Circulation Research

RESEARCH LETTER

Acute Blood Pressure-Lowering Effects of Nitrogen Dioxide Exposure From Domestic Gas Cooking Via Elevation of Plasma Nitrite Concentration in Healthy Individuals

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Air pollution is a major cause of cardiovascular and all-cause mortality. Disentangling the relative contributions of pollutants is challenging, as epidemiological data measuring exposure to one (eg, nitrogen dioxide [NO_2]) is inevitably confounded by exposure to others (eg, particulate matter). Animal studies suggest that inhaled NO_2 has the potential to increase plasma [nitrite][1]; a chemical originally considered to be physiologically inert before we found that its reduction to nitric oxide protects the myocardium against ischemia-reperfusion injury and lowers blood pressure in humans.[2]

We conducted an acute, randomized, controlled, crossover study to assess the impact of 90 minutes exposure to NO_2 (from sitting next to a domestic gas cooker with gas hobs lit and uncovered) versus control (room air) on plasma [nitrite] (primary end point) and blood pressure (secondary end points) in 12 healthy participants. All underwent both interventions/visits (interval 7–108 days) in a computer-generated randomized order. Baseline characteristics (mean±SD): 26±4years, 10/12 female, body mass index 21.9±3.0 kg/m^2, systolic blood pressure 113.8±7.9 mm Hg, diastolic blood pressure 72.8±5.7 mm Hg. The exposure phase was followed by a 90 minutes washout phase at background [NO_2]. Participants fasted for 12 hours before each visit and received 250 mL low-nitrate water at time 0 h/1.5 h. The study was powered for a difference in plasma [nitrite] of 27±40 nmol/L on repeated-measures, 2-way ANOVA (α, 0.05 and β, 0.2) following D'Agostino-Pearson normality-confirmation, with Sidak post-test (GraphPad Prism v8.2.1).[3]

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Relative to control, exposure increased ambient [NO_2]: 276.3±38.5 versus 27.6±2.8 ppb ($P<0.001$). Plasma [nitrite] was increased through both the 90 minutes NO_2 exposure and 90 minutes washout ($P<0.001$; Figure [A]). NO_2 exposure decreased both systolic blood pressure and diastolic blood pressure (both $P<0.001$; Figure [B] and [C]). The largest decrease in systolic blood pressure relative to control occurred at 45 minutes (4.6 mm Hg [95% CI, 0.2–8.9]; $P=0.032$) and 90 minutes (5.5 mm Hg [95% CI, 1.2–9.9]; $P=0.005$). The effect of NO_2 on diastolic blood pressure was maximal at 45 minutes (5.7 mm Hg [95% CI, 0.9–10.5]; $P=0.009$).

The temporal relationship between the increase in plasma [nitrite] and systolic blood pressure/diastolic blood pressure reduction (≈5 mm Hg) is consistent with studies investigating dietary nitrate.[2] Furthermore, whilst the level of NO_2 exposure (276.3±38.5 ppb) was ≈2.5-fold greater than recommended limits for exposure (eg, World Health Organization guideline 105 ppb 1-hour mean), it is less than that recorded adjacent to busy roads or in some domestic kitchens (≈2000 ppb).

Key Words: air pollution ■ blood pressure ■ nitrite ■ nitrogen dioxide ■ particulate matter

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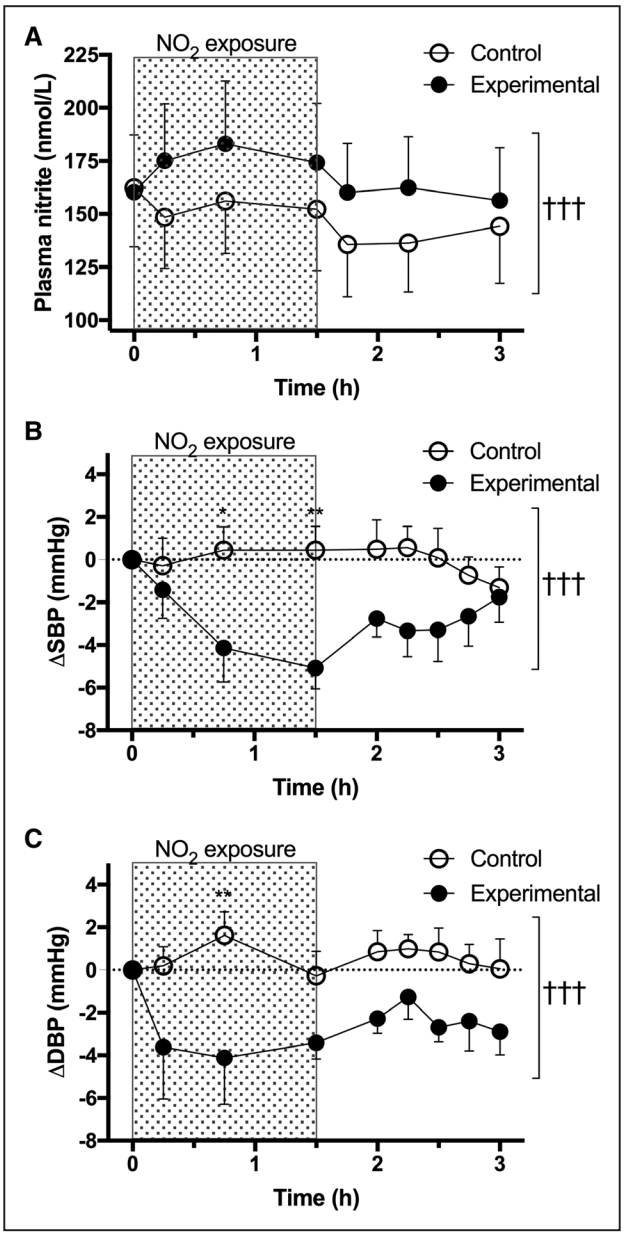

Figure. Effect of nitrogen dioxide (NO_2) exposure on plasma [nitrite] and blood pressure.
Plasma [nitrite] (**A**), systolic blood pressure (**Δ**SBP; **B**), diastolic blood pressure (**Δ**DBP; **C**). Comparison between experimental and control shown as †††P<0.001 and individual timepoints as *P<0.05 and **P<0.01. Data expressed as mean±SEM (n=12).

Our model is, therefore, conservative relative to real-world exposure.

Previously, an increase in plasma [nitrite] at 2 hours following diesel exhaust inhalation was thought to be due to particulate matter-mediated induction of inflammatory pathways.[3]

However, our data suggest a more rapid increase in plasma [nitrite] which favors chemical conversion from NO_2 (eg, via a nitrous acid intermediary) and presents a plausible mechanism through which inhaled NO_2 increases plasma [nitrite].[1] This novel ecophysiological NOx cycle may directly feed into the established nitrate-nitrite-nitric oxide pathway and contribute nitric oxide-mediated cardiovascular effects.[2] Adverse respiratory effects of inhaled NO_2 were not investigated here.[1]

These data must be considered in the context of the strong epidemiological association between NO_2 exposure and cardiovascular mortality.[1] However, particulate matter-free NO_2 does not appear to impair either vascular function, fibrinolysis, or affect heart rate variability in patients with coronary heart disease: parameters adversely affected by increased ambient NO_2 exposure in epidemiological studies.[4,5] This study expands our understanding of how inhaled NO_2 might impact the cardiovascular system, and the role of diet in disease: it is not just what you eat, but how you cook it that matters.

ARTICLE INFORMATION

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Disclosures

None.

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