Do nonsteroidal anti-inflammatory drugs affect blood pressure: a meta-analysis

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Authors' objectives
To study the effect of non-steroidal anti-inflammatory drugs (NSAIDs) on blood-pressure.

Searching
MEDLINE was searched from 1966 to 1990, EMBASE from 1974 to 1990, BIOSIS Previews from 1969 to 1990, Diogenes from 1976 to 1990, Science Citation Index from 1972 to 1990, International Pharmaceutical Abstracts from 1979 to 1990, IOWA Drug Information Service from 1966 to 1990, and the Combined Health Information Database from 1973 to 1990. Bibliographies, reference lists of all identified studies, and textbooks on hypertension, clinical pharmacology and NSAIDs, were also examined.

Study selection
Study designs of evaluations included in the review
Randomised placebo-controlled trials, and randomised non-placebo-controlled trials comparing 2 or more NSAIDs with each other.

Specific interventions included in the review
NSAIDs.

Participants included in the review
Hypertensive patients administered NSAIDs (24). Patients with controlled hypertension administered NSAIDs (462). Patients with uncontrolled hypertension administered NSAIDs (46). Normotensive volunteers given antihypertensive agents and administered NSAIDs (47). Normotensive volunteers administered NSAIDs (110).

Outcomes assessed in the review
Blood-pressure, weight, creatinine clearance, plasma renin activity, and daily urinary excretion of sodium and prostaglandins.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
Studies had to assess the potential interaction between NSAIDs and blood-pressure, and to have used a control group (either placebo or comparison of at least 2 NSAIDs; patients had to have been randomly allocated. Two authors made decisions based on the methods, blinded to the source of the articles. A quality assessment score was given to each study by one reviewer, and the second assessed a 20% random selection.

Data extraction
One reviewer extracted data from every trial, and a second reviewer extracted data from a 20% random selection of trials for all randomly assigned persons (intention to treat method).

Methods of synthesis
How were the studies combined?
The placebo-controlled trials were combined separately using a meta-analysis.
How were differences between studies investigated?
Randomised trials were subdivided into 5 population groups and analysis of variance was carried out. The analysis showed no significant difference among any of the groups in terms of the pooled effect of NSAIDs on blood-pressure, suggesting these groups were not statistically heterogeneous and could be pooled. Also, there were no significant differences between trials grouped according to race, duration of NSAID use, antihypertensive type, diet, study design, quality assessment score, location, patient drop-out or activity level. Separate meta-analyses were carried out for randomised, placebo-controlled trials and for randomised but not placebo-controlled trials.

Results of the review
Thirty-eight randomised, placebo-controlled trials, and 12 randomised non-placebo-controlled trials comparing at least 2 NSAIDs.

NSAIDs elevated supine mean blood-pressure by 5.0 mmHg (95% confidence interval, CI: 1.2, 8.7). NSAIDs had no significant effect on weight, creatinine clearance, plasma renin activity or daily urinary excretion of sodium and prostaglandins. NSAIDs antagonised the antihypertensive effect of beta-blockers (blood-pressure elevation 6.2 mm Hg, 95% CI: 1.1, 11.4) more than vasodilators and diuretics. Among the NSAIDs studied, piroxicam produced the most marked elevation in blood-pressure (6.2 mm Hg, 95% CI: 0.8, 11.5), whilst sulindac and aspirin had the least hypertensive effect.

Authors' conclusions
NSAIDs may elevate blood-pressure and antagonise the blood-pressure-lowering of antihypertensive medication to an extent that may potentially increase hypertension-related morbidity. Certain NSAIDs and hypertensive agents may be more prone to producing these effects, but the underlying mechanisms still require further study.

CRD commentary
A very thorough account of the methodology used; detailed tables are presented and the search strategy used is described. The number of patients recorded in the section of this abstract on included participants is taken from Table 1. There is a discrepancy between the number of patients included in the meta-analysis, shown in Figure 1, and the number reported in the table.

Implications of the review for practice and research
If the finding that NSAIDs significantly elevate blood-pressure has clinical relevance then such an effect could be associated with an increase in morbidity and mortality.

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