

ONE-YEAR DIOSMIN THERAPY (600 MG) IN PATIENTS WITH CHRONIC VENOUS INSUFFICIENCY – RESULTS AND ANALYSIS

Ivan V. Batchvarov,
Mariana G. Batselova¹,
Ivan I. Damyanov¹

*Division of Vascular Surgery,
St George University Hospital,
Plovdiv*

¹*Department of Physiology,
Medical University, Plovdiv
Bulgaria*

Corresponding Author:

Ivan V. Batchvarov
Division of Vascular Surgery
Medical University of Plovdiv,
66, Peshtersko Shosse bul.
Plovdiv, 4002
Bulgaria
e-mail: ivbatchv@hotmail.com

Received: June 13, 2010

Revision received: July 26, 2010

Accepted: July 29, 2010

Summary

Chronic venous insufficiency (CVI) is increasingly affecting more and more patients, usually in their prime of life. This is most often a result of negligent examination overlooking varicose veins in different stages of development that present with edema, subfascial tension of the lower legs and, in some cases, even restriction of leg movement. The authors evaluated the efficiency of diosmin (600 mg) received for one year (from November 2007 to February 2008) by 256 patients. These patients were allocated into 4 groups by severity of the respective subjective complaints. Patients in all phases of CVI demonstrated good tolerance to the drug, which was found to have the best effect in reducing the edema in group I and group II (patients with initial symptoms). It also had a very good effect on pain intensity in groups III and IV (patients feeling heaviness and continuous pains in the lower legs in walking).

Key words: diosmin (600 mg), chronic venous insufficiency, vasoprotective therapy

Introduction

Chronic venous insufficiency (CVI) affects an ever increasing number of people, usually in their prime of life. Its progress is most often due to negligent examination, overlooking varicose veins at different stages of development that present with edema, subfascial tension of the lower legs and, in some cases, even restriction of leg movement [1, 2, 3]. Although CVI is a progressive disorder, its terminal stages are not inevitable. The progress of the disease can be slowed down, especially if adequate treatment is used. The complications in CVI are usually associated with inflammatory and thromboembolic processes. Treatment for CVI at different stages requires different approaches: conservative, mini-invasive and surgical.

Conservative treatment aims at disrupting the pathological adhesion, activation and migration of leukocytes, ameliorating venous microcirculation and lymph drainage thus resolving the symptoms of heaviness and edema in the lower legs [4, 5]. We report the results of an evaluation study of diosmin (600 mg) which has been a vasoprotective

therapeutic agent of choice for several years.

The aim of our study was to assessment of the clinical and pathological dynamics of CVI of lower limbs for the specified period of time.

Patients and Methods

We report the results of a study on 256 patients, most of them presenting with chronic venous pathology. A relatively small number of them presented with acute venous pathology. The patients, recruited from Plovdiv and Plovdiv region, received diosmin (Phlebodia®) 600 mg, one tablet a day on an outpatient basis for 60 days from November 2007 to February 2008.

We followed up the following subjective symptoms: sensation of burning in the feet, heaviness in the lower legs, indurative skin

changes in more severe forms (recent history of thrombosis of the deep veins), occasional itching, seasonal cycle of complaints.

We studied following objective findings: lower leg swelling, subfascial muscle tension of the lower leg and expanded pathomorphological picture of post-thrombophlebitis syndrome (PTPS): scleroderma, skin induration, pigmentation and trophic varicose ulceration in the later stages.

As diosmin has a polyvalent action, we also followed up patients with initial (two or three days) history of phlebitis.

The PTPS did not exclude the possibility of continuous treatment of the trophic skin lesions including surgical treatment of the lesions. To facilitate the analysis we divided the patients into 4 groups by severity of clinical picture and pathomorphological findings (Table 1):

Table 1. Distribution of patients by CVI clinical pathomorphological findings

Groups	Clinical findings	Pathomorphological findings	Number of patients
I	Sensation of tension in lower legs in walking, Mild pain afternoons	Swelling up to 1-2 cm	105
II	Mild to moderate pain throughout the day, No skin lesions, Itching in the lower leg	Swelling > 2 cm, Reticular venous changes, Varices in the second and third stage	80
III	Seasonal dynamics in the clinical picture of groups 1 and 2 patients, Aggravation without trophic skin changes.	Subfascial tension in the lower leg	36
IV	Long term history of CVI with refractory lesions	Pathomorphological findings in PTPS, Varicose ulceration	35

Group I – lower leg edema but without phlebotic complications, subjective symptoms – sensation of tension in the leg

Group II – leg circumference bigger by more than 2 cm and predominantly reticular varices

Group III – exacerbation of existent CVI with subfascial tension in the lower leg

Group IV – pathomorphological findings in PTPS and refractory trophic lesions.

During treatment, we used a four-grade scale to assess pain:

0 points – no pain reported

1 point – slight pain

2 points – moderate pain

3 points – strong pain.

The lower leg edema was measured in centimeters.

The data obtained were processed by frequencies of descriptive statistics, while the significance of non-parametric features was measured by t-test and Wilcoxon test (SPSS 13).

Results

CVI was somewhat more frequent among female than among male – 1,9:1 (Fig. 1).

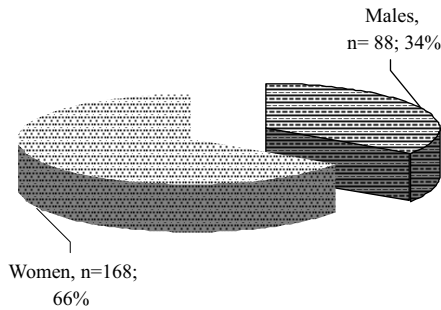


Figure 1. Distribution of patients by sex

The patients with CVI had positive family history and were mostly engaged in jobs featuring static load.

After the administration of the tested medication for 60 days, parameters of pain and edema in all groups were significantly improved ($p < 0.0001$).

Figure 2 shows a reduction of edema after 60 days therapy. The drug was most effective in Groups I and II patients. Edema, the commonest symptom, was managed in 90% (Group I), and 81% (Group II) of the patients. In Group IV (the group with the most severe manifestations) successful treatment was achieved in less than half of the patients (34%).

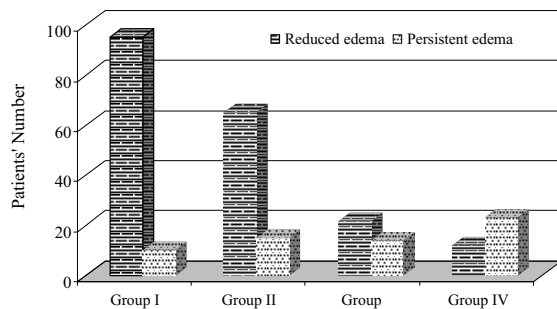


Figure 2. Reduction of the edema - Dynamics of edema

Figure 3 shows a reduction of pain intensity after 60 days treatment. One of the symptoms (usually associated with disability and confinement to bed for recovery) – a sensation of heaviness in the leg which became worse in walking – was best managed in PTPS patients of

groups III and IV. Only 19 (26%) of the 71 patients in these two groups continued to complain of symptoms, restricting their mobility. Of the Group IV patients, only three had trophic lesions in the distal third of lower leg, which were treated with the drug in combination with normal topical application.

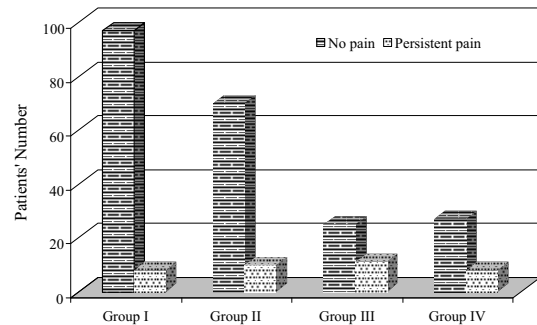


Figure 3. Reduction of pain intensity - Continuous pain and sensation of heaviness in the lower leg

Figure 4 shows a 54-year-old patient, who underwent surgical treatment for the lesion and received diosmin (600 mg) for 60 days. Beginning of healing is clearly visible in the 7 o'clock position. The epithelialization area before treatment was started is also clearly seen.



Figure 4. A 54-year-old patient receiving diosmin 600 mg and surgical treatment for the wound for 60 days

Discussion

Good tolerance to treatment with purified diosmin 600 mg was demonstrated, indicating that it can be used in all stages of CVI. The drug was most effective in reducing the edema in group I and group II patients (patients with initial symptoms). It was also very effective in reducing pain intensity in groups III and IV patients with PTPS. The conservative treatment using diosmin 600 mg as a vasoprotective therapy improved the subjective symptoms we followed up.

Our study showed that the therapeutic effect of long time treatment varied, depending on the severity of clinical picture. The best effect, as far as reduction of edema was concerned, was achieved in groups I and II. Decrease of pain severity was most discernible in group III and IV. According to literature data, the preparation is most effective in the treatment of group II and III patients (classification of chronic venous disease of lower extremities, CEAP) [6, 7].

Our study confirmed the positive restorative effect of the drug, as reported by other authors [8] in combined treatment with diosmin 600 mg and topical treatment in patients with PTPS.

Conclusions

The results of our one-year study indicate that:

Diosmin 600 mg administered in the dose of 1 tablet a day is effective in the management of pain, heaviness and swelling by reducing them, and it is especially effective in milder cases.

When applied for a longer period (2.5-3 months and combined with routine surgical treatment, Diosmin 600 mg has a good effect on severe trophic changes.

Diosmin 600 mg is an effective drug of choice in all stages of CVI, including aggravated forms of the disorder.

References

1. Topalov IB, Anastassov VG, Zanzov ID. Post-thrombophlebitis syndrome. In: Ilieva A, editor. *Physiology and regulation of blood flow*. Plovdiv: State Publishing House; 1986. p. 24-29 (In Bulgarian)
2. Zahariev TT. Modern treatment of chronic venous insufficiency. *Proceedings of the First National Discussion Week on Healthcare Issues*; 2001 March 15-20, Plovdiv, Bulgaria. Plovdiv: TRIMED; 2002
3. Sakakushev GE, Cheshmedzhieva BD. Lower leg varices – a medical and social problem. *Proceedings of the First National Discussion Week on Healthcare Issues*; 2001 March 15-20, Plovdiv, Bulgaria. Plovdiv: TRIMED; 2002
4. Shoab SS, Porter JB, Scurr JH, Coleridge-Smith PD. Effect of oral micronized purified flavonoid fraction treatment on leukocyte adhesion molecule expression in patients with chronic venous disease: a pilot study. *J Vasc Surg*. 2000;31(3):456-461
5. Arcelus JI, Caprini JA. Nonoperative treatment of chronic venous insufficiency. *Journal of Vascular Technology*. 2002;26(3):231-238
6. Kirienko AI, Bogachev Vyu, Zolotukhin IA, Golovanova OV. Semisynthetic Diosmin (Phlebodia 600) for therapy of lower limb chronic venous insufficiency. *Angiologia i sosudistaia khirurgia* 2006;12(2):73-75 (In Russian)
7. Pokrovskii AV, Sapelkin SV. Derivatives of semi-synthetic diosmine in the treatment of patients with chronic venous insufficiency. The results of a prospective study-using phlebodia 600. *Angiologia i sosudistaia khirurgia*. 2005;11(4):73-9 (In Russian)
8. Vakhart'ian PE, Gavrilenko AV, Kim EA. Combined therapy of lower limb variceal disease. *Angiologia i sosudistaia khirurgia* 2008;14(4):93-96 (In Russian)