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[Intervention Review]

# Pharmacotherapy for hyperuricemia in hypertensive patients

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## ABSTRACT

### Background

High blood pressure represents a major public health problem. Worldwide, approximately one-fourth of the adult population has hypertension. Epidemiological and experimental studies suggest a link between hyperuricemia and hypertension. Hyperuricemia affects 25% to 40 % of individuals with untreated hypertension; a much lower prevalence has been reported in normotensives or in the general population. However, whether lowering serum uric acid (UA) might lower blood pressure (BP) is an unanswered question.

### Objectives

To determine whether UA-lowering agents reduce BP in patients with primary hypertension or prehypertension compared with placebo.

### Search methods

The Cochrane Hypertension Information Specialist searched the following databases for randomized controlled trials up to February 2016: the Cochrane Hypertension Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (2016, Issue 2), MEDLINE (from 1946), Embase (from 1974), the World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov. We also searched LILACS up to March 2016 and contacted authors of relevant papers regarding further published and unpublished work.

### Selection criteria

To be included in this review, the studies had to meet the following criteria: 1) randomized or quasi-randomized, with a group assigned to receive a UA-lowering agent and another group assigned to receive placebo; 2) double-blind, single-blind or open-label; 3) parallel or cross-over trial; 4) cross-over trials had to have a washout period of at least two weeks; 5) minimum treatment duration of four weeks; 6) participants had to have a diagnosis of essential hypertension or prehypertension, and hyperuricemia (serum UA greater than 6 mg/dL in women, 7 mg/dL in men and 5.5 mg/dL in children/adolescents); 7) outcome measures assessed included change in clinic systolic, diastolic or 24-hour ambulatory BP.

### Data collection and analysis

The two review authors independently collected the data using a data extraction form, and resolved any disagreements via discussion. We assessed risk of bias using the Cochrane Collaboration' Risk of bias' tool.

### Main results

In this review update, we examined the abstracts of 349 identified papers and selected 21 for evaluation. We also identified three ongoing studies, the results of which are not yet available. Three other randomized controlled trials (RCTs) (two new), enrolling individuals with hypertension or prehypertension, and hyperuricemia, met the inclusion criteria for the review and were included in the meta-analysis. Low quality of evidence from three RCTs indicate no reduction in systolic (MD -6.2 mmHg, 95% CI -12.8 to 0.5) or diastolic (-3.9 mmHg, 95% CI -9.2

to 1.4) 24-hour ambulatory BP with UA-lowering drugs compared with placebo. Low quality of evidence from two RCTs reveal a reduction of systolic clinic BP (-8.43 mmHg, 95% CI -15.24 to -1.62) but not diastolic clinic BP (-6.45 mmHg, 95% CI -13.60 to 0.70). High quality of evidence from three RCTs indicates that serum UA levels were reduced by 3.1 mg/dL (95% CI 2.4 to 3.8) in the participants that received UA-lowering drugs. Very low quality of evidence from three RCTs suggests that withdrawals due to adverse effects were not increased with UA-lowering therapy (RR 1.86, 95% CI 0.43 to 8.10).

**Authors' conclusions**

In this updated systematic review, the RCT data available at present are insufficient to know whether UA-lowering therapy also lowers BP. More studies are needed.

## PLAIN LANGUAGE SUMMARY

### Drug therapy to treat high levels of uric acid in individuals with high blood pressure

**Background**

Uric acid is the natural end product produced by the breakdown of the body's tissues and a person's food, most notably protein. Uric acid is usually removed from the blood by the kidneys and eliminated from the body in the urine. However, if too much uric acid is produced or the kidneys are not able to remove it from the blood as usual, uric acid levels in the blood increase (termed hyperuricemia). A link between hyperuricemia and high blood pressure (a major health matter worldwide) has been recognized since the 19th century. Today, there is more evidence that this is an important association. The aim of this review was to evaluate whether lowering levels of uric acid in the blood could also lower blood pressure. Such an approach could represent a new goal and/or a therapeutic option for individuals with hypertension.

**Study characteristics**

In this update of a previous review, we examined the abstracts of 349 references, and selected 21 for evaluation. Only three studies were suitable for inclusion, two of which had not identified in a previous review in this topic. The studies in this review were from the USA; and evaluated adolescents and adults. The aim of these studies were to compare drug therapy to decrease uric acid with a placebo control in individuals diagnosed with high blood pressure.

**What the research says**

We found that drug therapy to lower uric acid did not result in a significant reduction in blood pressure in individuals who had high uric acid levels in the blood as well as high blood pressure compared with placebo. Drug therapy was superior to placebo to decrease blood levels of uric acid. Withdrawals due to side effects were not increased with drug therapy; however, in one study, one patient withdrew due to a severe cutaneous reaction.

Thus, there is insufficient evidence to demonstrate that the use of drugs that lower uric acid levels in the blood also reduce blood pressure in individuals with hypertension. More research on this question is needed. Because only three studies were suitable to be included, we cannot be certain that future studies will not change these conclusions.

**Quality of the evidence**

Overall, there was low quality evidence that failed to establish whether drug therapy to treat high levels of uric acid reduces blood pressure. The studies included in this review presented results not similar across studies for this outcome. In addition, we found a high quality of evidence that uric acid lowering drug therapy decreases uric acid. Finally, there was a very low quality of evidence that failed to establish whether drug therapy increased withdrawals due to side effects. The key reasons for this included issues with study design, lacking of data and results not similar across studies.