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## Multi-drug risk reduction strategy safe in peripheral artery disease

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## Keywords

Atherosclerotic risk factors, LDL cholesterol reduction, peripheral arterial disease

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## Context

In patients with peripheral arterial disease (PAD) is it both feasible and safe to modify multiple atherosclerotic risk factors with an intensive combination of drugs. The ADMIT (Arterial Disease Multiple Intervention Trial) investigators hope that this multi-faceted approach could offer benefits over the currently recommended low density lipid (LDL) cholesterol reduction and antiplatelet therapy only.

## Significant findings

The investigators report that niacin increased high density lipid (HDL) cholesterol levels by 30% and decreased LDL cholesterol and triglyceride levels by 12% and 28%, respectively. The majority of these effects were achieved at a dosage of 500 mg twice daily, and the addition of pravastatin further reduced LDL cholesterol levels. As expected, warfarin had an anticoagulant effect. The antioxidant vitamins resulted in a significant increase in vitamin E, C and beta-carotene plasma levels. Overall, compliance was high and few adverse effects were reported. Over the 48-week study period, ABI increased from 0.69 ± 0.16 at baseline to 0.71 ± 0.17 at the final visit (P = 0.018).

## Comments

The authors note that trials of statin monotherapy have found a residual risk of coronary heart disease events despite optimal LDL cholesterol reduction. They believe that, given the multifactorial nature of the pathogenesis of atherosclerosis and its complications, a combined approach offers the greatest potential benefit. 'The most promising interventions are the combinations of niacin and statins and vitamin E and C supplements. At this time, there is less evidence that the addition of beta-carotene or low-dose warfarin would be beneficial', the team concludes.

## Methods

ADMIT used a randomized 2 x 2 x 2 factorial design to investigate the feasibility and effect of combinations of low-dose warfarin, antioxidant vitamins, niacin and pravastatin in 468 patients with PAD. Inclusion criteria were: age  $\geq$  30 years; ankle-brachial index (ABI)  $<$ 0.85 and documented surgery or angiography for PAD; and LDL cholesterol  $<$ 190 mg/dl.

## Additional information

### References

1. Garg R, Elam MB, Crouse JR, Davis KB, Kennedy JW, Egan D, Herd JA, Hunninghake DB, Johnson WC, Kostis JB, Sheps DS, Applegate WB: Effective and safe modification of multiple atherosclerotic risk factors in patients with peripheral arterial disease. *Am Heart J* 2000, 140:792-803. 2000, 140: 792-803.