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LETTER TO THE EDITOR

Cochrane Corner: Withdrawal of antihypertensive drugs in older people

Cochrane Corner: Descontinuação de fármacos anti-hipertensores em idosos

A systematic review with meta-analysis of randomized controlled trials (RCTs) comparing withdrawal of antihypertensive medication with usual treatment in older adults (age ≥50 years) by Reeve et al. has been published in Cochrane Systematic Review Database.[1]

The authors aimed to investigate the effects of withdrawal of antihypertensive medications on mortality, cardiovascular outcomes (stroke or myocardial infarction), hospitalization, blood pressure, and adverse drug reactions in older people.

A total of 1073 patients were followed in six RCTs with study duration and follow-up ranging from four to 56 weeks. The odds ratios of all-cause mortality, hospitalization, myocardial infarction, and stroke are presented in Figure 1. The mean difference in blood pressure between the groups is presented in Figure 2. Antihypertensive discontinuation did not appear to increase the risk of adverse events. No studies reported data on falls. There was no significant difference between the groups in change in quality of life after 16 weeks.[1]

In this Cochrane Corner we provide our view and comments about the results of this systematic review.

To contextualize the controversial topic addressed by this review, there is overwhelming evidence supporting treating hypertension and controlling blood pressure to reduce cardiovascular morbidity and mortality.[2] For this purpose, non-pharmacological and/or pharmacological interventions are applied to hypertensive patients. Nevertheless, there are some patients who might not require pharmacological treatment; for example in those with low cardiovascular risk and grade 1 hypertension, delaying drug therapy may be reasonable, especially if blood pressure reduction can be achieved with lifestyle modifications,[3] such as decreasing sodium intake,[4,5] exercising,[6] and minimizing alcohol consumption.[7]

Regarding pharmacological treatment, one of the largest meta-analyses of RCTs of blood pressure reduction, by Law et al., showed that lowering systolic blood pressure by 10 mmHg or diastolic blood pressure by 5 mmHg reduces coronary heart disease events (fatal and non-fatal) by about a quarter and stroke by about a third.[8] Evidence from other RCTs has also shown that in old and very old patients, antihypertensive treatment substantially reduces cardiovascular morbidity and all-cause mortality.[9,10] However, intensive blood pressure treatment can cause adverse events.[11] In particular, older patients are more likely to have comorbidities such as renal impairment, severe polyvascular atherosclerotic disease, and postural hypotension, which may be worsened directly by blood pressure-lowering drugs,[12] as is the risk of syncope.[13] In this context, antihypertensive drugs are a major contributor to polypharmacy, which has a substantial burden of adverse drug events, disability, hospitalization, and even death.[14]

Therefore, the decision to start or continue treatment should be especially cautious when approaching frail old people (>60 years) or very old people (≥80 years), so that low drug doses and monotherapy can be considered.[15]

The European Society of Cardiology (ESC) guidelines state that blood pressure-lowering drug treatment and lifestyle interventions are recommended for fit older patients (65-80 years old) when systolic blood pressure is in the grade 1 range (140-159 mmHg), provided that treatment is well tolerated. Also, withdrawal of antihypertensive drugs based on age is not recommended, even in patients aged ≥80 years, if treatment is well tolerated. However, it is important to recognize that the ESC guidelines scope mainly fit and independent old patients, because physically and mentally frail as well as institutionalized patients have been excluded from most RCTs.[12]

In their Cochrane systematic review, Reeve et al. suggest that withdrawal of antihypertensives in older people may have no effect on clinically important outcomes such as mortality or cardiovascular events, albeit with low certainty in this result (see GRADE evaluations in Figures 1 and 2).

However, it should be borne in mind that the central estimates of all outcomes support an increased risk of death and cardiovascular events in the discontinuation group and that the wide range of the confidence intervals are much more in favor of an increased risk of all-cause mortality than a reduced risk. Furthermore, there was a mean increase of 9.75 mmHg in systolic blood pressure, which means that the potential benefits shown by Law et al. in their meta-analysis could be reduced.[8]

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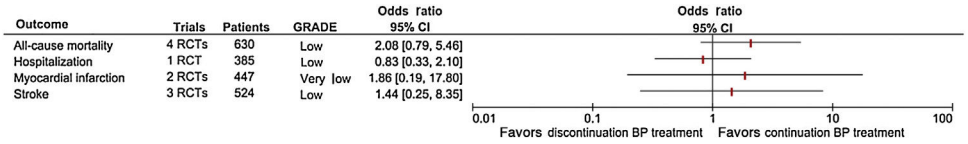

Figure 1 Results of the meta-analysis for all-cause mortality, hospitalization, myocardial infarction and stroke risks according to treatment allocation.[1] BP: blood pressure; CI: confidence interval; RCT: randomized controlled trial.

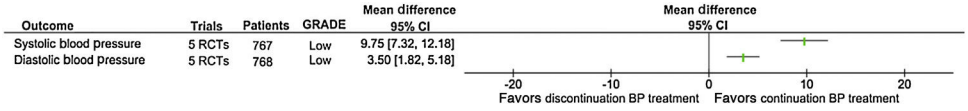

Figure 2 Results of the meta-analysis showing the magnitude of blood pressure increase with discontinuation of antihypertensive medication.[1] CI: confidence interval; RCT: randomized controlled trial.

Additionally, we should emphasize that all the studies analyzed in this systematic review considered adults aged over 50 years (mean age 58-82 years), which includes a not inconsiderable proportion of non-elderly people. It is likely that the included patients may not be representative of those frail polymedicated elderly patients in whom doubts are raised in clinical management of antihypertensive drugs. For these cases, in the absence of robust evidence, functional and autonomy status may be important in the decision process.[16,17]

In conclusion, this systematic review suggests that withdrawal of antihypertensive drugs is potentially harmful. More studies are needed to clarify with greater robustness the effects of discontinuing hypertensive treatment in frail elderly patients with multiple comorbidities.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Filipa Reis[a,1], Mariana Alves[a,b,c,1], Daniel Caldeira[b,d,e,*]

[a] *Serviço de Medicina III, Hospital Pulido Valente, CHLN, Lisboa, Portugal*
[b] *Laboratory of Clinical Pharmacology and Therapeutics, Faculdade de Medicina, Universidade de Lisboa, Portugal*
[c] *Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Portugal*
[d] *Centro Cardiovascular da Universidade de Lisboa – CCUL, CAML, Faculdade de Medicina, Universidade de Lisboa, Portugal*
[e] *Serviço de Cardiologia, Hospital Universitário de Santa Maria – CHULN, Portugal*

[*] Corresponding author.
E-mail address: dgcaldeira@hotmail.com (D. Caldeira).
[1] Co-first authors.