THE EFFECT OF A COMBINATION COMPLEMENTARY MEDICATION ON VENOUS TONE

A Research Dissertation presented to the Faculty of Health Sciences, University of Johannesburg, as partial fulfilment for the Master's Degree in Technology: in the programme Homoeopathy

by

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Abstract

Low venous tone (LVT) occurs when the veins in the lower limbs can no longer sufficiently pump enough blood back to the heart. Symptoms may include dull aching and cramping, itching or tingling in the calves, swelling redness or any colour changes as well as thickening of the skin in the lower limbs (Comerota, 2009). The most common indication of LVT is dilated veins known as varicose veins(Glovicski et al., 2011). LVT is a disorder found more commonly in females. Conventional treatment for LVT includes vein ligation or stripping, elastic compression, valve reconstruction and sclerotherapy venous bypass(Van den Bos et al., 2009). Amongst other treatment, exercise has also proven to be effective as it increases circulation, by increasing blood returning to the heart (Behrens and Michlovitz, 2006). A variety of herbal supplements have been proven to be safe and effective in the treatment of LVT.A combination complementary medication of red leaf extract, butcher's broom extract, horse chestnut extract and vitamin B6 has been formulated as an over-the-counter product in South Africa, to treat LVT without any anticipated adverse effects (Venavine-Nativa, 2014). Red vine leaf extract has also been proven to be useful in the treatment of LVT. Previous studies on the red vine leaf extract have shown that it is an effective and safe source of treatment (Kaluset al., 2004). Studies done on horse chestnut extract have stated that the extract increases venous tone and decreases capillary permeability, and butcher's broom extract has been proven to be effective in the treatment of LVT (Lim and Davies, 2009). There are currently no studies done on the combination of red vine leaf extract, butcher's broom extract, horse chestnut extract and vitamin B6 on symptoms associated with LVT.

The aim of this study is to determine the efficacy of a combination complementary medication of red vine leaf extract (360 mg), horse chestnut extract (60 mg), butcher's broom extract (35 mg) and pyridoxine (vitamin B6) (3.2 mg) in the treatment of symptoms associated with LVT, using a venous clinical severity score questionnaire (VCSS).

A double-blinded, placebo-controlled design will be conducted at the University of Johannesburg (UJ) Health Centre, over 12 weeks. This research sample will be shared with another researcher, Miss Xoliswa Mazibuko, who evaluated the quality

of life with the use of CIVIQ questionnaire when treating LVT with the combination of red leaf extract, butcher's broom extract, horse chestnut extract and vitamin B6. This study investigated any changes in physical symptoms.

Forty one female participants between the ages of 30 and 55 years were recruited via advertisement placed at the UJ Health Centre and on the University of Johannesburg Doornfontein campus. A total of thirty three participants had completed the study. At the initial consultation, all respondents will be screened to see if they qualify to participate in the study. After the screening procedure, participants were paired according to the severity of their symptoms. This was determined by the number of symptoms experienced by each participant as mentioned in the inclusion criteria; and their current age. Each participant was paired with another participant experiencing the same or similar severity of pain and current age, according to matched pairs and placed in group A or B. Participants in group A had received a placebo capsule consisting of starch amyral white, di calcium phosphate DC and magnesium stearate as in-actives (Venavine-Nativa, 2014) and participants in group B had received the capsule that contained the active ingredients red vine leaf extract (360 mg), horse chestnut extract (60 mg), butcher's broom extract (35 mg) and pyridoxine (vitamin B6) (3.2 mg). Once they qualified to participate in the study, a consent form was signed and completed. Participants then completed a VCSS questionnaire, with the help of the researcher, to assess their symptoms. Participants were given medication for the next thirty days and were instructed to take one capsule every morning. Follow up consultations took place after every thirty days at which participants completed the VCSS questionnaire, with the help of the researcher, underwent a physical assessment and receive additional medication for the next thirty days. The final consultation took place after 12 weeks.

The Friedman test showed that the experimental group had a statistically significant improvement for the pain outcome measure and total combined score of the VCSS questionnaire after the 12-week period. The Mann Whitney U test for inter-group analysis showed that there were statistically significant differences between the experimental group and the control group for the pain outcome measure after the 12-week period, and for the venous oedema outcome measure at week 8 and week 12; and for the total combined sores of the VCSS questionnaire after the 12-week

period.

Results from this study shows the herbal combination complementary medication, containing red vine leaf extract, horse chestnut extract, butcher's broom extract and vitamin B6 is effective in treating physical symptoms of LVT, when using the total combined scores of VCSS questionnaire, thus accepting the hypothesis. Further research is however needed to validate and support these findings.

Introduction

Definition

Low venous tone (LVT) occurs when the veins in the lower limbs cannot pump sufficient blood back to the heart, causing accumulation of blood and increasing venous pressure (Turpie, 2011).

Epidemiology

The prevalence of LVT is higher in females than in males; 40% of females experience symptoms of LVT whereas 17% of males may experience symptoms (Miessner et al., 2007). Approximately 50% of women between the ages of 40-50, and 75% of women between the ages of 60-70 experience some symptoms of LVT during their lifetime (Beede-Dimmer, 2005).

Aetiology

The usual and most likely cause of LVT is venous hypertension usually due to incompetent valves. Factors which contribute to this are prolonged standing, pregnancy, trauma, surgery and genetics (Durham and Hebert, 2012). Genetics my also plays a crucial part in the formation of varicose veins. Various studies have shown that varicose veins are much more prevalent in older people and may be asymptomatic for a long period of time (Krysa et al., 2012). Venous hypertension, due to incompetent valves takes place in either superficial veins, deep veins or perforating veins. Incompetent valves are due to weakness of the valves or damage to the valves caused by certain venous diseases such as thrombosis. Valvular incompetence takes place once the vein wall has been weakened or dilated preventing the normal functioning of valves in the vein (Glovicski et al., 2011). Once blood is not sufficiently transported back to the heart, venous blood starts to

accumulate and increases the pressure within the lower limbs. As pressure starts to increase, venous hypertension develops. Venous hypertension may cause valvular incompetence, reflux and even venous obstructions. Accumulation of venous blood may affect superficial veins as well as deeper veins (Eberhardt and Rafelto, 2005). Valvular incompetence or weakened valves with increased venous pressure cause superficial veins to become dilated or tortuous; these are known as varicose veins (Glovicski et al., 2011).

Signs and symptoms

LVT is a disorder affecting the lower limbs commonly presenting as dilated veins such as telangiectasia, reticular veins and varicose veins (Eberhardt and Rafelto, 2005). Once the superficial and deep veins become affected, clinical manifestations such as oedema, cutaneous hyperpigmentation, fibrosis, dermatitis, pruritus and subcutaneous tissue damage start to occur. Venous oedema occurs when there is an accumulation of fluid between the interstitial spaces; pitting oedema occurs when there is protein in the interstitial fluid while turgor skin indicates that the symptom is more chronic (Behrens and Michlovitz, 2006). Patients experiencing LVT commonly complain about heavy, tired and painful legs which tend to worsen throughout the day; these are typical signs that the disease is progressing and becoming more chronic (Butcher, 2005).

Treatment

Initial treatment in most cases of LVT, is to reduce any primary symptoms in order to prevent any secondary complications; such as CVI that may arise (Goldman et al., 2011). A non-invasive and most common treatment technique of LVT is elevation of the lower limbs (Cooper, 2013). Compression therapy is used to decrease any oedema in the lower extremities. It causes a compression in the greater part of the lower part of the limb and gradually reduces the oedema, by pushing fluid upwards, towards the knee and towards the heart (Moffat et al., 2009). Pharmacological treatment has also been effective in the treatment of LVT. Certain drugs have proven to have venoactive properties causing an improvement in venous tone and capillary permeability (Eberhardt and Rafelto, 2005). Ablative therapy is the use of thermal energy to create radiofrequency directly over the veins. This type of therapy is usually used when bigger veins such as the saphenous vein becomes distended due

to the accumulation of blood (Merchant and Pichot, 2005). Exercise is another effective treatment, as calf and foot muscles contact causing an increase in the upward flow of blood in the peripheral circulatory system. Exercise tends to rehabilitate muscles responsible for contraction, thereby reducing symptoms of LVT (Eberhardt and Rafelto, 2005).

Venavine Intensive® is a combination of red vine leaf extract, butcher's broom extract, horse chestnut extract and vitamin B6 that have been researched separately for the treatment of LVT resulting in mild to moderate CVI. It is available over the shelf for self-medication purposes and it has no recorded side effects, provided that the recommended dosage and frequency is used.

Materials and method

Research design

This 12-week double-blinded, placebo-controlled study was conducted to explore the efficacy of a herbal combination complementary medication, containing red vine leaf extract, horse chestnut extract, butcher's broom extract and vitamin B6 in the improvement of physical symptoms associated with LVT, using the VCSS questionnaire as an evaluation tool.

Participants

Forty one female participants between the ages of 30 and 55 years, were recruited via advertisements placed at the UJ Health Centre and on the University of Johannesburg Doornfontein campus.

Selection of participants

The initial consultation (week 0), consisted of signing of the Participant Information and Consent form, followed by a screening test which confirmed if participants qualified to participate in the study.

Inclusion criteria

Participants were included in the study if they were;

- Female
- Between the ages of 30 and 55 years
- Experienced at least three symptoms from CEAP C1-C4 of LVT which includes varicose veins, tired or heavy legs, pain in the legs, tingling calves, venous oedema, induration of the legs, brown discolouration in the legs, skin changes such as erythema in the legs
- Symptoms were aggravated by walking/standing and symptoms were ameliorated by rest and limb elevation.

Exclusion criteria

Respondents were excluded from this study if they;

- Were pregnant or lactating
- Were on chronic medication for cardiovascular disorder
- Had any chronic diseases that was not sufficiently managed
- Experienced CEAPC5-C6 of LVT symptoms including venous ulceration
- Had a previous history of deep vein thrombosis
- Were on Warfarin or blood thinning medication
- Had any liver or kidney pathologies
- Were hypersensitive to any/all herbal extracts
- Were on any treatment (herbal or conventional) for LVT
- Used compression stockings or Kinesio Taping therapy.

Materials

A modified University of Johannesburg case taking form was used to record results from the physical examination. The venous clinical severity score (VCSS) has been previously validated (Vasquez and Muschauer, 2010) but was not created to replace CEAP but rather to compliment it as an assessment for LVT and CVI. Participants than completed the VCSS questionnaire, with the assistance of the researcher.

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Method

Each participant was paired with another participant experiencing the same or similar severity of pain and current age, according to matched pairs. One participant from each pair was then placed into group A and one participant was placed into group B,

thereby placing the participant in either the experimental group or the control group. Medication was labelled as A or B. The researcher, supervisor and all participants were blinded as to which group was the experimental and control group. At the initial consultation (week 0), after signing the consent form and the screening took place , a physical examination was conducted. The physical examination included vital signs as well as a physical examination. Participants than completed the VCSS questionnaire, with the assistance of the researcher. Follow up consultations took place at week 4, week 8 and week 12. Participants were given medication for the following 30 days at follow-up consultations. Participants in the experimental group and the control group were given 30 capsules at each consultation (week 0, week 4 and week 8) (ninety capsules in total) and instructed to take one capsule each morning after breakfast for a 12 week period.

Data analysis

Data was collected from the questionnaire and analysed statistically with the assistance of a statistician at STATKON UJ.

Results

Definitions of statistical tests used

- **The Friedman test**- is a non-parametric test used to analyse results which have been repeated over a period of time. This test aims at analysing repeated measures of variance in the experimental group and the control group.
- **The Mann-Whitney U test**- is used to test independent variables. The Mann-Whitney U test is used when variables are not normally distributed. It analyses changes across groups.
- **The Wilcoxon signed-rank test**- is a non-parametric test used when comparing two related samples, when analysing any changes or differentiating between two mean ranks from related samples or matched pairs (Pallant, 2007).

Results of age distribution

The Shapiro-Wilk test was used to determine whether age was normally distributed ($p>0.05$).

Table 4.1 The Shapiro-Wilk test for age distribution

Group		Sig	Mean
Age	Control	0.174	43,06 years
	Experimental	0.026	43,13 years

Results from the Shapiro-Wilk test shows that age was normally distributed in the control group ($p= 0.174$) but was not normally distributed in the experimental group ($p= 0.026$)

Results of pain outcome measure

The mean value for the control group at initial consultations (week 0) was 1.61. After 4 weeks, the mean value for the control group had a slight decrease to 1.22. Mean values showed an increase in pain from week 8 (mean= 1.39) to week 12 (mean= 1.56) for the control group. According to the Friedman test results, the control group had an insignificant decrease of $p= 0.317$.

On initial consultation (week 0), the pain outcome measure in the experimental group was 1.80. After the 12-week period the pain outcome measure decreased to 0.80.

Results of varicose vein outcome measure

After the 12-week period, the mean rank increased to 2.53. In the control group, symptoms increased at week 4 (mean= 2.56) as well week 12 (mean= 2.33), when compared to week 8 (mean= 2.44).

At the Initial consultation (week 0), the mean rank for the experimental group showed a value of 2.33 and at week 4 (mean rank=2.87) there was an increase in the appearance of varicose veins. Symptoms associated with varicose veins had decreased at week 8 (mean rank=2.47) and returned to 2.33, matching results at week 0 (mean= 2.33) after the 12-week period.

Results of venous oedema outcome measure

After the 12-week period, the control group had an increase in venous oedema outcome measure. Venous oedema increased after week 8 (mean rank= 2.67) and week 12 (mean rank= 2.69) for the control group.

In the experimental group, on initial consultation (week 0), the mean rank for venous oedema outcome measure was 2.73; after the 12-week period it decreased to 2.17. Although there was a decrease in the mean rank of the experimental group, there was no statistically significant difference in either the experimental (p= 0.164) and control group (p= 0.246).

Results of skin pigmentation

Results obtained from Friedman test for both the control group and the experimental group for skin pigmentation outcome measure had decreased over the 12-week period. The control group had a mean rank of 2.64 at week 0, which had decreased to 2.44 after the 12-week period. The control group had a skin pigmentation outcome measure increase at week 8 (mean rank= 2.58). The experiment group had a mean rank of 2.57 at the initial consultation (week 0); this remained the same at week 4 and decreased at week 8 (mean rank= 2.43). After a 12-week period the mean rank was 2.43.

Results of inflammation outcome measure

Symptoms of inflammation ranked higher in the control group than in the experimental group at week 0. Mean ranks of inflammation outcome measures, at initial consultation (week 0) was 2.78 for the control group. There was a decrease in the mean rank of the control group at week 4 (mean rank= 2.56) and week 8 (mean rank= 2.33). There was no further decrease after the 12-week period for the control group (mean rank= 2.33).

At the initial consultation (week 0) the experimental group had mean rank of 2.57, which had remained the same at week 4. At week 8 the inflammation outcome measure had decreased (mean rank= 2.43) and remained the same after the 12-week period (mean rank= 2.43) in the experimental group.

Results of shin circumference outcome measure

Measurements were taken after participants were seated for 30 minutes.

In the control group, the right leg had a mean of 29.81 cm. After the 12-week period, the mean had increased to 30.22 cm. The experimental group had a higher circumference. At week 0, the mean was 29.86 cm. The shin circumference decreased at week 4 (mean= 29.62 cm) and at week 8 (mean= 29.37 cm). After the 12-week period the mean was 29.23 cm (right leg).

At the initial consult (week 0), in the control group, the mean of the shin circumference of the left leg was 29.99 cm. After the 12-week period, the mean for the shin circumference outcome measure of the left leg had increased (mean= 30.48 cm). In the experimental group at the initial consultation (week 0), the mean for the shin circumference was 29.71 cm; at week 4 (mean= 29.71 cm) had remained the same; and decreased after week 8 (mean= 29.33 cm). After the 12-week period the mean for the shin circumference of was 29.29 cm.

Results of total combined scores of VCSS questionnaire

Results showed that at week 0, the control group had a mean rank value of 2.72. At week 4, the mean rank decreased (mean rank= 2.00). The total combined score in the control group had increased at both week 8 (mean rank= 2.50) and after the 12-week period of the study (mean rank= 2.78).

At week 0, the experiment group showed a mean rank of 3.37. This decreased consecutively at week 4 (mean rank= 2.80), at week 8 (mean rank= 2.17) and after the 12-week period (mean rank= 1.67) in the experiment group.

Discussion

Age outcome measure

The Shapiro-Wilk test was used to analyse whether the variable age, in either group, was normally distributed ($p>0.05$). Results showed the variable age in the control group was normally distributed ($p= 0.174$), but was not normally distributed in the experimental group ($p= 0.026$).

Pain outcome measure

Results after a 12-week period showed that the combination complementary medication significantly decreased the pain outcome measure of the experimental group when compared to the control group. The mean value for pain experienced was 1.80 at week 0 and after the 12-week period, the mean value had decreased to 0.80. The Friedman test showed a statistically significant change, p=0.001 for the experiment group after the 12-week period.

Results according to the Mann-Whitney U test shows a statistically significant difference (p=0.016) after the 12-week period.

After the 12-week period, the Wilcoxon signed rank test showed significant statistical changes in the pain outcome measure, after the 12-week period (p= 0.016).

Varicose vein outcome measure

After the 12-week period, the mean rank was 2.33, showing no change in symptoms of varicose veins, according to the Friedman test (p= 0.947). The mean rank for the experimental group after week 4 and week 8 showed that there was a slight aggravation in symptoms associated with varicose veins, but the aggravation was short lived and the appearance of the varicose veins returned to their initial state (week 0) in the experimental group. Results from Table 4.7 showed that after the 12-week, the control group had a p-value of p= 0.947 and the experimental group had a p-value of p= 0.079, showing no statistical significant changes over time.

When comparing results in the control group, the mean rank at week 0 was 2.47, and after the 12-week period, the mean rank was 2.53, showing an aggravation of varicose veins.

Results show that the combination complementary medication was unsuccessful in removing varicose veins but may have prevented aggravations associated with existing varicose veins, further long term studies are required to confirm this.

There was also no statistically significant difference for the Mann-Whitney U (inter-group) test (p= 0.196) for varicose vein outcome measure after the 12-week period.

Venous oedema outcome measures

Results according to the Friedman test shows that the control group had a statistically insignificant difference of p=0.246 and the experimental group had a statistically insignificant difference of p=0.164 after the 12-week period. However, results obtained from the Mann-Whitney U test, show there was a statistically significant difference at week 0, showing a higher incidence of venous oedema in the experimental (mean rank at week 0 was 2.73) when being compared to the control group (mean rank at week 0 was 2.53). Later results from the Mann-Whitney U test show a statistically significant decrease at week 8 (p= 0.030) and after the 12-week period (p= 0.012).

After the 12-week period, the Wilcoxon signed rank test showed a statistically significant change in venous oedema, after week 0 (p= 0.043), after week 8 (p= 0.030) and after the 12 week period (p= 0.012).

Skin pigmentation outcome measure

In the experimental group, there was no increase of skin pigmentation. At week 0, the experimental group had a mean rank of 2.57 and had remained the same at week 4. Skin pigmentation outcome measures decreased at week 8 (mean rank= 2.43) and remained the same after the 12-week period in the experimental group. Although the decrease was not constant, there was no aggravation or increase of skin pigmentation.

After the 12-week period, the control group had a statistically insignificant difference of p= 0.439 and the experimental group had an insignificant significant difference of p= 0.392 according to Friedman test. Results from the Mann-Whitney U test show a statistically insignificant difference of p= 0.190 between the groups after 12-weeks.

Although there is no statistically significant difference according to Friedman test and the Mann-Whitney U test, subjective results reported by participants show that the herbal complementary combination slightly decreased the skin pigmentation and prevented any further pigmentary changes in the experimental group (mean rank at week 0= 2.57; week 4= 2.57; week 8= 2.43 and week 12= 2.43).

Inflammation outcome measure

Results from the Friedman test showed that the presence of inflammation in the control group was 2.78. Inflammation outcome measures in the control group decreased at week 4 (mean rank= 2.56) and week 8 (mean rank= 2.33). After the 12-week period, the mean rank in the control group remained the same as week 8 (mean rank= 2.33).

After the 12-weeks period, according to the Mann-Whitney test, there was no statistical significant difference, p=0.361.

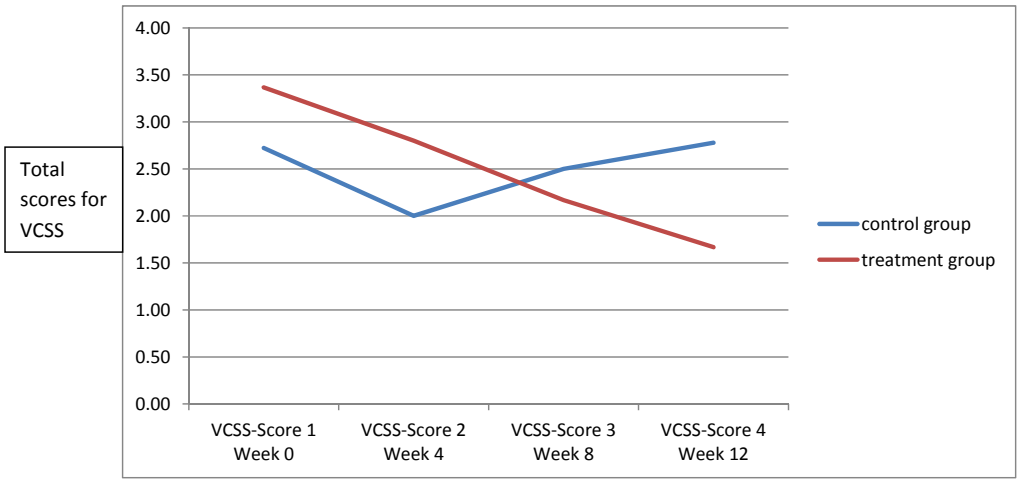
Results after the 12-week period had showed the herbal combination complementary medication had no effect on inflammation as both the control and experimental groups decreased from week 4 to week 8; however this did not change from week 8 to week 12.

Shin circumference outcome measure

According to Friedman test results for the shin circumference outcome measure, in the control group, both the right and left leg had increased in circumference. This increase was consecutive and increased at week 4, 8 and 12. In the experimental group shin circumference for the left leg had remained the same from week 0 (mean= 29.71cm) to week 4 (mean= 29.71cm) for the experimental group. The shin circumference outcome measure for the experimental group had decreased at week 8 (mean= 29.33cm) and 12 (mean= 29.29cm) in the left leg. The shin circumference outcome measure in the experimental group for the right leg had decreased at week 4 (mean= 29.62cm), week 8 (mean= 29.37cm) and after the 12-week period (mean= 29.23cm)

Even though the shin circumference in both legs of participants in the experiment group had decreased successively results from the Mann-Whitney U test showed no significant difference, p=0.198 for the right leg and p=0.138 for the left legafter the 12-week period.

Overall results of VCSS questionnaire



In the experimental group, results from the Friedman test showed that there was a statistically significant difference (p=0.000) in the total combined score of the VCSS questionnaire after the 12-week period. The control group had a statistically insignificant difference (p= 0.129) after the 12-week study.

After the 12-week period the Wilcoxon signed rank test showed a statistically significant change in total combined scores of the VCSS questionnaire had after week 8 (p= 0.024) and after the 12-week period (p= 0.001).

Results from the Mann-Whitney U test shows a statistically difference at week 8 (p= 0.024) and after the 12-week period (p= 0.001)showing overall significant improvement in the experimental group when compared to the control group.

Results from this study shows the herbal combination complementary medication, containing red vine leaf extract, horse chestnut extract, butcher's broom extract and vitamin B6 is effective in treating physical symptoms of LVT, when using the total combined scores of VCSS questionnaire, thus accepting the hypothesis. Further research is however needed to validate and support these findings.

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