MITOCHONDRIAL-TARGETED ANTIOXIDANT IMPROVES VASCULAR FUNCTION AND EXERCISE TOLERANCE IN PERIPHERAL ARTERY DISEASE PATIENTS

Elizabeth J. Pekas, Won-Mok Son, Ronald J. Headid III, TeSean Wooden, and Song-Young Park

University of Nebraska at Omaha, School of Health and Kinesiology, Omaha, NE

Vascular Research Lab

BACKGROUND

• Peripheral arterial disease (PAD) is an atherosclerotic disease in the leg arteries which results in reduced blood perfusion in the leg skeletal muscle and causes leg pain

•Vascular dysfunction and leg pain in patients with PAD may in part due to endothelial dysfunction, which may be result from attenuated mitochondrial function and excessive mitochondria-produced reactive oxygen species (ROS) in the vascular endothelial cells

•Previous studies have shown that mitoquinol mesylate, a mitochondrial-targeted antioxidant, can improve both vascular endothelial and mitochondrial function in older adults and animal models, however the impacts of mitoquinol mesylate on vascular function in patients with PAD have not been elucidated

PURPOSE

•To examine the impacts of acute mitoquinol mesylate intake on endothelial function (flow-mediated dilation, FMD), resting heart rate (RHR), blood pressure (BP), arterial stiffness (pulse-wave velocity, PWV; augmentation index, AIx), and exercise tolerance in patients with PAD

•It was hypothesized that acute mitoquinol intake would improve vascular function and exercise tolerance in these patients

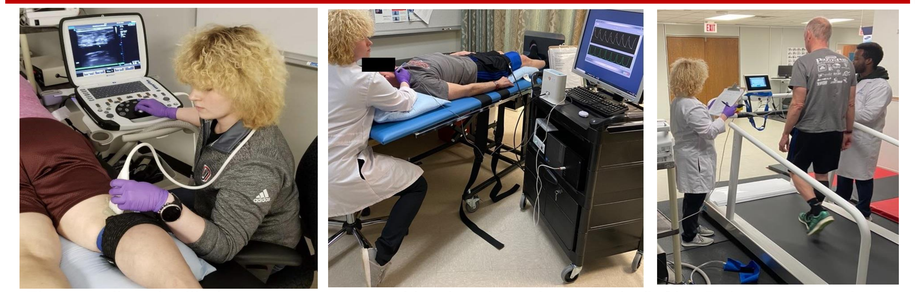
METHODS

•In 2 study visits, 10 patients with PAD (stage II-III, 5 males) received either mitoquinol mesylate (80 mg) or placebo (PL, similar in appearance and taste) in a randomized crossover study design

•At each visit measurements of height, weight, body composition, hand grip strength, RHR, BP, brachial and popliteal FMD, PWV, AIx, maximal walking capacity, and time to claudication onset (COT) were measured before and after mitoquinol and placebo intake

•Data were analyzed using a 2 x 2 repeated measures analysis of variance (ANOVA). A probability of type I error less than 5% ($p < 0.05$) was considered significant, and paired *t*-tests were used for *pos hoc* comparisons

METHODS



Flow-mediated dilation assessment with doppler ultrasound (left). Pulse-wave velocity assessment with applanation tonometry (center). Maximal walking test (right).

RESULTS

Table 1. Participant characteristics at both the placebo (n=10) and mitoquinol (n=10) visits. Values are Mean ± SD.

	Placebo (n=10)			Mitoquinol (n=10)		
Age, y	66.1	±	10.5	66.1	±	10.5
Height, cm	163.5	±	13.8	163.5	±	13.8
Body mass, kg	80.1	±	19.7	79.7	±	19.3
BMI, kg/m^2	30.0	±	6.8	29.9	±	6.7
Body fat, %	37.4	±	8.5	37.6	±	8.6
R handgrip strength, kg	33.0	±	13.3	32.0	±	12.8
L handgrip strength, kg	28.4	±	11.5	28.0	±	11.2

Table 2. Participant characteristics at both the placebo (n=10) and mitoquinol (n=10) visits. Values are Mean ± SEM.

	Placebo (n=10)		Mitoquinol (n=10)	
	Pre	Post	Pre	Post
RHR, bpm	68.2 ± 4.8	67.7 ± 4.3	69.3 ± 4.2	66.7 ± 3.6
Systolic BP, mmHg	134.6 ± 5.2	135.1 ± 5.4	133.3 ± 5.3	130.6 ± 5.0
Diastolic BP, mmHg	80.8 ± 2.6	81.4 ± 2.6	82.9 ± 2.5	79.8 ± 2.7
Carotid-to-radial PWV, m/s	9.2 ± 0.3	9.3 ± 0.3	9.2 ± 0.4	9.4 ± 0.4
Carotid-to-ankle PWV, m/s	10.4 ± 0.5	10.3 ± 0.5	10.3 ± 0.5	9.5 ± 0.6
Carotid-to-femoral PWV, m/s	9.7 ± 0.8	9.7 ± 0.9	10.0 ± 0.7	9.9 ± 0.7
Deceleration time, ms	685.9 ± 61.2	675.7 ± 61.9	674.2 ± 50.0	650.8 ± 77.2
Max dP/dt, mmHg/s	683.6 ± 43.4	720.9 ± 67.9	668.2 ± 65.4	669.4 ± 49.9
Peripheral PP, mmHg	47.4 ± 4.5	47.5 ± 4.7	47.9 ± 4.3	49.9 ± 4.7
Central PP, mmHg	43.5 ± 4.3	44.6 ± 4.4	41.5 ± 4.0	40.1 ± 3.9
AP, mmHg	21.9 ± 13.6	21.7 ± 14.1	20.8 ± 12.9	21.1 ± 12.9
AIx, mmHg	19.7 ± 3.5	21.5 ± 4.5	21.1 ± 3.5	20.7 ± 4.8
Max walking time, s	457.2 ± 35.7	435.2 ± 35.7	442.7 ± 52.6	516.5 ± 47.1

RESULTS

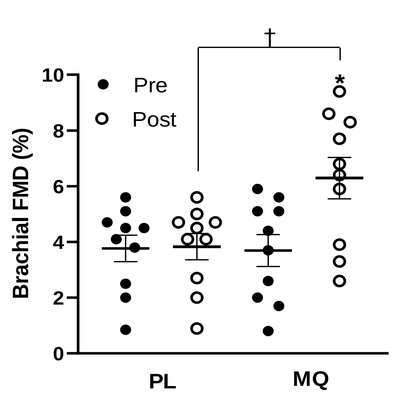


Figure 1. Brachial artery FMD (%) pre- and post-PL and mitoquinol intake (n=10)
Values are presented as Mean±SEM
*p<0.05 vs. Pre, † p<0.05 vs. placebo

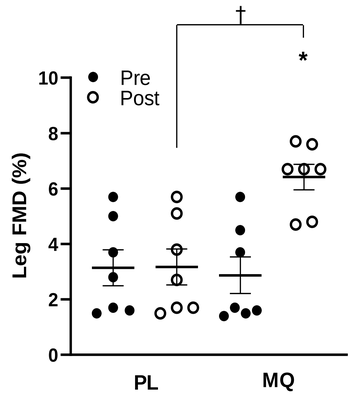


Figure 2. Popliteal artery FMD (%) pre- and post-PL and mitoquinol intake (n=7)

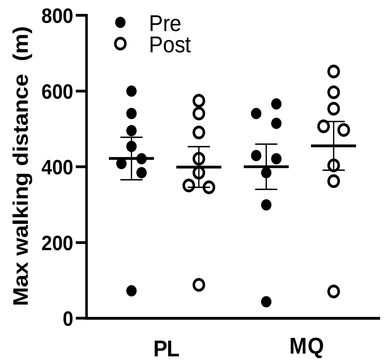


Figure 3. Maximal walking distance (m) pre- and post-PL and mitoquinol intake (n=8)

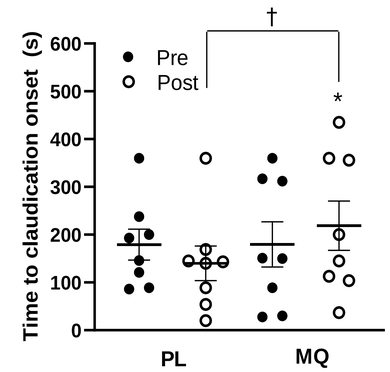


Figure 4. COT (s) during the maximal walking test pre- and post-PL and mitoquinol intake (n=8)

CONCLUSIONS

•Mitoquinol mesylate intake may be an effective therapeutic strategy for targeting mitochondrial-derived ROS, which may be useful for treating endothelial dysfunction, leg pain, and improving walking time in patients with PAD

This project was funded by the University Committee on Research and Creative Activity (UCRCA), Graduate Research and Creative Activity (GRACA) Grant and the NASA Nebraska Space Grant (#NNX15AI09H).