

# Nonnarcotic analgesic use and the risk of hypertension

Dedier J, Stampfer MJ, Hankinson SE, Willett WC, Speizer FE, Curhan GC. Nonnarcotic analgesic use and the risk of hypertension in US women. *Hypertension* 2002;40:604-8.

**Background:** ASA, acetaminophen and ibuprofen are the most commonly used medications among adults, according to a national survey of US households.<sup>1</sup> Short-term prospective studies suggest that NSAIDs can cause acute elevations of blood pressure,<sup>2</sup> and ASA and acetaminophen can influence prostaglandin homeostasis.<sup>3</sup> The Nova Scotia Heart Health study has shown that 21% of women aged 35–64 years have hypertension,<sup>4</sup> thus, even small elevations in blood pressure caused by nonnarcotic analgesic use could result in cardiovascular morbidity and mortality. To date, there has not been strong evidence of an association between nonnarcotic analgesic use and hypertension.<sup>5,6</sup>

**Question:** Is there an association between ASA, acetaminophen and other NSAID use and incident hypertension?

**Design:** Participants in the Nurses' Health Study<sup>7</sup> have completed a mailed questionnaire every 2 years, starting in 1976. The study by Dedier and colleagues is based on data collected between 1990 and 1998. In 1990, 85 625 women in the cohort returned the mailed questionnaire: 51 630 of them were included in the study, and the remaining women were excluded because of a reported history of hypertension ( $n = 27\ 344$ ), chronic kidney failure ( $n = 10$ ), failure to answer any of the questions on analgesic use ( $n = 336$ ), no physical examination between 1988 and 1990 ( $n = 735$ ) and no physical examination during the study period ( $n = 5570$ ). The women were asked how many days on average each month they took any of ASA, acetaminophen or other NSAIDs. Dosage and prior duration of analgesic use were not ascertained. Body mass index (BMI), smoking status, age and physical activity were ascertained from the 1990 questionnaire and were updated with each subsequent biennial questionnaire. Alcohol and sodium intake were obtained from the 1990 questionnaire and again in

1994. Diabetes was diagnosed if it had been reported on any biennial questionnaire through 1990, and information on family history of hypertension was obtained from the 1992 questionnaire. Incident hypertension was determined based on answers in biennial questionnaires as to whether a physician had made a new diagnosis of hypertension in the preceding 2 years.

Incident rates were computed by dividing the number of new cases of hypertension by the number of person-years in that analgesic use category. Odds ratios were used as the measure of association. Multivariate pooled logistic regression allowed control for confounding factors, including concurrent use of other analgesic types. Subjects were censored after being diagnosed with hypertension or at the time of death.

**Results:** The median age of the cohort was 55 (interquartile range 49–61) years. The women who used ASA, acetaminophen or other NSAIDs at any frequency had a higher age-adjusted risk of hypertension than nonusers. The sizes of the odds ratios were similar across analgesic types by frequency of use. The relative risk of incident hypertension increased for all 3 categories of analgesic with increasing frequency of use, although it appeared to plateau over 14 days/month. This association remained after adjusting for age and after multivariate adjustment for age, BMI, sodium and alcohol intake, physical activity, family history of hypertension, diabetes and smoking status.

**Commentary:** This large prospective cohort study identified an association between the frequency of use of nonnarcotic analgesics and incident hypertension. The individuals studied were female nurses from the 11 most populous US states. The information on analgesic use was obtained from questionnaires. The definition of incident hypertension had previously been demonstrated to be highly correlated with the documented diagnosis of hypertension in the medical record.

There are limitations to this study. The Nurses' Health Study cohort is predominantly derived from the middle so-

cioeconomic class and white. Of the women who answered the 1990 questionnaire, 32% reported having hypertension (and were excluded from the analysis) and a further 20% acquired hypertension during the subsequent 8 years. This combined rate is much higher than the 21% among women aged 35–64 years in the Nova Scotia Health Heart study.<sup>4</sup> It is not known when the hypertension was first noted. Comparisons were only carried out for each type of analgesic, and not with a group of nonusers of any drug. Doses and duration of analgesic use before 1990 and after 1992 are not reported.

**Practice implications:** This study does suggest that the risk of hypertension is increased by nonnarcotic analgesic use, but there still remain a number of questions concerning dose and duration of use and whether the use of analgesics is a surrogate marker for the conditions for which they were used. Some conditions that could be associated with hypertension could include premenstrual syndrome, headache, primary or secondary prevention of vascular disease, or arthritis.

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## References

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