2019

Reply to OM Shannon et al

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10.1093/ajcn/nqy246
Originally published as:
Blekkenhorst, L.C., Lewis, J.R., Prince, R.L., Devine, A., Bondonno, N.P., Bondonno, ... Hodgson, J.M. (2018). Reply to OM Shannon et al. *The American Journal of Clinical Nutrition, 108*(6), 1353–1354.
Original article available here.

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Response to Letter, "No effect of 4 weeks nitrate-rich vegetable consumption on blood pressure: Reflections for future research"

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Response to letter:

We would like to thank Shannon and colleagues for their interest in our recent publication (1). Our approach to increasing nitrate intake was to have participants consume high nitrate vegetables, rather than supplements. The estimated increase in nitrate intake of ~150 mg/d was in addition to an estimated background intake of ~85 mg/d (1). This represents a substantial increase in habitual nitrate intake. With typical median habitual nitrate intakes of ~100 mg/d (2), a nitrate intake of >200 mg/d would represent high nitrate intake within most populations. We believe that an increase in nitrate intake of >100 mg/d is readily achievable for the wider population. Although a very high nitrate intake (>500 mg/d) can be achieved through dietary means, this is unrealistic on a long-term basis for the majority of the general population. Such intakes usually require supplementation with nitrate salts ($NaNO_3$; KNO_3) or concentrated beetroot juice. The feasibility of translation of findings to shift behaviours of the wider population should be taken into account in designing future studies.

Many trials have now investigated the effects of increased nitrate intake on blood pressure (3-6). Results of acute studies are largely consistent and indicate dose-related blood pressure lowering with increased nitrate intake. The chronic effects following a sustained increase in nitrate intake are less consistent (3-5). Several previous trials indicate that a short-term increase in nitrate intake does not result in lower blood pressure (7-10): results that align with our recent trial (1). However, other short-term trials have demonstrated blood pressure lowering effects following sustained short-term increases in nitrate intake (3-5, 11).

The reasons for the inconsistent results from short-term trials are unclear. We agree that nitrate dose may be a factor, but counterintuitively, a meta-analysis of short-term studies indicated smaller effect sizes for blood pressure among trials with the highest nitrate intakes (3). This contrasts with data from acute studies (4), and suggests that factors other than dose

may account for the inconsistent findings. One explanation may be that sustained higher nitrate intakes can result in down-regulation of nitric oxide synthase leading to reduced endogenous nitric oxide production and/or reduced sensitivity of cellular targets to nitric oxide (12). Another possibility is an interaction between sulphur-containing compounds and nitrate (13, 14). In a study by Dewhurst-Trigg and others (14), the ingestion of vegetables with high thiocyanate (a sulphur-containing compound) attenuated the blood pressure lowering-effects of nitrate-rich vegetables. Several of the high nitrate vegetables consumed by the participants in our study were also likely to include sulphur-containing compounds. Furthermore, the age and health status of participants may be important. Older individuals and those at an increased risk of cardiovascular disease may respond differently to healthy populations (3-5, 7-9). This is supported by Ashor and colleagues who reported that when short-term trials that recruited active, healthy individuals were excluded from their meta-analysis, effects on blood pressure became non-significant (3).

In summary, we agree with Shannon and colleagues that dose of nitrate may be a contributing factor to the inconsistencies in nitrate intervention trials. However, we believe that factors other than nitrate dose are more likely to explain the inconsistent findings in this field.

Disclosures: None.

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