



# Efficacy and safety of inhaled sodium nitrite in pulmonary hypertension associated with heart failure with preserved ejection fraction



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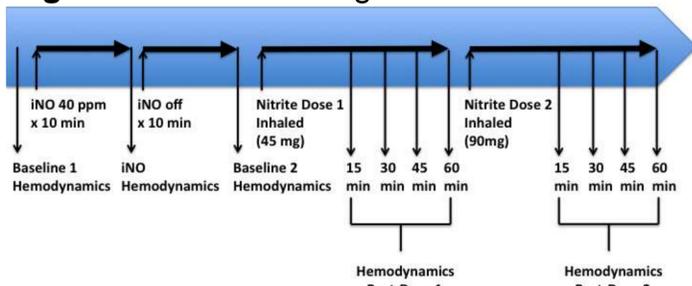
## Rationale

- Pulmonary hypertension (PH) is associated with poor functional capacity and outcomes regardless of etiology.
- Nitrite is a source of nitric oxide, with growing evidence that exogenous administration reduces pulmonary pressures and improves functional capacity.<sup>1-4</sup>
- This is the first study of the acute hemodynamic effects of inhaled nitrite in patients with PH due to heart failure with preserved ejection fraction (HFpEF).

## Methods

- After informed consent, PH patients underwent a standard right heart catheterization with inhaled nitric oxide (iNO) vasodilator challenge.
- Aerosolized sodium nitrite was administered at the first dose of 45 mg.
- Hemodynamics were recorded every 15 minutes for 1 hour.
- If stopping criteria were not met (decrease in systemic systolic blood pressure > 40 mm Hg, decrease in peripheral oxygen saturation > 10%, methemoglobin level > 5%, severe bronchospasm or dyspnea), then a second dose of 90 mg aerosolized sodium nitrite was administered and hemodynamics were recorded every 15 minutes for 1 hour (Figure 1).
- Primary analysis was a mixed effect model.

Figure 1. Protocol design.



## Results

### Patient Characteristics

- N=10
- Age 67 ± 7
- 6 female
- LVEF 61 ± 7%
- Functional class II (n=1), III (n=8) or IV (n=1)
- NT-Pro-BNP median 195 pg/mL (IQR 139-572)

### Acute Hemodynamic Effects

- Inhaled sodium nitrite significantly lowered right atrial, right ventricular systolic and diastolic, pulmonary artery (PA) systolic/diastolic/mean, and pulmonary artery occlusion (PAOP) pressures (Figure 2).
- Of note, right atrial, PAOP and mean PA pressures markedly decreased (Figure 2).
- PA compliance (stroke volume/PA pulse pressure) substantially increased (Figure 2).
- Minimal change in pulmonary vascular resistance (Figure 2).
- Cardiac output decreased significantly, with a modest decrease in mean arterial pressure but no change in heart rate.
- Methemoglobin levels increased modestly in all patients but did not meet stopping criteria (<5%) of the study.

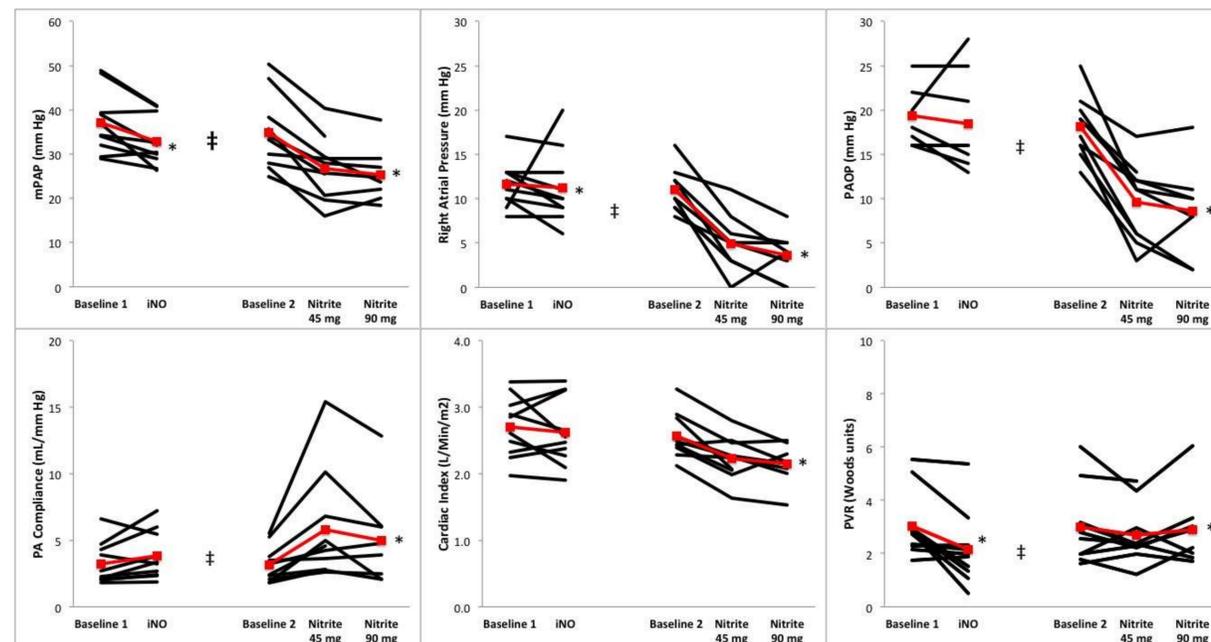


Figure 2. Effect of inhaled nitric oxide and aerosolized sodium nitrite. \*P<0.05 for effect of iNO or nitrite compared to baseline; ‡ P<0.05 for effect of nitrite compared to effect of iNO.

## Results

- The resistance-compliance (RC) relationship was significantly shifted up and to the right by nitrite (Figure 3), indicating an increase in pulmonary artery compliance for any given resistance.

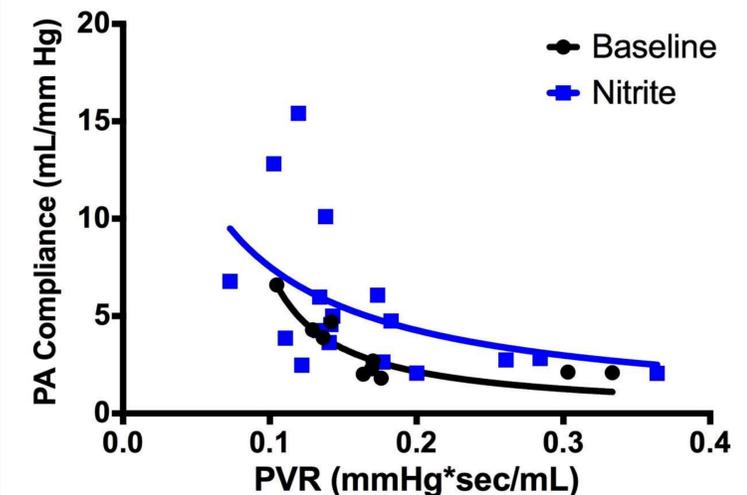


Figure 3. Resistance-compliance relationship at baseline and after administration of inhaled nitrite.

## Conclusion

- Inhaled sodium nitrite significantly lowers PA pressures in patients with PH due to HFpEF by a marked vasodilatory effect (lowering filling pressures) across the pulmonary vascular bed resulting in increased PA compliance, which may explain the functional benefits reported.
- Administration is well tolerated.

## References

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