Effects of a Novel Delivery Device for Inhaled Nitric Oxide On Ambulatory Exercise Induced Increases in Pulmonary Pressures

R. A. Davey*, A. Raina†, R. L. Benza†.

*Western University, London, ON, Canada. †Cardiovascular Institute, Allegheny General Hospital, Pittsburgh, PA.

PURPOSE

Pulmonary arterial hypertension (PAH) is characterized by progressive increases in pulmonary vascular resistance (PVR) and subsequent reductions in cardiac output (CO); these changes are further exacerbated by exercise. Inhaled nitric oxide (iNO) can decrease PVR and improve CO.

We sought to investigate the effects of a novel ambulatory delivery device for iNO (iNOPulse DS) (Fig. 1) in patients with the CardioMEMS implantable hemodynamic monitor both before and after exercise.

Our primary endpoint was to detect a difference in pulmonary artery pressures (PAP) and total pulmonary resistance (TPR) before and after exercise, with and without iNO. We also sought to measure surrogate markers of exercise such as: 6 minute walk test (6MWT) distance, O2 saturations, Borg dyspnea scale, and other RV derived parameters from the CardioMems device.

METHODS

10 subjects were consented and enrolled in the study with PAH from any cause (4=connective tissue disease, 5=idiopathic, 1=familial) and previously had a CardioMEMS device implanted as part of the ongoing VITA study. CardioMEMS readings were taken at 6 time points: baseline, immediately after a 6MWT, after 30 minutes rest (then started on iNO), 30 minutes after drug wash-in, immediately after repeat 6MWT and a final reading 30 minutes after drug discontinuation to ensure return to baseline.

RESULTS

With exercise, parameters including PAP (mean PAP 7.72±1.80mmHg,p=0.002), cardiac index (CI) (0.61±0.25 L/min/m2,p=0.04), and RV stroke work index (RVSWI) (3.39±1.03 g/m2/beat, p=0.01) all significantly increased whereas effective compliance significantly decreased (Ceff) (-1.01±0.23, p=0.002).

The effect of iNO at rest did not reach significance but did show a consistent trend toward improvement in PAP, CI, RVSWI, TPR and Ceff and this trend was preserved and demonstrated a blunting effect with exercise. In comparing the absolute differences in measured characteristics in the pre/post exercise group with and without iNO, again the trend was preserved (Fig. 2).

Furthermore, iNO administration did not appear to have any impact on systemic blood pressures, heart rates, or respiratory rates.

Importantly, there were no significant negative effects recorded: oxygen requirements, 6MWT distances, and subjective dyspnea scores all remained stable. It should be noted that 3 of the 10 subjects were on long-term oxygen therapy. This therapy was continued during the study in addition to study drug and there were no significant differences in outcomes or adverse effects in this group.

Fig. 1
iNOPulse Delivery System

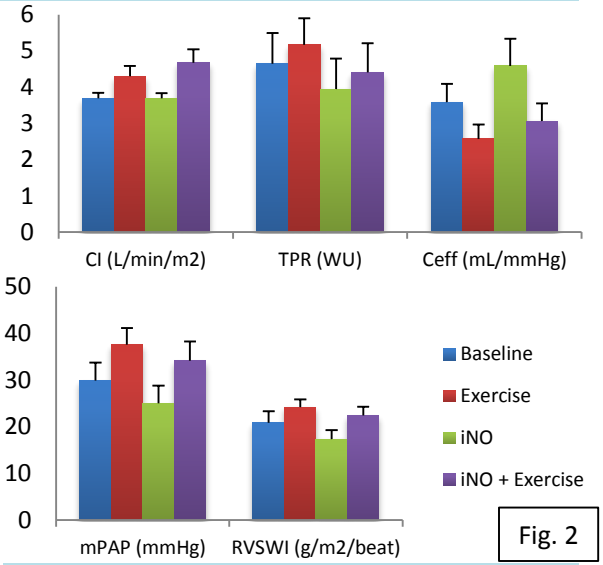

Fig. 2

CONCLUSIONS

This study provides important information for further exploration of a novel delivery device for iNO in an ambulatory setting.

iNO appears to have a role in blunting pulmonary pressures both with and without exercise as delivered by the iNOPulse DS.

This study reinforces existing knowledge about the effects of iNO with exercise but provides vital "real world" information about their effects. This information can form a framework for further investigations into the use of ambulatory iNO and its potential role in mitigating the paradoxical effects of exercise in patients with PAH.