radcliffe cardiology

Title: Nicotinamide Riboside in PAD for Improved Walking
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Dr Mary McDermott

"Mary McDermott and I am at the Northwestern University Feinberg School of Medicine.

NR Supplementation in Patients with PAD

So, nicotinamide riboside, or NR, is rapidly metabolised in humans to NAD. And NAD is an essential co-factor and enzyme for mitochondrial activity. It reduces oxidative stress, and it increases nitric oxide through eNOS, and NAD declines with age. And for patients with peripheral artery disease, all of those three actions that I mentioned, increasing mitochondrial activity, reducing oxidative stress, and increasing nitric oxide to improve blood flow, all have the potential to help people with peripheral artery disease walk better.

Study Design and Outcome Measures

This was a phase two, randomised clinical trial. We randomised 90 people with peripheral artery disease to nicotinamide riboside alone, nicotinamide riboside with resveratrol, or placebo. And the rationale for the resveratrol with nicotinamide riboside was that resveratrol may increase the effects of NR on certi-one, an enzyme that increases nitric oxide. And people were randomised for six months. They took the study drug for six months; it was double-blinded, and our primary outcome was a six-month change in the six-minute walk distance.

Baseline Characteristics

So we randomised 90 people in this phase two clinical trial, 47% were women, so nearly half women, and we had 48% black, so we did have a diverse population.

Data Presented at AHA 23

So for our primary outcome, six-month change in six-minute walk distance, we found that nicotinamide riboside alone meaningfully improved six-minute walk distance by 17.6 metres. In our primary analyses, the NR plus resveratrol did not have a meaningful effect. But when we looked at the subset of people who adhered to their study drug, that is, they had 75% or greater adherence, then we actually found a 35-metre improvement in the NR alone group and a 30-metre improvement in the NR plus resveratrol group compared to placebo.

We also found meaningful improvements in six-minute walk at three-month follow-up, 22 and 20 metres in the NR alone and the NR with resveratrol group. And we found that both interventions had significant effects on treadmill walking time.

Unexpected or Surprising Results

Well, it was surprising that there was such a difference in results by adherence. So the two-thirds of people that took 75% or more, the mean improvements were substantially increased, while those who didn't adhere actually declined in all three groups. And also among those who did adhere, the magnitude of the effect size was quite large. The 35 and 30 metres that I mentioned, that's similar to what supervised exercise does for patients with peripheral artery disease.

Take-Home Messages

Well, it was a phase two trial, so it's not definitive, but it's preliminary evidence of a potential for a very strong signal of benefit for nicotinamide riboside on improvement in walking performance and peripheral artery disease. But resveratrol did not add to the nicotinamide riboside.

Next Steps

So we would like to design a phase three, multicenter randomised clinical trial to see whether in a larger sample size, these findings hold up close."