SPRINT), involving 9,361 people with an increased risk of cardiovascular events, found intensive therapy (SBP target 120 mmHg) was associated with a lower incidence of adverse cardiovascular events and mortality compared with standard therapy (SBP target 140 mmHg). People in the intensive treatment arm were at increased risk of acute kidney injury (AKI).
- Sub-group analysis of SPRINT participants with CKD (n=2,646) found no significant difference in the primary composite cardiovascular disease endpoint (hazard ratio 0.82, 95% CI 0.63 to 1.07). However, the study was not designed or powered to determine the benefits and risks of intensive control in people with CKD.

What does this evidence add?

- This large systematic review and meta-analysis found that in people with CKD stages 3 to 5, more intensive BP lowering therapy was associated with a lower risk of all-cause mortality compared with less intensive therapy (odds ratio [OR] 0.86, 95% confidence interval [CI] 0.76 to 0.97) after a median follow-up period of 3.6 years.
- The review did not report or discuss adverse event rates across the intensive and less intensive treatment arms. Adverse events are of concern when considering more aggressive BP lowering strategies. The SPRINT study found that people treated with more intensive BP therapy had higher rates of serious adverse events, including hypotension, syncope, electrolyte abnormalities, and AKI or failure.
- The authors were not able to evaluate the effect of intensive BP lowering on mortality stratified by CKD severity. The majority people in the studies had CKD stage 3, the effect of more intensive BP lowering in people with more severe CKD is not known.
- Baseline BP and reductions in BP varied by study, preventing the authors from estimating the optimal target for people with CKD.
- The authors noted some difficulty in obtaining CKD-only results from authors of RCTs that included a mixed population, meaning a number of studies had to be excluded from the review.

Study details

Participants:

- The systematic review included open-label and double-blind RCTs of adults with CKD stages 3 to 5 (eGFR <60 ml/min/1.73 m^2). The review included a total of 18 RCTs, involving 15,924 participants.
- If the study included a mixed of population of people with and people without CKD, results for the CKD group were extracted. If sub-group analysis was not reported in the original publication, the authors were contacted.
- The majority of studies were published after 2000.

Intervention and comparison:

- Trials were required to have randomised participants to two defined BP targets (either more intensive *vs.* less intensive BP control, or active BP treatment *vs.* placebo or no treatment).
- BP targets varied across studies.
- The median follow-up period was 3.6 years (interquartile range 2.8 to 4.9 years).

Outcomes and results:

- At baseline, the mean SBP was 148 mmHg (standard deviation [SD] 16). In the more intensive treatment arm the mean SBP decreased by 16 mmHg to 132 mmHg, and in the less intensive arm the mean SBP decreased by 8 mmHg to 140 mmHg.
- Across the 18 studies, there were 584 deaths (7.8%) in the intensive arm and 709 deaths (8.4%) in the less intensive arm. Compared with less intensive therapy, people treated with intensive BP lowering therapy had a 14% lower risk of all-cause mortality (OR 0.86, 95% CI 0.76 to 0.97, p=0.01).
- There was no evidence of heterogeneity between trials (I^2=0%) or publication bias. Excluding the large SPRINT study did not materially affect the outcome of the meta-analysis.
- Further analysis found that the effect of more intensive therapy on mortality was consistent irrespective of:
    - type of treatment in the comparator arm (placebo or less intensive BP target)
    - median follow-up duration (<3 *vs.* ≥3 years)
    - inclusion of diabetic patients (yes or no)
    - CKD severity
    - baseline SBP of the entire cohort (<140mmHg *vs.* 140-160mmHg *vs.* >160mmHg)
- A trend towards a greater difference in all-cause mortality in studies that achieved larger differences in SBP between the treatment arms (≥ 12 mmHg *vs.* 6 to 12 mmHg *vs.* < 6 mmHg) was observed, although this difference was not statistically significant.
- The rates of adverse events are not reported by the authors of the systematic review.

Level of evidence:
Level 1 (good quality patient-oriented evidence) according to the SORT criteria.

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