

Usefulness of A-Lipoc Acid, Leucoselect and Ginkgoselect Phytosoma in Chronic Venous Insufficiency

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Abstract

Background: Chronic venous insufficiency (CVI) is a frequent pathology that affects quality of life of the patients due to several symptoms such as pain, leg cramps, aching and itch. Our scope was to verify the usefulness of a supplement based on α -lipoc acid, Leucoselect® and Ginkgoselect® phytosome in patients with CVI.

Methods: From July to November 2015, 30 consecutive patients with CVI received once a day a tablet containing the supplement for a period of 4 weeks. A control group of 30 subjects taking placebo and matched for CVI class, age and sex was also recruited. Clinical evaluation using VCSS and microcirculatory assessment with perimalleolar capillaroscopy were performed. A questionnaire consisting of two questions investigating presence of pain and itch/paraesthesia was also given to the patients. Each question was scored on a dichotomous Likert scale (0=no; 1=yes).

Results: A significant reduction of VCSS from baseline to 4-weeks was observed in the group of treatment respect to control group (2.70 ± 0.95 vs 0.93 ± 0.74 and 2.87 ± 0.86 vs 2.60 ± 0.81 , $p < 0.0001$). Itch and paresthesias resolved in 86.7% of patients vs 26.7% of control ($p < 0.0001$) while leg pain improved in 70% of cases vs 23.3% of control ($p < 0.001$). No significant changes were found between baseline and 4-weeks capillaroscopic pattern in both groups.

Conclusions: After 4-weeks of treatment with α -lipoc acid, leucoselect and ginkgoselect phytosoma we observed clinical improvement of CVI symptoms, especially itch and paresthesias.

Keywords: Chronic venous insufficiency; α -Lipoic acid; Leucoselect; Ginkgoselect; Phytosome

derivatives have been shown as vascular protective agents to attenuate oxidative stress damage [7].

Introduction

Chronic venous insufficiency (CVI) is a common pathology affecting mainly lower limbs [1]. Vein-related problems include a wide spectrum of a several clinical signs that vary from minimal superficial venous dilation to chronic skin changes with ulceration. Symptoms usually reported by patients are pain, leg cramps, aching and itch. Particularly, itch has been shown to significantly influencing the quality of life of CVI patients [2].

The aim of our work was to verify the usefulness of α -lipoc acid, Leucoselect® and Ginkgoselect® phytosome in patients with CVI. Leucoselect® Phytosome® is a formulation of lower procyanidin oligomers from grape seed and soy lecithin to further improve their absorption. Alterations in the venous microcirculation are the main risk factors in CVI and procyanidin supplement has shown to improve the microcirculation and increase the capillary resistance [3]. Also, Leucoselect® Phytosome® has been proven able to reduce oxidative stress [4]. The α -Lipoic acid is a cofactor essential to the functioning of all the dehydrogenase of the human body. Some reports suggested a protective effect of α -Lipoic acid on endothelial cell damage [5] and antioxidant proprieties [6]. In the same fashion, Ginkgo biloba extract

Methods

Population

This was a single center study that included 30 consecutive patients with novel clinical diagnosis of CVI (CEAP 0-3,) [8] admitted to our ambulatory from July to November 2015. Patients with history of previous thromboembolic events were excluded.

Patients received a tablet (Blunorm Forte, Laborest Italia srl, Milano, IT) containing α -lipoc acid (400 mg), Leucoselect® Phytosome (200 mg), Ginkgoselect® Phytosome (80 mg), vitamin B6 and B12 (1 mg and 0.5 μ g, respectively), Folic acid (100 μ g) and Selenium (18.3 μ g). Treatment was administered once every day, orally, for a period of 4 weeks. We also selected a control group of consecutive subject with CVI symptoms matched for CVI class, age and sex recruited from April to May 2016 that received placebo administered in a single-blind manner for the period of the study.

The study complied with the Declaration of Helsinki. A written informed consent was achieved from all subjects. The local Ethical committee approved this study.

Clinical evaluation

Baseline (T0) and 4-weeks (T1) clinical assessment using Venous Clinical Severity Score (VCSS) was performed. The VCSS system includes 10 clinical descriptors (pain, varicose veins, venous edema, skin pigmentation, inflammation, induration, number of active ulcers, duration of active ulceration, size of ulcer, and compressive therapy use), scored from 0 to 3 (total possible score=30) [9]. A questionnaire consisting of two questions investigating presence of pain and itch/paraesthesia was also given to the patients at baseline and after 4 weeks. Each question was scored on a dichotomous Likert scale (0=no; 1=yes).

Microcirculation evaluation

Baseline (T0) and 4-weeks (T1) microcirculation assessment by capillaroscopy was performed. Peri-malleolar medial region was examined putting a video microscopy system (Charm View, Moritex Corporation, Tokyo, Japan) 1-cm up to the malleolus. Six parameters of capillaries' network were then evaluated: 1) capillaries architecture; 2) avascular fields; 3) capillary density; 4) abnormal capillary density; 5) haemorrhages; 6) apical capillary dilatation. Three Venous Hypertensive Microangiopathy (VHM) stages were identified according to the microcirculatory pattern [10].

Statistical analysis

Continuous variables are presented as mean ± standard deviation while dichotomous parameters as frequencies and percentages. The normal distribution of continuous parameters has been evaluated with the Kolmogorov-Smirnov test. Continuous data was compared using Student's unpaired or paired T-test, as appropriate. Categorical data was compared using the chi-square or the Fisher's test, as appropriate. SPSS 20 (IBM SPSS, Chicago, IL) was used for statistical analysis. P<0.05 was considered statistically significant.

Results

All patients included completed the study. Table 1 summarizes baseline clinical characteristic of patients.

	Treatment n=30	Control N=30	p
Age (years), mean ± SD	45.33 ± 11.55	46.80 ± 13.18	0.65
Gender (Male), n (%)	7 (23.3)	6 (20)	0.75
BMI, mean ± SD	24.15 ± 2.33	25.01 ± 2.90	0.21
CEAP, mean ± SD	1.73 ± 0.74	1.60 ± 0.81	0.51
VCSS, mean ± SD	2.70 ± 0.95	2.87 ± 0.86	0.48

BMI: Body Mass Index; CEAP: Clinical-Etiology-Anatomy-Pathophysiology; VCSS: Venous Clinical Severity Score

Table 1: Baseline characteristics

Females represented the majority of population (76.7%). Distribution of CVI according to VCSS classification is shown in Figure 1.

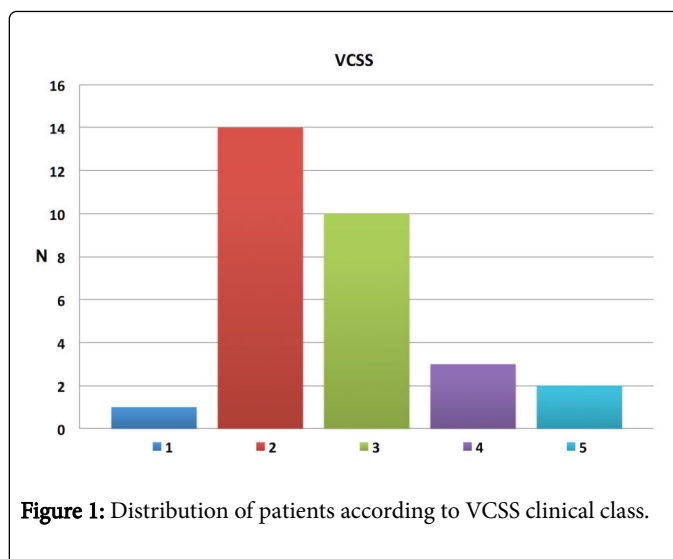


Figure 1: Distribution of patients according to VCSS clinical class.

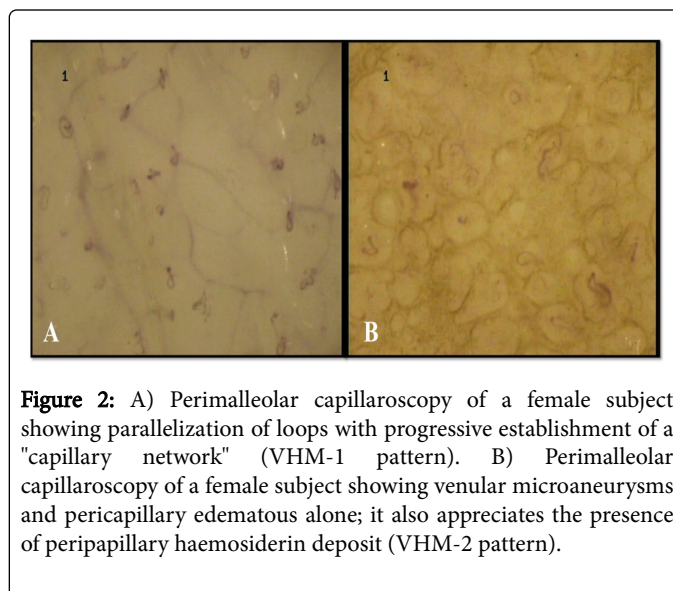


Figure 2: A) Perimalleolar capillaroscopy of a female subject showing parallelization of loops with progressive establishment of a "capillary network" (VHM-1 pattern). B) Perimalleolar capillaroscopy of a female subject showing venular microaneurysms and pericapillary edematous alone; it also appreciates the presence of peripapillary haemosiderin deposit (VHM-2 pattern).

The capillaroscopic baseline evaluation showed a VHM stage-1 in majority of patients (83.3%) (Figure 2A) followed by a VHM stage-2 in the remaining population (16.7%) (Figure 2B). In none of the patients VHM stage-3 pattern was highlighted confirming the venous insufficiency in non-advanced stage in most subjects.

After 4 weeks of treatment, there has been a significant reduction of VCSS in patients treated with supplement compared to control group (2.7 ± 0.95 vs 0.93 ± 0.74 in treatment group, 2.87 ± 0.86 vs 2.60 ± 0.81 in control group). Figure 3 shows the reduction of the classes from baseline to 4 weeks in treatment group.

Itch and paresthesias were referred by 20 patients in both groups (66.7%) and resolved in 86.7% of patients vs 26.7% of control (p<0.0001) (Figure 4) while leg pain was described in almost all patients (100% in supplement group, 96.7% in controls) and improved in 70% of cases treated vs 23.3% of control (p<0.001) (Figure 5).

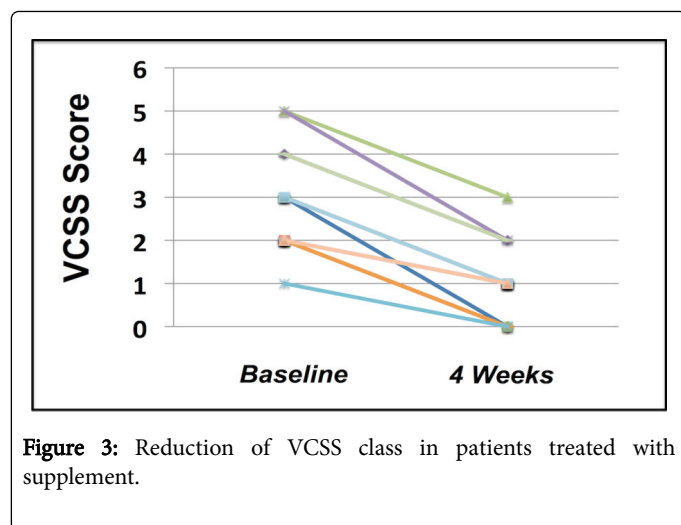


Figure 3: Reduction of VCSS class in patients treated with supplement.

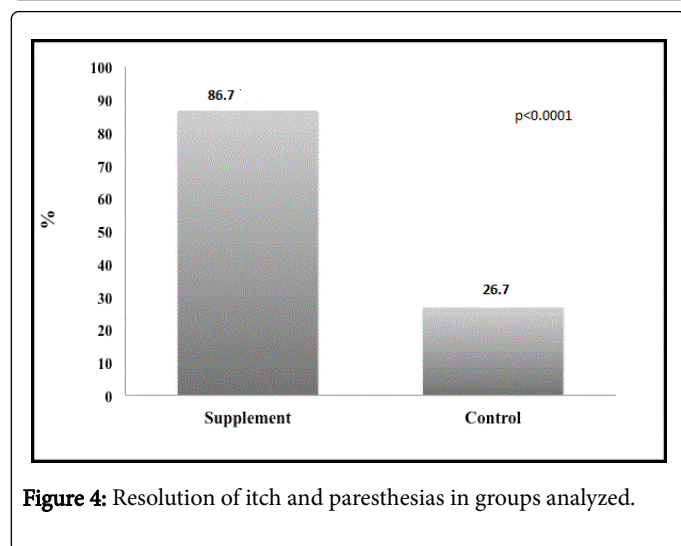


Figure 4: Resolution of itch and paresthesias in groups analyzed.

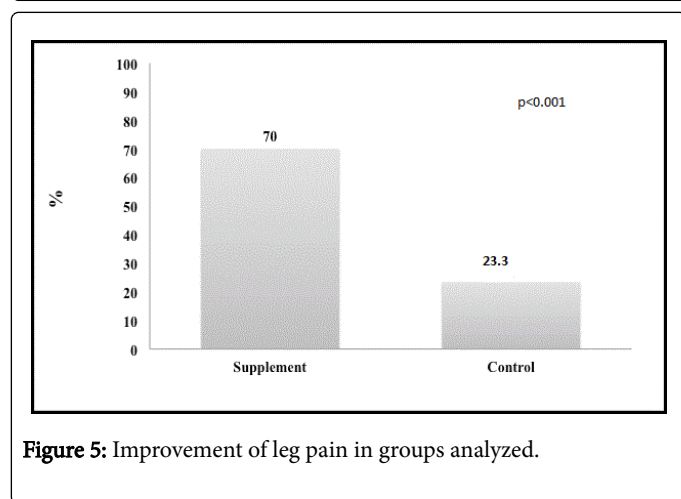


Figure 5: Improvement of leg pain in groups analyzed.

Of note, no significant changes were found between baseline and 4-weeks capillaroscopic pattern in both groups. In particular, only one patient in treatment group shifted from VHM stage-2 to stage-1 while all patients in VHM stage-1 did not show variation of pattern (p=NS).

Discussion

After 4 weeks of treatment there has been a significant clinical improvement of CVI symptoms in patients treated with supplement as evaluated with VCSS.

Interestingly, there has been a significant improvement of symptoms, particularly as regards the itching and paresthesias. In addition, there was a significant reduction of leg's pain, albeit of lesser impact respect to the reduction of itching / paresthesia.

The positive effect on the symptoms can be attributed to anti-inflammatory and antioxidant properties of the complex-Ginkgo biloba / alpha-lipoic acid and the antioxidant activity and affinity of Leucoselect complex for the rich districts of glycosaminoglycans (GAGs) such as venous vessels. In a previous study Leucoselect[®] Phytosome[®] has been proven able to reduce oxidative stress [4] while some reports suggested a protective effect of α -Lipoic acid on endothelial cell damage [5] and antioxidant proprieties [6]. In particular, the alpha-lipoic acid plays cytoprotective action against free radicals [6,11], especially protecting the nerves in the case of induced degeneration (itching / paresthesia symptomatology). The leucocianidine (Leucoselect) shows an activity of reducing vascular permeability, savings of vitamin E, chelation of iron and copper, inhibition of protease (hyaluronidase, collagenase, elastase). Then, the protective action against venular endothelium is expressed through the adhesion of leucocianidine at internal vessel walls with consequent improvement of the elasticity and resistance to breakage [4].

In the same fashion, Ginkgo biloba extract derivatives have been shown as vascular protective agents to attenuate oxidative stress damage [7]. Ginkgo-biloba performs a regulating action on the arterial tone and increase in capillary permeability (increased nitric oxide concentration), therefore it provides vasoprotective action both on venules and arterioles [12]. Furthermore, it has been shown that the synergic use of α -lipoc acid, Leucoselect[®] and Ginkgoselect[®] phytosome is accompanied by an improvement in the levels of numerous cytokines and factors involved in inflammation [11,13].

The absence of significant change to the capillaroscopic pattern may be due to many factors: first, we believe that the four-week time may be insufficient to make a significant improvement to the microcirculation; second, in the majority of cases the patients showed an early stage of microcirculatory alteration and capillaroscopy could not adequately assess the slight microcirculatory improvement. We believe that the study of microcirculation with advanced imaging as laserdoppler or Laser Speckle Contrast Imager could provide further data.

Limitations

This study has the following limitations: First, the relatively small cohort of patient and lack of randomization may have limited the observations. Second, a longer FU is needed to fulfill assess the clinical outcome of such patients. Lastly, the possible positive effect on microcirculation should be assessed also with alternative imaging technique that could analyze minimal variation in microcirculatory pattern.

Conclusion

We have shown clinical improvement of CVI symptoms after 4-weeks of treatment with α -lipoc acid, leucoselect and ginkgoselect

phytosoma. Further researches are needed to evaluate the long-term effect on microcirculation.

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