Response to Letter Regarding Article, “Acetaminophen Increases Blood Pressure in Patients With Coronary Artery Disease”

We thank Dr Nguyen for his interest in our study and share his view that the findings may have major public health implications. As is usual for multiple end points, a Bonferroni correction was made at the end of the study. Bonferroni corrections for an interim analysis are important to decide whether to stop a study preliminarily, but are not necessarily useful for extending a study that is not dependent on statistical significance values alone but rather on trends and power analysis. We disagree with Dr Nguyen’s statement about $P$ values, given that statistical significance was defined as $P<0.05$, and $P$ values of 0.021 and 0.024 for systolic and diastolic blood pressure (BP), respectively, were observed.1 Of note, the crossover design allowed for exposing all 33 patients to acetaminophen, thus substantially increasing the power of the study and the validity of the results. As already outlined,1 the number of patients and the time of exposure to acetaminophen had to be limited to the minimum required by sample size calculation because the patients included in this study did not present with arthritis or chronic pain and thus would potentially not benefit from the study drug.

The “biological and mechanistic basis to explain the BP effect of acetaminophen” was discussed in the article: There is an increasing body of evidence indicating that the hypertensive effect of acetaminophen is at least in part mediated by cyclooxygenase-2 inhibition, in a manner similar to traditional nonsteroidal antiinflammatory drugs.2

The 3 previously published studies mentioned by Dr Nguyen, 1 demonstrating a 4-mm Hg increase and 2 no change in BP associated with the use of acetaminophen, were also cited and thoroughly discussed.1 In contrast to our trial, these studies included patients with hypertension only, but excluded patients with established coronary artery disease, in whom the evidence of cardiovascular safety of acetaminophen is still absent.

We also disagree with Dr Nguyen that the results of the recently published Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD-BP) trial3 would suggest that the demonstrated rise in BP induced by acetaminophen in patients with coronary artery disease might not be harmful. Although the results of the ACCORD-BP trial demonstrated that targeting a systolic BP of $<120$ mm Hg did not further reduce the rate of a composite of cardiovascular events, with the exception of stroke, in patients with type 2 diabetes mellitus,3 there is abundant evidence that BP is strongly and directly related to vascular (and overall) mortality, particularly in patients at increased cardiovascular risk.4,5

Notwithstanding that BP is a surrogate of clinical outcomes, randomized, placebo-controlled clinical trials specifically addressing the safety of acetaminophen are currently lacking and probably unlikely to be performed. For this reason, our study, by providing the first prospective evidence that acetaminophen increases ambulatory BP in patients with coronary artery disease to a similar extent as traditional nonsteroidal antiinflammatory drugs, is of particular clinical relevance. The use of acetaminophen should therefore be evaluated as rigorously as all traditional antiinflammatory drugs, and we agree with Dr Nguyen that we may decide to continue prescribing acetaminophen while more closely monitoring BP and adapting the antihypertensive treatment, if necessary.

Disclosures

None.

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References


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Disclosures

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