Angina (chronic stable) (updated)

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Single-drug treatment

Beta-blockers as monotherapy

In this section:

Summary | Benefits | Harms | Comment

Top

Summary

Symptom improvement

Beta-blockers compared with placebo We don't know whether propranolol is more effective at reducing the frequency of angina attacks, at reducing serious cardiac events (cardiac death, MI, or angina deterioration), or at improving the duration of exercise at 6 months (very low-quality evidence).

Beta-blockers compared with calcium channel blockers We don't know whether beta-blockers are more effective at reducing the frequency of angina attacks or improving exercise duration at 6 months, at improving exercise capacity at 32 weeks, or at improving a composite outcome of non-fatal cardiovascular events or mortality at 3.4 years, or the combined outcome of unstable angina, MI, or mortality, at 2 years (very low-quality evidence).

Mortality

Beta-blockers compared with calcium channel blockers Metoprolol and verapamil seem equally effective at reducing mortality after a median follow up of 3.4 years (high-quality evidence).

Quality of life

Beta-blockers compared with calcium channel blockers Metoprolol and verapamil seem equally effective at improving quality-of-life scores (moderate-quality evidence).

Note

There is consensus that beta-blockers are effective for treating the symptoms of stable angina.

For GRADE evaluation of interventions for angina (stable), see table.

Top

Benefits

We found one systematic review (search date 1996). [22]

Beta-blockers versus placebo:

The review [22] identified one RCT [23] (191 people aged less than 70 years with abnormal exercise stress test or previous MI). It compared three treatments: beta-blockers (propranolol; 78 people), calcium channel blockers (bepridil; 78 people), and placebo (35 people). It found no significant difference between propranolol and placebo in the reduction in frequency of angina attacks, or improvement in duration of exercise at 6 months (mean reduction in weekly angina attacks from baseline: 71% with propranolol *v* 77% with placebo; P reported as not significant; increase in exercise duration from baseline: 24% with propranolol *v* 8% with placebo; P = 0.09). Serious cardiac events (cardiac death, MI, or angina deterioration) were more common with propranolol than with placebo, but the significance of this difference was not reported (AR for serious cardiac events: 8/78 [10%] with propranolol *v* 2/35 [6%] with placebo; P value not reported).

Beta-blockers versus calcium channel blockers:

The systematic review [22] identified five RCTs that met our inclusion criteria (1818 people). The first RCT (191 people ages less than 70 years, with abnormal exercise stress test or previous MI), [23] compared three treatments: beta-blockers (propranolol 60–240 mg/day; 78 people), calcium channel blockers (bepridil 100–400 mg/day; 78 people), and placebo (35 people). It found no significant difference between propranolol and bepridil in the reduction in the frequency of angina attacks or improvement in duration of exercise at 6 months (reduction in weekly angina attacks from baseline: 69% with bepridil *v* 71% with propranolol; P reported as not significant; increase in exercise duration from baseline: 24% with propranolol *v* 31% with bepridil; P = 0.26). The incidence of serious cardiac events (cardiac death, MI, or angina deterioration) was similar with propranolol and bepridil (AR for serious cardiac events: 8/78 [10%] with propranolol *v* 6/78 [8%] for bepridil; P value not reported). The second RCT (80 people aged up to 80 years with abnormal exercise stress test) [24] compared a beta-blocker

(nadolol 40–160 mg once daily) versus a calcium channel blocker (amlodipine 2.5–10 mg once daily) in people with stable angina. It found no significant difference in the reduction in frequency of angina attacks or change in exercise duration at 6 months (change in median number of angina attacks/week from baseline to 6 months: from 3.0 to 0.3 with nadolol *v* from 4.0 to 0.3 with amlodipine; P reported as not significant; change in total exercise treadmill time from baseline to 6 months: 490 seconds to 475 seconds [–3%] with nadolol *v* 454 seconds to 462 seconds [+2%] with amlodipine; P reported as not significant). The third RCT (56 people aged less than 80 years with abnormal exercise stress test) compared a beta-blocker (metoprolol 100 mg twice daily; 26 people) with a calcium channel blocker (diltiazem 120 mg twice daily; 30 people) in people with stable angina. [25] It found no significant difference between groups at 32 weeks in the change in exercise capacity (39 people evaluable: 19 people with metoprolol *v* 20 people with diltiazem; analysis not by intention to treat; mean change in duration of exercise from baseline to 32 weeks: +0.2 minutes with metoprolol *v* +0.3 minutes with diltiazem; P reported as not significant). The effect of treatments on the frequency of angina symptoms was not reported. The fourth RCT (809 people aged less than 70 years selected on the basis of typical clinical history and response to nitroglycerin or, if history was not typical, an abnormal stress test) compared a beta-blocker (metoprolol 200 mg once daily) with a calcium channel blocker (verapamil 240 mg twice daily). [26] It found no significant difference in either mortality or the combined outcome of mortality or non-fatal cardiovascular event between metoprolol and verapamil after a median follow up of 3.4 years (AR for mortality: 22/406 [5%] with metoprolol *v* 25/403 [6%] with verapamil; OR 0.87, 95% CI 0.48 to 1.56; AR for mortality or non-fatal cardiovascular event: 128/406 [32%] with metoprolol *v* 123/403 [30%] with verapamil; OR 1.03, 95% CI 0.84 to 1.30. It also found no significant difference in three quality-of-life variables between metoprolol and verapamil (Cornell Medical Index psychomatic symptom index, score range 39–195: mean score change –1.1 with metoprolol *v* –2.2 with verapamil; P = 0.34; overall life satisfaction, score range 0–120: mean score change –3.0 with metoprolol *v* –2.5 with verapamil; P = 0.85; sleep disturbances, score range 9–36: mean score change –0.7 with both treatments: P = 0.97). The fifth RCT (682 people with stable angina who were not immediately being considered for coronary revascularisation) compared three treatments: atenolol (50 mg twice daily), nifedipine (20 or 40 mg twice daily as tolerated), and atenolol plus nifedipine. [13] It found no significant difference between atenolol alone and nifedipine alone in the combined outcome of mortality, MI, or unstable angina, after a mean follow-up of 2 years (AR for combined death, MI, or unstable angina: 29/226 [13%] with atenolol *v* 25/232 [11%] with nifedipine; log rank P = 0.32).

Beta-blockers versus nitrates or potassium channel openers:

We found no RCTs.

Top

Harms

Beta-blockers versus placebo:

The RCT identified by the review found no significant difference between propranolol and placebo in the proportion of people experiencing at least one non-cardiac adverse effect (AR 23/78 [29%] with propranolol *v* 6/35 [17%] with placebo; P = 0.08). [23] There was no significant difference between groups in treatment withdrawal caused by lack of efficacy or severe adverse effects (17/78 [22%] with propranolol *v* 6/35 [17%] with placebo; P = 0.58).

Beta-blockers versus calcium channel blockers:

The first RCT identified by the review found that the proportion of people experiencing at least one non-cardiac adverse event was significantly higher with propranolol than with bepridil (AR for at least one non-cardiac adverse event: 23/78 [30%] with propranolol *v* 9/78 [12%] with bepridil; P = 0.003). [23] This was mostly due to an increased incidence of fatigue in the propranolol group (14/78 [18%] with propranolol *v* 6/78 [8%] with bepridil; P = 0.05). However, there was no significant difference between groups in treatment withdrawal caused by lack of efficacy or severe adverse effects (17/78 [22%] with propranolol *v* 15/78 [19%] with bepridil; P = 0.69). The second RCT found that significantly more people taking nadolol than amlodipine had adverse effects (AR 33/40 [83%] with nadolol *v* 17/40 [43%] with amlodipine; P less than 0.0001). [24] However, similar numbers of people in both groups were withdrawn from treatment owing to adverse effects (4/40 [10%] with nadolol *v* 3/40 [8%] with amlodipine; P value not reported). The third RCT reported that most adverse events were mild, and that there was no significant difference in the incidence of adverse events between metoprolol and diltiazem (figures not reported, P reported as non-significant). [25] The fourth RCT (809 people) found that significantly more people withdrew from the study because of gastrointestinal upset with verapamil than with metoprolol (AR 22/403 [6%] with verapamil *v* 10/406 [3%] with metoprolol; P = 0.029). However, it found no significant difference between the two treatments in overall withdrawal due to adverse effects (AR 59/403 [15%] with verapamil *v* 45/406 [11%] with metoprolol; P = 0.13). The fifth RCT (682 people) found that, over an average of 2 years' follow-up, significantly more people stopped treatment because of adverse effects in the nifedipine group than in the atenolol group (AR 93/232 [40%] with nifedipine *v* 60/226 [27%] with atenolol; log rank P = 0.001). [13]

Beta-blockers versus nitrates or potassium channel openers:

We found no RCTs.

Top

Comment

Many of the RCTs included in the review were unlikely to have been sufficiently powered to detect a clinically important difference between groups. [22]

Clinical guide:

There is consensus that beta-blockers are effective for treating the symptoms of stable angina.

References

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