Effect of Nitrate Ingestion on Central Hemodynamics in Hypoxia

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Acute hypoxia results in local vasodilation that may temporarily unload the left ventricle (LV) through nitric-oxide (NO)-mediated mechanisms. Whether increasing NO levels augments LV unloading and improves ventricular-vascular coupling in hypoxia remains unknown. **PURPOSE:** Investigate the effect of nitrate ingestion on central hemodynamics in hypoxia. **METHODS:** 20 Healthy men (23±3 yrs, BMI 24.6±2.8 kg·m-2) consumed 70 mL of either a) a 0.45 g nitrate (NIT) or b) an inert placebo (PLA) prior to 105 min of normobaric hypoxia (11.6±0.1%) in this randomized, double-blind, crossover-design study. Central hemodynamic variables were derived from the aortic blood pressure (BP) waveform at normoxic baseline and in hypoxia. Wave reflection index (RIx; ratio of forward to reflected wave pressure), augmentation index (AIx75) and pulse wave velocity were assessed as measures of wave reflection and aortic stiffness, respectively. LV wasted pressure effort (WPE) was calculated as an index of LV work due to wave reflections, and subendocardial viability ratio (SEVR) as a measure of myocardial O2 supply/demand ratio. Arterial O2 saturation was measured to quantify the hypoxic stimulus. **RESULTS:** Hypoxia significantly reduced arterial oxygen saturation compared to normoxia ($p<0.05$). Aortic diastolic BP, RIx, AIx75, and LV WPE significantly decreased in hypoxia compared to normoxia ($p<0.05$). SEVR and PWV were unaffected by hypoxia ($p>0.05$). Nitrate ingestion did not significantly alter central hemodynamics in hypoxia ($p<0.05$). **CONCLUSIONS:** Acute hypoxic exposure unloads the LV and reduces myocardial energetics without disturbing myocardial O2 supply-demand ratio via reductions in pressure from wave reflections and not from changes in aortic stiffness per se. Nitrate ingestion did not improve LV unloading or ventricular-vascular coupling in acute hypoxia.

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Table 1: Central hemodynamics, wave reflections, and indices of left ventricular work across treatments and conditions (mean ± SD)

	Placebo (PLA)		Nitrate (NIT)		
	Normoxia	Hypoxia	Normoxia	Hypoxia	*n*
Aortic SBP (mmHg)	97 ± 8	97 ± 7	97 ± 7	96 ± 10	20
Aortic DBP (mmHg)	69 ± 6	74 ± 7*	70 ± 6	72 ± 8*	20
Heart rate ($b \cdot min^{-1}$)	59 ± 9	64 ± 7*	57 ± 8	64 ± 8*	20
AIx75 (%)	-10 ± 11	-19 ± 7*	-13 ± 10	-22 ± 12*	20
LV WPE	-542 ± 856.0	-1089.7 ± 691.1*	-534.0 ± 902.1	-1312.0 ± 932.6*	14
Aortic SEVR (%)	176 ± 37	178 ± 29	183 ± 31	177 ± 31	20
Aortic PWV ($m \cdot s^{-1}$)	6.6 ± 0.8	6.2 ± 0.6	6.4 ± 0.7	6.2 ± 0.6	15
Aortic RIx	40 ± 8	32 ± 7*	36 ± 7	32 ± 5*	16

SBP, systolic blood pressure; DBP, diastolic blood pressure; AIx75, augmentation index at 75 bpm; WPE, wasted pressure effort; SEVR, subendocardial viability ratio; PWV, pulse wave velocity; Rix, wave reflection index.

* $p<0.05$ time effect, significantly different vs normoxia