Diabetes

Diabetes: treating hypertension

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- Interventions
- Key points
- About this condition
- Updates (2)
- Guidelines (7)
- References
- Your responses

Treatments

Diuretics

In this section:

Summary | Benefits | Harms | Comment

Top

Summary

One RCT found that chlorthalidone (a diuretic) reduced cardiovascular events compared with placebo plus usual care in people with diabetes and isolated systolic hypertension. One RCT found that chlorthalidone was at least as effective as lisinopril (an angiotensin-converting enzyme inhibitor) for reducing cardiovascular events. Two RCTs found no significant difference in overall cardiovascular events between diuretics (chlorthalidone or co-amilozide) and calcium channel blockers (nifedipine or amlodipine). However, one of the RCTs found that chlorthalidone reduced heart failure compared with amlodipine. One RCT found that chlorthalidone reduced the risk of cardiovascular events compared with doxazosin (an alpha-blocker). We found no RCTs comparing diuretics versus beta-blockers, angiotensin II receptor antagonists, or combinations including diuretics.

Top

Benefits

We found no systematic review of diuretics for hypertension in people with diabetes.

Diuretics versus placebo:

We found one RCT in people with isolated systolic hypertension, which conducted a prespecified subgroup analysis in people with diabetes (583 people with type 2 diabetes; mean age 70 years; mean blood pressure 170/77 mm Hg). [9] It compared diuretic-based treatment (chlorthalidone alone, with added atenolol or reserpine if needed) versus placebo. People in the placebo group already receiving an active antihypertensive drug for persistent high blood pressure (46% of people; type of antihypertensive drugs used not reported) continued to receive their prescribed treatment (usual care). The RCT found that diuretic-based treatment significantly reduced the risk of cardiovascular events compared with placebo plus usual care (RR 0.66, 95% CI 0.46 to 0.94; ARR 8%, 95% CI 1% to 14%). [9]

Diuretics versus beta-blockers:

We found no RCTs.

Diuretics versus alpha-blockers:

See benefits of alpha-blockers versus diuretics.

Diuretics versus angiotensin-converting enzyme (ACE) inhibitors:

We found one RCT, which conducted a prespecified subgroup analysis in people with diabetes (12,063 people with type 2 diabetes; mean age 66.9 years; mean blood pressure 146/84 mm Hg). [18] It compared three treatments: a diuretic (chlorthalidone), a calcium channel blocker (amlodipine), and an ACE inhibitor (lisinopril). It found that chlorthalidone reduced cardiovascular disease compared with lisinopril, although the difference was of borderline significance at 4.9 years' follow-up (RR 0.92, 95% CI 0.85 to 1.00; absolute risks not reported for people with diabetes). Most of the benefit was attributable to a significantly lower risk of heart failure with chlorthalidone than with lisinopril (RR 0.82, 95% CI 0.70 to 0.95).

Diuretics versus calcium channel blockers:

We found two RCTs. [18] [19] The first RCT, which conducted a prespecified subgroup analysis in people with diabetes (1302 people with diabetes; mean age 65 years), found no significant difference in cardiovascular event rates between nifedipine (a calcium channel blocker) and co-amilozide (a diuretic; AR: 54/649 [8.3%] with nifedipine *v* 55/653 [8.4%] with co-amilozide; RR 0.99, 95% CI 0.69 to 1.42). [19] The second RCT, which also conducted a prespecified subgroup analysis in people with diabetes (12,063 people with type 2 diabetes; mean age 66.9 years; mean blood pressure 146/84 mm Hg), compared three treatments: chlorthalidone (a diuretic), amlodipine (a calcium channel blocker), and lisinopril (an ACE inhibitor). [18] It found no significant difference in cardiovascular events (including death from coronary heart disease, non-fatal myocardial infarction, stroke, angina, heart failure, or peripheral arterial disease) between amlodipine and chlorthalidone at 4.9 years' follow-up (RR 1.06, 95% CI 0.98 to 1.15). However,

chlorthalidone significantly reduced heart failure compared with amlodipine (ARs not reported; RR 1.42, 95% CI 1.23 to 1.64).

Diuretics versus angiotensin II receptor antagonists:

We found no RCTs.

Diuretics alone versus combinations including diuretics:

We found no RCTs.

Top

Harms

Diuretics versus placebo:

The RCT found that chlorthalidone increased glucose, cholesterol, and uric acid levels after 1 year compared with placebo plus usual care (glucose: 182 mg/dL [10.1 mmol/L] with chlorthalidone v 165 mg/dL [9.2 mmol/L] with placebo plus usual care; cholesterol: 236 mg/dL [6.1 mmol/L] with chlorthalidone v 231 mg/dL [6.0 mmol/L] with placebo; uric acid: 5.8 mg/dL [345 mmol/L] with chlorthalidone v 5.4 mg/dL [321 mmol/L] with placebo; P values not reported) . [9] The chlorthalidone group also had lower potassium levels (4.2 mmol/L with chlorthalidone v 4.4 mmol/L with placebo plus usual care; significance not reported).

Diuretics versus beta-blockers:

We found no RCTs.

Diuretics versus alpha-blockers:

See harms of alpha-blockers versus diuretics.

Diuretics versus ACE inhibitors:

The RCT found that diuretics (chlorthalidone) increased rates of hypokalaemia compared with ACE inhibitors (lisinopril; 9% with chlorthalidone v1% with lisinopril; P less than 0.001), and increased cholesterol (197.2 mg/dL [5.1 mmol/L] with chlorthalidone v 195.0 mg/dL [5.0 mmol/L] with lisinopril; P = 0.005) and fasting glucose levels (126.3 mg/dL [7.0 mmol/L] with chlorthalidone v 121.5 mg/dL [6.7 mmol/L] with lisinopril; P = 0.002). [18]

Diuretics versus calcium channel blockers:

The first RCT did not report any harms data for the diabetic population. [19] The second RCT found that diuretics significantly increased cholesterol (197 mg/dL [5.1 mmol/L] with chlorthalidone *v* 195 mg/dL [5.0 mmol/L] with amlodipine; P = 0.009) and reduced potassium levels (4.1 mEq/L with chlorthalidone *v* 4.4 mEq/L with amlodipine; P less than 0.001) compared with calcium channel blockers, but these findings were considered to be of minimal clinical significance. [18] It did not report on clinical adverse effects.

Diuretics versus angiotensin II receptor antagonists:

We found no RCTs.

Diuretics alone versus combinations including diuretics:

We found no RCTs.

Top

Comment

The first RCT comparing diuretics versus calcium channel blockers did not specify the type of diabetes of people included in the study. [19] This study also allowed the administration of ACE inhibitors and other antihypertensive drugs if blood pressure remained higher than 140/90 mm Hg. People in the co-amilozide group required more additional medication than those in the nifedipine group (49% with co-amilozide *v* 43% with nifedipine; P = 0.027). However, when results were analysed separately for those who received additional medication and those who did not, there was no significant difference between treatments in primary or secondary outcomes for either population. Diuretics have, in some cases, been grouped together with beta-blockers as "conventional" therapy. We found four such RCTs, two comparing ACE inhibitors [20] [21] and two comparing calcium channel blockers [20] [22] versus conventional therapy (beta-blockers, diuretics, or beta-blockers plus diuretics). However, none analysed results of diuretics alone, and so they were excluded from this review.

Clinical guide:

Diuretics are effective in reducing cardiovascular risk in people with diabetes, and are a reasonable first-line treatment option.

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