# Antioxidants improve Ankle-Brachial Index in Patients with Peripheral Vascular Disease

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**Abstract:**

**Objective:** The study was designed to evaluate the effects of vitamin C (250mg/ daily ) plus vitamin E (100 mg/daily ) for three months on the ankle – brachial index (ABI) in 20 male patients with peripheral vascular disease (PVD) .

**Setting:** Department of pharmacology and department of medicine , College of Medicine ,AL-Mustansiriyah University and AL-Yarmouk Teaching Hospital.

**Design:** Prospective, randomized, intervention study .Outcome measures: Ankle –brachial index is calculated using Doppler ultrasound probe and standard sphygmomanometer .

**Results:** Data showed that vitamin C plus vitamin E were statistically significant increase in the mean values of ABI after three months treatment in comparison with pretreatment values in patients with peripheral vascular disease. While the results of the treatment with aspirin (100mg / daily ) showed no significant difference in ABI after three months treatment in comparison with pretreatment values .

**Conclusion:** Combined double therapy of daily vitamin C (250mg ) plus vitamin E (100 mg) can be useful and effective therapeutic strategy in treating patients with peripheral vascular disease.

**Key wards:** Vitamin C, Vitamin E, ABI, PVD

## Introduction:

Peripheral vascular disease (PVD) is a chronic progressive atheromatous disease affecting blood vessels of the lower and upper limbs as a part of diffuse alterosclersis and/or secondary to diabetes mellitus[1]. PVD is a common Macro vascular complication in diabetic patients and is regarded as a major source of morbidity[2]. PVD affects arteries of the upper and lower extremities in addition to the carotid arteries[3].

In the United Kingdom, PVD affects 5% of men and women by late middle age[4] & it occurs in about 18% of people above 70 years of age[5].

There are 2 types of PVD[6]. The first type is Peripheral Arterial Diseases (PAD) is the most common type of PVD which refers to diseased Peripheral arteries and is a type of atherosclerosis. The second form of PVD is the Peripheral venous disorder which refers to problems in Peripheral reins e.g thrombophlebitis, varicose veins and chronic venous insufficiency[6]. Disease of the Peripheral arteries is most commonly due to atheroma. A variant of atheromatous PVD occurs in diabetics[7]. Atherosclerosis is the descriptive term of thickened and hardened lipid-rich lesions of the medium and large muscular elastic arteries[8]. Patients with PVD have higher levels of blood cholesterol, triglycerides, LDL, V LDL, fasting glucose, fibrinogen, haematocrit and white cell count[9]. PVD is a multifactorial condition, in which many causes and risk factors interact to produce vascular changes, these include: age[10]. Gender[11], hypertension[12]. Diabetes mellitus[13] and smoking[14]. In addition lipid peroxidation and oxidative modification of LDL have been implicated as causal factors in the pathogenesis of atherosclerosis[15]. Prevention of LDL antioxidants by oxidation may be effective strategy to inhibit the progression of the disease[15] so decreasing antioxdants defense may play an important role in the pathogenesis of peripheral vascular disease. This study was designed to show the benefit of using some antixidants like Vitamin C plus Vitamin E in patients with PVD.

## Patients :

This study was a prospective, single blind intervention randomized, study. Our study was conducted at the Department of Pharmacology, college of Medicine, AI-Mustansiriah Univerity &AI-Yarmouk Teaching Hospital for the period from 1st October 2002 to 1st October 2003. Patients recuited for the study were selected from a group of 50 patients complaining from intermittent claudication. Forty-three of them were diabetics [35 patients with (NIDDM) and 8 patients with (IDDM), All patients were examined both clinically and by Doppler ultrasonography to determine the presence of peripheral vascular disease (PVD) in them. Twenty patients were diagnosed to have

(PVD) (all were males with NIDDM) & were included in the study. The other patients were not included. The 20included male patients were randomly divided into 2 groups; Groups 1 (double therapy): given vitamin C 250mg daily & vitamin E 100mg daily, & Group 2 (monotherapy): given aspirin 100mg daily only. All patients were advised to strictly follow of their therapeutic regime. Written informed consents were obtained from patients & all possible risks & adverse effects were explained to them.

Patients were supplied with their treatments monthly & follow up was carried out monthly for 3 months.

**Drugs:**

Drugs used in this were obtained from local pharmacies. They included: Aspirin 100mg table (SDI), Vitamin C250mg table(SAMA VIT-C) (SDI), & Vitamin E 100mg capsule (BARKAVIT-E)(BARKAT).

**Doppler Ultrasonography:**

In this study, VOLUSON 530 DKRTZ type of instrumentation for echo-Doppler study was utilized. The instrument is equipped with 3.5 MHz frequency probe. Ankle-Brachial Index (ABI) is calculated using Doppler ultrasound probe and standard sphygmomanometer for the measurement of supine ankle systolic pressure (posterior tibial artery), and brachial systolic pressure( brachial artery). The ratio of ankle systolic pressure to the brachial systolic pressure is considered as the ankle-brachial index[16,17].

**Results:**

Included patients aged between 42 to 65 years and their mean age was 59± 7.4 yr. Duration of the disease ranged between 3 months to 12 years. All patients were diabetic, Non smoker and non obese(according to their BMI and WHR). Regarding drug history, 7 patients with IHD are on glyceryl trinitrate and/or isosorbide dinitrate. All patients were on gilbenclamide (5mg).

**Ankle-Brachial Index:**

Normally the ABI should not be less than 0.9 (Young et.al, 1993). The results showed that the mean values of the 2 treatment groups before therapy were less than the normal value. The mean (± SD) ABI in group 1 was 0.79 (± 0.15), & in group was 0.89 (± 0.18) (table 1). Both right and left ABI measurement for all patients were pooled together.

Data showed a statistically significant increase in the mean ABI following treatments ($p< 0.05$). paired t-test revealed a significant increase in the double therapy group($p< 0.05$) in the third months after treatments in comparison with pretreatment value. While aspirin monotherapy showed no significant difference in ABI after 3 months in comparison with pretreatment value(table 1).

**Table 1: Ankle-brachial index (ABI) for the different groups according to different periods of the study.**

| Timing | Double therapy mean +SD | P value | Aspirin mean+ SD | P value |
|---|---|---|---|---|
| **Before** | 0.7± o.152 | | 0.89± 0.185 | |
| **1month** | 0.28± o.148 | > o.o5 | 0.87± 0.164 | >0.05 |
| **2 month** | 0.85± o.135 | < o.o5 | 0.87±0.149 | >0.05 |
| **3 month** | 0.85± o.16 | < o.o5 | 0.87±0.14 | >0.05 |

**Discussion:**

The present study aimed to find whether there is any therapeutic usefulness of combination of vitamin C (250mg/day) and vitamin E (100mg/day) on patients with PVD. Effects of two therapeutic regiments on ankle/brachial systolic pressure index were evaluated.

In the present study, all patients were diabetic. The high incidence of PVD in diabetic patients is the results of many factors like high levels of serum cholesterol and triglycerides, oxidative stress, increased blood viscosity, hyperglycemic effects on vascular structure…etc.[18].

Many studies have tried to find possible useful effect of antioxidant drugs in the prevention of atherosclerosis. Evidence that antioxidant drugs may prevent atherosclerosis

disease is growing [19]. A potential role for the micronutrients (vitamin C and vitamin E) in modifying the risk of conditions resulting from oxidative stress has stimulated intense research efforts[20].

In our patients, pretreatment baseline mean values of ABI were lower than normal(should be> or= 1.0) and values less than 1.0 are a diagnostic feature of PVD.

After initiation of therapy, a significant increase was recorded in the double therapy group in the 3rd month in comparison with pretreatment values ($p< 0.05$). No significant increase appeared following aspirin monotherapy in the 3 months of the study. Therefore, it may be concluded that antioxidants may have a role elevating ABI values. Data obtained by [21] in their study on 4367 patients have shown that vitamin C intake was inversely & significantly associated with PVD and a 100mg increase in intake was associated with a 0.013 increase in ABI. Vitamin E intake was also inversely associated with PVD (but not significantly) and a 10-mg increase in intake was associated with a 0.015 increase in ABI.

The propable mechanism of the beneficial effects obtained in this study in Doppler parameters is propably related to the antioxidant effects of the compounds that have reduced the process of lipid peroxidation and retarded the process of atherosclerosis.

**Conclusions:**

Combined doubler therapy of daily vitamin C (250mg), vitamin E (100mg) could be a useful and effective therapeutic strategy in treating patients with PVD that result in reduction in Ankle/Brachial Index.

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