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Is Polidocanol Foam Sclerotherapy Effective in Treating Varicose Veins as Compared to Conventional Treatments?

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ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not Polidocanol foam sclerotherapy is effective in treating varicose veins as compared to conventional treatments.

STUDY DESIGN: Review of three randomized controlled trials. All three studies are published in English between 2008 – 2012.

DATA SOURCES: Three randomized control trials were found using PubMED and Medline. The sources were selected based on the outcomes measured and how the studies and outcomes mattered to patients (POEMS).

OUTCOMES MEASURED: The patients' assessment for quality of life analyzed by logistic regression model, Chronic Venous Insufficiency Questionnaire (CVIQ), EQ-5D model, Visual analog scale and Venous clinical severity score (VCSS) and ordinal scale.

RESULTS: Three randomized controlled trials were included in the review. The first study, Rabe et al study showed statistically significant evidence in patient satisfaction ($p= 0.008$) in reduction of symptoms of varicose veins among the polidocanol foam sclerotherapy group as compared to liquid treatment. The second study Shadid et al showed that patient satisfaction of venous symptoms was higher in surgical intervention group (66.1%) as compared to the polidocanol foam sclerotherapy group (59.6%). However, when other factors like cost and cosmetic evidence of scars were considered; polidocanol foam sclerotherapy reflected as a better option. The third study, Ukritmanoroat demonstrates that polidocanol foam sclerotherapy has greater efficacy for venous sclerosis and venous symptoms as compared to polidocanol liquid therapy ($p=0.002$).

CONCLUSION: The systemic review concludes that polidocanol foam sclerotherapy is an effective treatment in treating varicose veins. When compared to different conventional treatments; there are different factors like cost, quality of life post treatment, cosmetic effects of individual treatments that should also be considered when considering the efficacy of the Polidocanol foam sclerotherapy.

KEY WORDS: Polidocanol foam sclerotherapy, varicose veins.

INTRODUCTION

Chronic venous disease has often not been highlighted and it goes unnoticed in the medical field by primary and cardiovascular health care providers because of an under representation of how big the impact and magnitude of the problem on patient lifestyle. There are a lot of people affected by chronic venous disease and the importance of the disease is directly related to the number and the socioeconomic impact of the more severe complications.[1] Lower Extremity venous disease is a very common vascular disorder seen in people as they get older. Chronic venous disease is classified by the presence of morphological (venous dilation) or functional (venous reflux) abnormalities in the veins due to venous insufficiency. The initial clinical presentation of the disease is highly variable and the most common symptoms consist of lower extremity pain or discomfort. Moreover, some of the physical findings include abnormal venous dilation such as telangiectasia, varicose veins, edema, inflammation, dermatitis, or ulceration.[1,2] Moreover, venous insufficiency is also associated with chronic disability, diminished quality of life, and high health care costs. It is seen that periods of high venous pressure due to prolonged standing or heavy lifting are major contributing factors. The highest incidence is seen in women post-partum. The superficial veins are most commonly involved, typically the great saphenous vein.[3,4] The standard treatment used in treating varicose veins was surgical stripping of the vein. However, this paper evaluates three randomized control trials (RCTs) comparing the safety, and efficacy of Polidocanol foam sclerotherapy with other conventional interventions like liquid treatment or surgical interventions.

LE venous insufficiency is a common health problem in Western countries. Varicose veins are very prevalent in the adult population with an estimated prevalence between 5% to 30%, with a female to male majority of 3:1.[4] The Framingham Heart Study, found an annual incidence rate of 2.6% in women and 1.9% in men.[5] The disease has a substantial impact on quality of life,

resources and budgets of healthcare systems. However, the exact cost of treatment of VV is not known; the use of surgery and other interventions cost approximately $2,500 for each patient.[4] As per Eberhardt et al[1], in the year 2002-03, 51,456 of hospital consultant episodes were for VV of LE. Of those consultant episodes 98% required hospital admissions. Moreover, serious complications of venous insufficiency like venous ulcers cost more than $3 billion yearly in US.[1]

Inadequate muscle pump function, incompetent venous valves (reflux), and venous thrombosis or obstruction are causes of elevated venous pressure.[5] The risk factors include advancing age, family history of venous disease, ligamentous laxity, prolonged standing, increased BMI and pregnancy. The factors responsible for a transition from mild to more severe manifestations, and whether or not there is necessarily a sequential progression of the condition, are not well known and the treatment varies based on the severity of the condition. For mild symptoms compression stockings are helpful. However, for more severe form of the disease, different conventional therapies are used such as liquid sclerotherapy, surgical intervention, surface laser therapy, electrodessication, PIN stripping and ambulatory phlebotomy.[4]

All the treatment options mentioned above are effective in treating varicose veins but the long-term efficacy and recurrence varies for each patient and is not studied well. The use of polidocanol foam sclerotherapy has been shown to be cost-effective and less invasive as compared to surgery. It also has a shorter recovery period as compared to the surgical and other interventions.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not Polidocanol foam sclerotherapy is effective in treating varicose veins as compared to conventional treatments?

METHODS

All three studies were randomized controlled trials (RCTs) that evaluated Polidocanol foam sclerotherapy as an effective treatment for treating varicose veins as compared to other conventional interventions. The three studies included in this review used specific criteria for selection of studies. The population included men and women with symptomatic varicose veins over the age of 18 years. All studies excluded any patients with a history of Deep vein thrombosis, venous ulcer, severe arterial hypertension, patients being treated with anti-coagulation medications.

The intervention used in all three studies was Polidocanol foam sclerotherapy. The treatment group was compared to the control groups who were given other conventional interventions such as Polidocanol liquid treatment or surgery interventions. The outcomes measured were safety, efficacy, quality of life and patient satisfaction of polidocanol foam sclerotherapy in treating varicose veins.

Keywords used when searching for articles consisted of varicose veins, polidocanol, foam sclerotherapy. All the articles were in English and in peer-reviewed journals. The articles were researched by the author and obtained through PubMed and Medline. The articles were selected based on the types of studies, its relevance to the clinical question being asked and the patient oriented outcomes (POEMS). The statistics that were utilized and reported included p-value, relative benefit increase (RBI), absolute benefit increase (ABI) and numbers needed to treat (NNT). Table 1 displays the demographics and characteristics included in studies.

Table 1 - Demographics & Characteristics of included studies [2,6,7]

Study	Type	#of pts	Age (yrs)	Inclusion criteria	Exclusion criteria	W /D	Intervention
Rabe[6] 2008	RCT	101	18-70	- Age of 18 and 70 yrs with an incompetent Great Saphenous Vein (GSV) with a diameter <12 mm measured 3 cm below the sapheno-femoral junction (SFJ) - Reflux duration of ≥1 second measured 3 cm below the SFJ under Valsalva maneuver.	Patients with a history of deep vein thrombosis, superficial thrombosis, major leg edema, known patent foramen ovale, were excluded from the trial.	2	Therapeutic treatment with 3% Polidocanol foam vs. 3% Polidocanol liquid
Shadid[7] 2012	RCT	460	20-87	- Presence of 1 or more venous symptoms along with incompetence of the SFJ and GSV and a reflux time >0.5s. -Normal deep venous system on duplex imaging.	-Incompetent deep venous system, signs of deep vein thrombosis on duplex imaging. -Active ulcer or contradiction to the use of polidocanol	26	3% Polidocanol foam vs. surgery
Ukritmanoroat[2] 2011	RCT	50	19-66	- Patients with primary reticular varices (>2mm of diameter) or postoperative varices that did not involve the SFJ.	Patients with truncal varices, post-thrombotic varices with incompetence, Chronic ischemia of the LE. Severe arterial hypertension (blood pressure >180/95mm Hg. Patients on anti-coagulants, anti-inflammatories and/or diuretics	0	Therapeutic treatment with 0.5mL Polidocanol (foam 2mL) vs. baseline matched 0.5ml polidocanol liquid.

OUTCOMES MEASURED

Study outcomes measured were the safety, efficacy of the treatment and health related quality of life of the patients. Outcomes were measured by using different methods. Rabe et al measured outcomes using a Chronic Venous Insufficiency Questionnaire (CVIQ) that consisted of 19 questions and 5 possible answers per question (i.e "not affected", "somewhat affected", "moderately affected", "highly affected", "impossible") that was completed by the patient 3 months after the last treatment. CVIQ is a verified tool for measuring quality of life in patients with venous disease. These were then analyzed using a logistic regression model and analysis of covariance (ANCOVA) scale.[6]

Shadid et al measured outcome based on symptoms reduction, health related quality of life, adverse events and direct hospital costs using a EQ-5d method. The evaluations were done at baseline, 3 months, 1 year and 2 years after the treatment. Patients were asked about the presence of venous symptoms such as pain, cramps, heavy and restless legs. EQ-5D consists of five dimensions (mobility, self-care, usual activities, pain and mood), each of which is rated at three levels (no problems, some problems, severe problems) that yields a possibility of 243 combination health states. Each health state has a utility score from worst possible (0) to best possible (100).[7]

Ukritmanoroat T., measured treatment safety and efficacy in treating varicose veins and venous symptoms such as sclerosis, pain, inflammation, skin pigmentation that was graded on an ordinal scale (absent, mild, moderate or severe). The evaluations were done at 13, 30, and 90 days by research team other than the doctor who performed the treatment. Analysis was done using chi-square test or Fishers' exact test.[2]

RESULTS

All the selected articles are randomized controlled trials. In all three articles Polidocanol foam sclerotherapy is used as an intervention for treating varicose veins. The p-value was significant at $p<0.05$ in all the trials. Rabe et al[6] study comprised of 108 patients with an incompetent GSV. The patients were randomized into two groups; Polidocanol foam (55 patients) and Polidocanol liquid (53 patients). Of the 108 patients who entered the trial, 2 (1.85%) exited the study early due to violation of entry criteria. "Worst-case" analysis was not done on the participants that did not complete the trial. The patient's self-reported assessment of the outcome showed that "improved nicely" or "improved excellent" was selected by 36 patients out of the 55 (66%) who were treated with Polidocanol foam; whereas 22 out of the 53 (42%) patients selected that in the Polidocanol liquid group. The patient satisfaction was significantly ($p=0.0008$) higher in the foam group than in the liquid group. Table 2 shows the treatment effects of Polidocanol foam sclerotherapy and patient satisfaction. Relative benefit increase (RBI) was calculated to be 0.57. Absolute benefit increase (ABI) was calculated to be 24%. Numbers needed to treat (NNT) was calculated 5 patients, indicating that 5 patients need to be treated with Polidocanol foam rather than Polidocanol liquid to see one more patient who had "improved excellently" than compared to liquid treatment.[6]

Table 2: Treatment effect of Polidocanol foam on varicose veins (Rabe et al)

CER	EER	RBI	ABI	NNT	P
42%	66%	0.57	24%	5	0.0008

Shadid et al[7] study comprised of 430 patients with great saphenous varicose veins. The patients were randomized into groups of Polidocanol foam (230) and surgery (200). Of the 430

patients who entered the trial, 40 (9.30%) did not continue with the follow-up. "Worst-case" analysis was not done on the participants that did not complete the trial. Complete patient satisfaction with the reduction in venous complaints was reported by 59.6% of patients in the Polidocanol foam group and 66.1% of those having surgery. P-value was 0.207. Table 3 shows the treatment effects of Polidocanol foam sclerotherapy and patient satisfaction. Relative benefit increase (RBI) was calculated to be -9.8%. Absolute benefit increase (ABI) was calculated to be -6.5%. Numbers needed to treat (NNT) was calculated as -15 patients, indicating that for every 15 patients treated with Polidocanol foam one fewer would have patient satisfaction by the end of their treatment as compared to the surgery treatment.[7]

Table 3: Treatment effect of Polidocanol foam on varicose veins (Shadid et al)

CER	EER	RBI	ABI	NNT	P
66.1%	59.6%	-9.8%	-6.5%	-15.38*= -15	0.207

*Outcome measured was efficacy of foam polidocanol sclerotherapy, so this negative value means that for every 15 patients who took foam polidocanol sclerotherapy, 1 fewer patient was satisfied as compared to the surgery intervention.

Ukritmanoroat[2] study comprised of 50 patients who had more than 1 varicose vein. Each patient received Polidocanol foam at one site and polidocanol liquid treatment at the other site. At the end of the trial all subjects who started the trial were accounted for. No losses to follow-up were noted. Efficacy of treatment and resolution of varicose vein was evaluated at the end of 90 days after the treatment and 92% decrease was noted in the Polidocanol foam treated location and 76% in the liquid treated location. Relative benefit increase (RBI) was calculated to be 21.1%. Absolute benefit increase (ABI) was calculated to be 16%. Numbers needed to treat (NNT) was calculated 7 patients, indicating that 7 patients need to be treated with Polidocanol foam rather than Polidocanol liquid to see one more patient who had "improved excellently" than compared to liquid treatment.[2]

CER	EER	RBI	ABI	NNT	P
76%	92%	0.21	16%	7	0.002

DISCUSSION

This selective evidence based medicine review investigated three randomized controlled trials to determine whether Polidocanol foam sclerotherapy is effective in treating varicose veins as compared to other conventional treatment.

All three trials concluded that when analyzed individually Polidocanol foam is effective in treating varicose veins. When the analysis was done in comparing Polidocanol foam to other conventional treatment like the liquid and surgical intervention the results varied. It was seen that patient satisfaction was significantly higher in Polidocanol foam as compared to the Polidocanol liquid. Whereas, Surgical intervention has higher patient satisfaction in reduction of venous complaints as compared to Polidocanol foam sclerotherapy.

The results of Rabe et al[6] study are generalized to adult patients with varicose veins in the GSV and SFJ and suggests that Polidocanol foam sclerotherapy is very effective in treating varicose veins as compared to liquid intervention. The ABI suggests that 24% of patients receiving Polidocanol foam will have improvement in varicose veins when compared to patients receiving liquid treatment. Some limitations of this study were not being able to follow a “double-blind” protocol due to the mechanism and application of the treatments. Polidocanol foam therapy is easily identified on ultrasound due to it being more echogenic as compared to liquid polidocanol.[6]

The results of Shadid et al[7] study generalized to adult population with varicose veins in the GSV and SFJ. The principal finding was that Polidocanol foam sclerotherapy was not inferior to

surgical intervention when reflux associated venous symptoms and patient satisfaction was considered as the clinical outcome of interest. Hospital costs were also considerably reduced in the foam sclerotherapy group. The ABI of this study was -6.5% which suggests that surgical intervention will have more improvement as compared to foam sclerotherapy. The p-value in this study was 0.207, suggesting that the results are not statistically significant. Also, when comparing other factors like cost and cosmetic effects; surgical intervention as costlier and left bigger scars as compared to polidocanol foam which was cheaper, easily applicable and no scars were left on the skin. The study had some limitations where blinding was not feasible due to the visible scars of post-surgery. However, the analyst assessing the outcome using venous duplex was not involved in the study. Other limitation was the high dropout rate (9.30%) which were mainly from the surgery group.[7]

Ukritmanoroat[2] study is generalized to the adult Thai population and shows that efficacy of foam sclerotherapy is higher than that of liquid injection. The p-value was 0.002 and the ABI suggests that 16% of patients receiving Polidocanol foam will have improvement in varicose veins when compared to patients receiving liquid treatment. The study concludes that polidocanol foam sclerotherapy is more effective in treating varicose veins as compared to liquid polidocanol treatment. The limitation in the study was the population size (50) and demographic where it was confined to only Thai population.[2]

CONCLUSION

Based on this systemic review and chosen studies, Polidocanol foam sclerotherapy is an effective treatment for varicose veins. The efficacy and patient satisfaction is consistent in all three trials and suggest that foam therapy is significant as compared to liquid and surgical intervention.

No serious adverse effects were noted in any of the studies. Some limitations noted were the short term follow-ups of the studies used, smaller population size in one of the study and the demographic limitation in one of the studies used. For a better research and evaluation of treatments for reflux and venous symptoms of recurrent varicose veins, longer follow-up is required for definitive conclusions. As factors such as recurrence, long term adverse-effects, quality of patient life after treatments can be better assessed in longer studies.

Future research should be designed to compare the long term effects of foam sclerotherapy as compared to other conventional interventions specifically surgical intervention.

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