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Hirudotherapy in deep vein thrombosis

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Abstract
In Deep vein thrombosis (DVT) the clot gets adhered within the venous lumen. It is most commonly found in lower limb and this entity can lead to complication like pulmonary embolism. This condition is usually precipitated after orthopaedic surgery, post traumatic, after pregnancy or after chronic ailment. Acute DVT is a well-recognized contributor to increased morbidity and mortality fallowing trauma and elective musculoskeletal procedures. Doppler study reveals the distribution of thrombus and one can go for probe compressibility and vessels diameter to diagnose DVT. Colour Doppler is more sensitive and also facilitates localization of vessels. We are able to identify the morphology of thrombus according to echogenicity whether it is anechoic or hypoechoic as a criteria to determine the chronicity of thrombus which correlated with the duration of complaints of the patient. In Unani system of medicine is based on the principal of humours and these body humours should be restored with adequate quantity and quality. The derangement in the four humours leads to different disease conditions. It is believed that in DVT the thrombotic material is formed due to derangement of the different humours which leads to the deposition of waste material / blood clots in venous system and the most prone vessel is great siphonous vein. The aim of the study is to evaluate the role of Hirudotherapy to resolve the thrombus.

Keywords: DVT, patency of vascular lumen, hirudotherapy, leeching, doppler

Introduction
Deep venous thrombosis is the clot formation in deep vein and the most common vein involved is great saphenous vein, femoral vein, popliteal vein and iliofemoral vein. Most often it comes up with symptoms like swelling, pain, redness or warmth over the affected areas, discoloration and distention of the surface veins. A large number of patients with DVT are symptoms free. The formation of the thrombus can be due to surgery, trauma, sedentary status, chronic illness, lack of exercise, pregnancy, hormonal birth control. Some genetic factors like deficiencies of antithrombin, protein C and S, factor V, leiden mutation. The risk of deep vein thrombosis can be estimated by wells score. The differential diagnosis of DVT include hematoma, tumors, venous or arterial aneurysms and certain connective tissue disorders [1]. Phlegmasia cesulea dolens is a very and serious type of DVT [2]. This type of DVT has acute and almost complete venous ocedusion of entire extremity including the iliac and femoral vein. Anticoagulation (blood thinners) is the standard treatment [3]. Typical medications include low-molecular-weight heparin, warfarin, or a direct oral anticoagulant [4]. Wearing graduated compression stockings may reduce the risk of post-thrombotic syndrome. Preventive efforts following surgery may include early and frequent walking, calf exercises, aspirin, anticoagulants, compression stockings and intermittent pneumatic compression [5]. The rate of DVTs increases from childhood to old age; in adulthood, about one in 1000 adults are affected per year [6]. About 5% of people are affected by a VTE at some point in time [7].

Technique for lower extremity venous ultrasound examination
Step 1: The iliac segment identify the external iliac vein at the groin and follow it cephalad with long axis images. Locate the iliac bifurcation or its approximate position. Follow the common iliac vein cephalad to the inferior vena cava. If you lose track of the vein start at the inferior vena cava and follow the iliac vein inferiorly.

Step 2: The femoral segment use long axis images to identify the external iliac vein at the groin and follow it distally into the common femoral vein. Note the entrance of great saphenous vein. Check Doppler characteristics at the common femoral level. Identify the deep femoral vein and confirm its patency. Return to the groin and check vein compressibility with short axis images and intermittent from the femoral level to the adductor canal. Watch for superficial femoral vein duplication.

Step 3: The great saphenous vein confirm that the proximal portion of the great saphenous vein is patent with long axis color flow veins. Examine as much of the vein as is clinically indicated using short axis intermittent compression.

Step 4: The popliteal segment using long axis veins, locate distal portion of the superficial femoral vein as high as possible in the adductor canal. Follow the superficial femoral vein distal into the popliteal segment to the junction of the tibial trunks confirm the compressibility of the popliteal vein and the tibial trunks with short axis views and intermittent compression watch for popliteal vein duplication.

Step 5: The calf vein examining the posterior tibial veins in their entirety starting either at the popliteal space or at the ankle. Use short axis intermittent compression as the primary mode and supplement with long axis color flow images parallel to veins, examine the peroneal veins similarly. Examine the anterior tibial veins with long axis color flow images. Examine the gastrocnemius and soleal veins as clinically indicated, using long or short axis veins.

Diagnosis

Individuals suspected for DVT is assessed initially clinically and is supported by using wells Score [4, 7] and D-dimer test. D-dimers are a fibrin degradation product, and an elevated level can result from plasmin dissolving a clot-or other conditions [8]. Hospitalized patients often have elevated levels for multiple reasons [9, 10]. When individuals are at a high-probability of having DVT, diagnostic imaging is preferred to a D-dimer test [11, 12]. The UK National Institute for Health and Care Excellence (NICE) recommends D-dimer testing prior to proximal vein ultrasound **[11]** CT scan venography, MRI venography, or MRI of the thrombus are also possibilities [9, 13]. The gold standard for judging imaging methods is contrast venography, which involves injecting a peripheral vein of the affected limb with a contrast agent and taking X-rays, to reveal whether the venous supply has been obstructed, however the diagnosis is more accurately done by color Doppler study with having sensitivity of 97% [14].

Pathophysiology

Virchow's triad i.e. venous stasis, hypercoagulability and change in endothelial blood vessel lining usually contribute to DVT. DVT usually grows in the direction of venous flow which is towards heart. If thrombus is very small it must often dissolves of its own by fibrinolysis [15]. A large and extensive DVT can reach to the inferior vena cava [16]. It is also experienced that veins of arm may also be involved due to local catheterization and due to Paget-Schrötter disease [17]. The beginning of venous thrombosis is said to be caused by tissue factor, which leads to conversion of prothrombin to thrombin fallowed by fibrin deposition [8]. DVT often begins in the valvular part of the veins however white blood cells play a role in the resolution of these clots [15]. Hypoxemia also results in the production of reactive oxygen species, which can activate these pathways, as well as nuclear factor-κB, which regulates hypoxia-inducible factor-1 transcription**.** Hypoxia-inducible factor-1 and early-growth-response protein 1 contribute to monocyte association with endothelial proteins, such as P-selectin, prompting monocytes to release tissue factor-filled microvesicles, which presumably begin clotting after binding to the endothelial surface [18].

Material and Methods

This study is a pilot study done on seven patients of DVT, diagnosed clinically and confirmed by Colour Doppler scanning. Six leeches were applied locally on the site for a period of 40 minutes. The leech therapy repeated after every seven days. It has been observed that DVT was resolved in three to five leech therapies. No recurrence or relapse was observed after following the patients for six months.

Sample Size: Seven Patients.
Duration of therapy: Five weeks.
Fallow up: After one week.
Assessment of efficacy

- Colour Doppler
- Clinically

Distribution of patients

Table 1: According to Mizaj (Temperament)

	***Mizaj* (Temperament)**	**Number of patients**	**Percentage of patients**
1	*Damawi*	1	14
2	*Safrawi*	2	29
3	*Balghami*	3	43
4	*Saudawi*	1	14

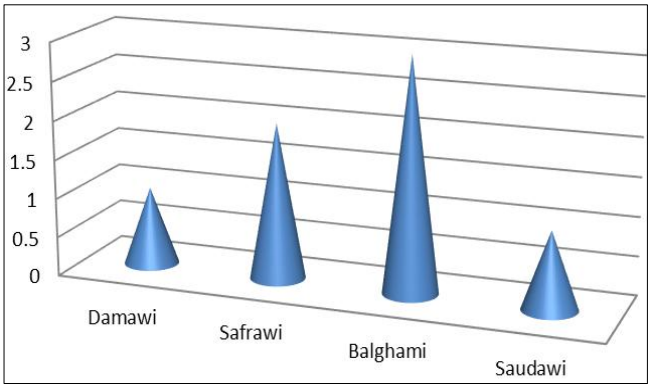

Fig 1: Number of patients according to *mizaj*

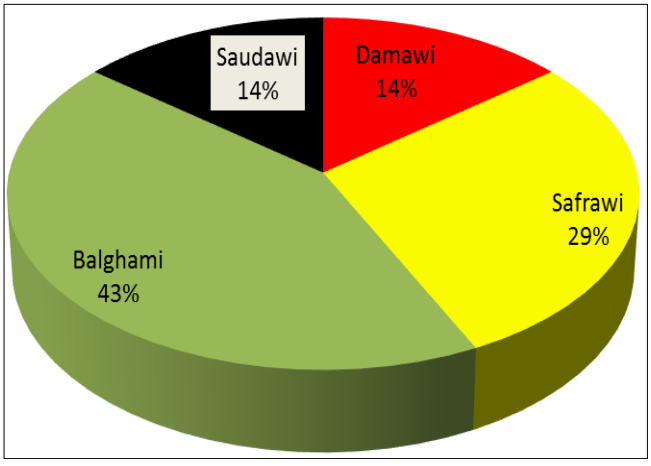

Fig 2: Percentage of patients according to *Mizaj*

Table 2: According to gender

	Gender	**Number of patients**	**Percentage of patients**
1	Male	3	43
2	Female	4	57
3	Transgender	0	00

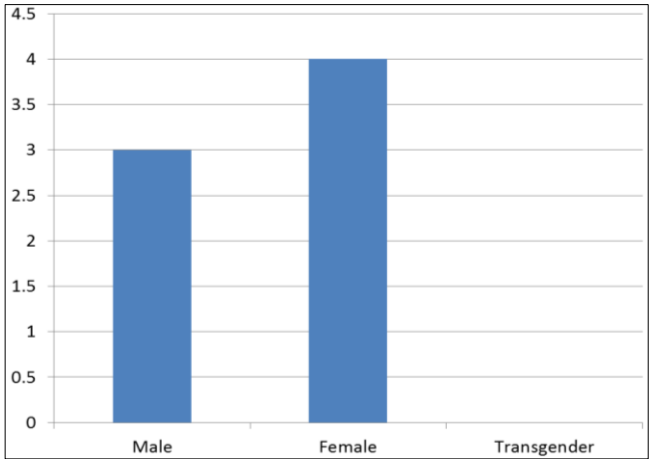

Fig 3: Number of patients according to gender

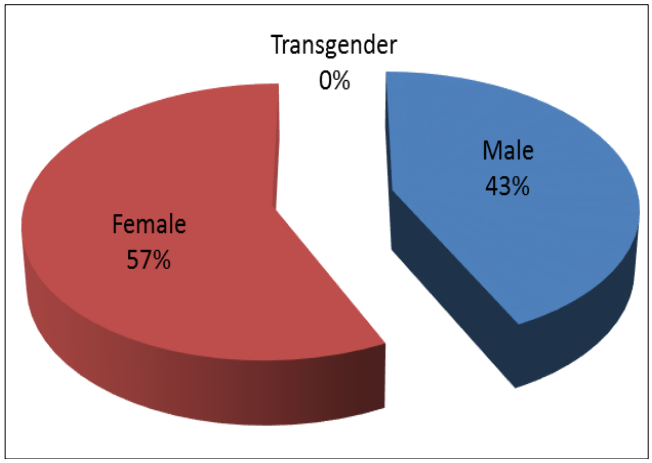

Fig 4: Percentage of patients according to gender

Table 3: According to age group

	Age group	Number of patients	Percentage of patients
1	35-40	2	29
2	41-45	3	43
3	46-50	1	14
4	51-55	1	14

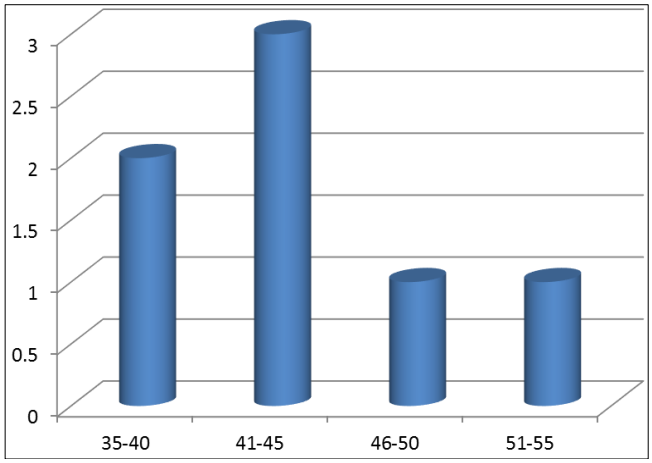

Fig 5: Number of patients according to age group

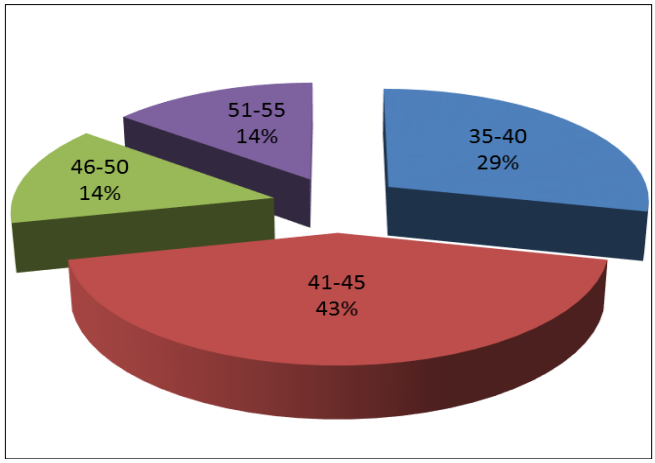

Fig 6: Percentage of patients according to age group

Table 4: According to socio economic status

	Socio economic category	Number of patients	Percentage of patients
1	Upper Class	1	14
2	Middle Class	3	43
3	Lower Class	3	43

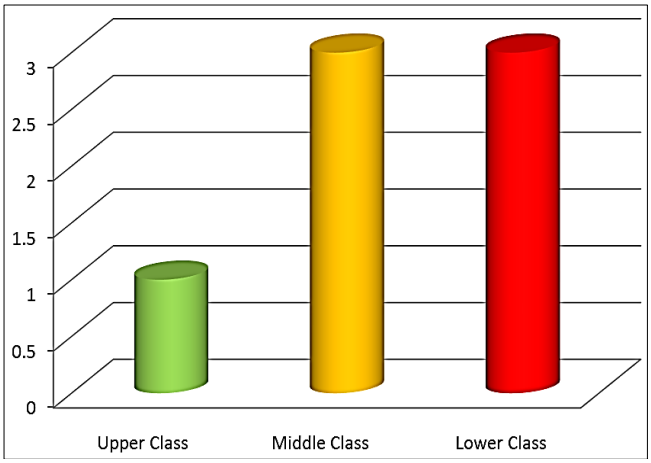

Fig 7: Number of patients according to socio economic status

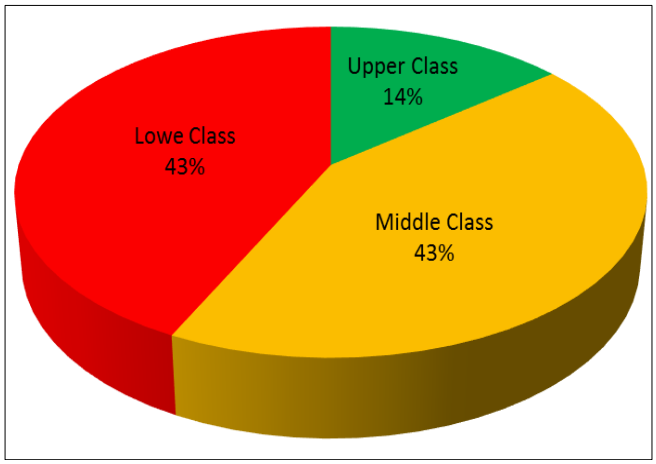

Fig 8: Percentage of patients according to socio economic status

Table 5: According to duration of chief complain

	Duration of Chief Complain	Number of Patients	Percentage of Patients
1	Up to 1 month	4	57
2	Up to 3 month	2	29
3	Up to 6 month	1	14

Table 6: According to intensity of pain (VAS score)

	VAS Score (For Pain)	Number of Patients	Percentage of Patients
1	0-3	4	57
2	3-6	2	29
3	Above 6	1	14

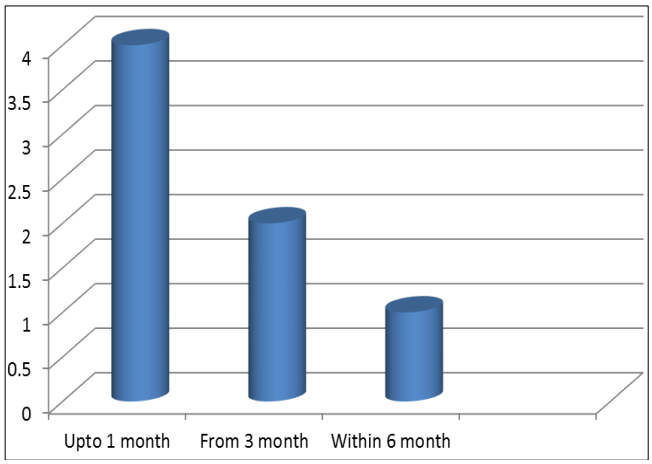

Fig 9: Number of patients according to duration of chief complain

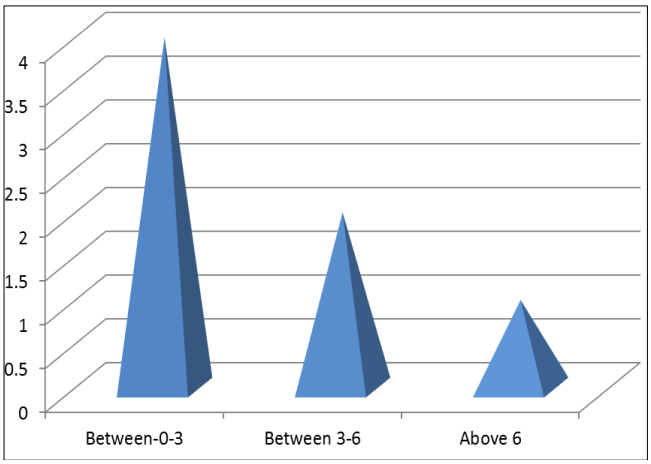

Fig 11: Number of patients according to VAS score

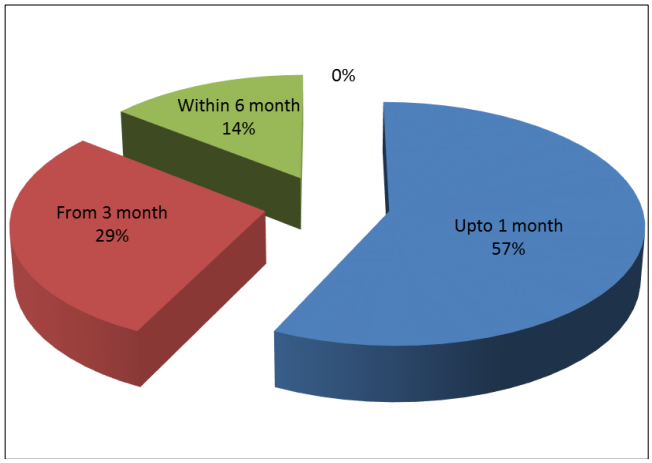

Fig 10: Percentage of patients according to duration of chief complain

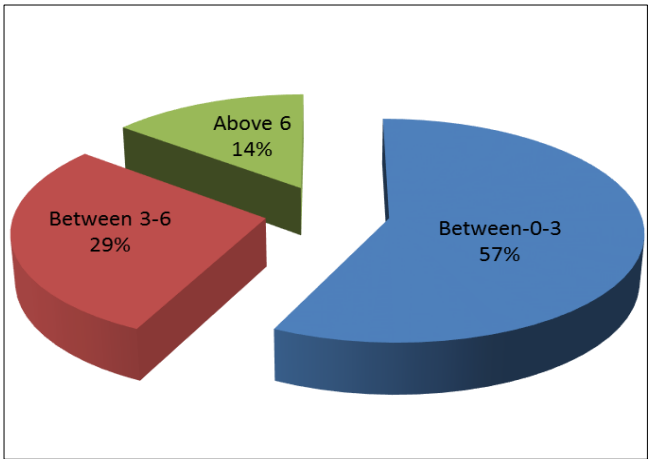

Fig 12: Percentage of patients according to VAS score

Statistical analysis

Table 7: Patency of Vascular lumen after thrombus formation on base line

S. No.	Base Line	Ist fallow up	IInd fallow up	IIIrd fallow up	IVth fallow up	Last fallow up
1	1 mm	1 mm	2 mm	3 mm	3 mm	3.5 mm
2	1.25 mm	1.65 mm	2.10 mm	2.90 mm	3.10 mm	3.4 mm
3	2 mm	2.20 mm	2.96 mm	3.30 mm	3.98 mm	4.4 mm
4	1.5 mm	1.90 mm	2.40 mm	2.45 mm	2.49 mm	2.5 mm
5	3 mm	3.40 mm	3.90 mm	4.20 mm	4.80 mm	5 mm
6	3.6 mm	3.90 mm	4.30 mm	4.80 mm	4.90 mm	5 mm
7	2.2 mm	2.65 mm	2.90 mm	3.25 mm	3.85 mm	4.1 mm

Table Analyzed	Data 1				
Repeated Measures ANOVA					
P value	< 0.0001				
P value summary	***				
Are means sign if different? (P < 0.05)	Yes				
Number of groups	6				
F	52.89				
R squared	0.8981				
Was the pairing significantly effective?					
R squared	0.5558				
F	61.40				

P value	< 0.0001				
P value summary	***				
Is there significant matching? (P < 0.05)	Yes				
ANOVA Table	SS	df	MS		
Treatment (between columns)	20.03	5	4.006		
Individual (between rows)	27.90	6	4.651		
Residual (random)	2.272	30	0.07574		
Total	50.21	41			
Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Base Line vs Ist fallow up	-0.3071	2.953	No	ns	-0.7546 to 0.1404
Base Line vs IInd fallow up	-0.8586	8.254	Yes	***	-1.306 to -0.4111
Base Line vs IIIrd fallow up	-1.336	12.84	Yes	***	-1.783 to -0.8882
Base Line vs IVth fallow up	-1.653	15.89	Yes	***	-2.100 to -1.205
Base Line vs Last fallow up	-1.907	18.33	Yes	***	-2.355 to -1.460
Ist fallow up vs IInd fallow up	-0.5514	5.301	Yes	**	-0.9989 to -0.1039
Ist fallow up vs IIIrd fallow up	-1.029	9.888	Yes	***	-1.476 to -0.5811
Ist fallow up vs IVth fallow up	-1.346	12.94	Yes	***	-1.793 to -0.8982
Ist fallow up vs Last fallow up	-1.600	15.38	Yes	***	-2.048 to -1.152
IInd fallow up vs IIIrd fallow up	-0.4771	4.587	Yes	*	-0.9246 to -0.02964
IInd fallow up vs IVth fallow up	-0.7943	7.636	Yes	***	-1.242 to -0.3468
IInd fallow up vs Last fallow up	-1.049	10.08	Yes	***	-1.496 to -0.6011
IIIrd fallow up vs IVth fallow up	-0.3171	3.049	No	ns	-0.7646 to 0.1304
IIIrd fallow up vs Last fallow up	-0.5714	5.493	Yes	**	-1.019 to -0.1239
IVth fallow up vs Last fallow up	-0.2543	2.445	No	ns	-0.7018 to 0.1932

From the ANOVA and the Tukey's test thereafter, it is evident that there is a significant difference between the base line parameters and the successive follow up parameters which means that Vascular lumen goes on increasing while as thrombus formations goes on decreasing indicating that the treatment is clinically effective.

Discussion

Hirudotherapy is an age old method of bloodletting under regimental therapy and is a widely practiced method of evacuation of morbid humours. Hirudotherapy has been effectively used for the management of different diseases by maintaining the blood perfusion and resolving the vascular thrombotic lesions by way of different important bioactive enzymes including anti-coagulants, vasodilators, anaesthetics etc. Hirudin a potent anticoagulant in leech saliva inhibits the conversion of fibrogen to fibrin, preventing blood from clotting. Since leeches are effective in increasing blood circulation and breaking the vascular deposits and clots. Leeching is of paramount importance in treating cardiovascular and circulatory disorders. Hyaluronidase and collagenase helps in extracellular matrix degradation and in the penetration of drug to the target. Acetylcholine helps in increasing the blood flow. Saratin, calin, apyrase and decorsin are bioactive substances help in inhibition of platelet function and hirudin, gelin, factor Xa inhibitor, destabilase are the substances found in leech saliva and while Hirudotherapy gets transmitted into the body and thus having prominent anticoagulant effect and thus helping in resolving the occluding material in DVT.

Conclusion

Deep venous thrombosis has been a problem reported around 600-900 BC, however it is nowadays a commonest manifestation due to change in life style and work culture. Various pharmacological therapies used in 20th century like oral anticoagulants, subcutaneous LDUH, LMWH and plethysmography were later replaced by surgical intervention and superseded by venous sclerotherapy, endovenous laser ablation, radiofrequency ablation, ambulatory, phlebectomy, foam sclerotherapy and cutaneous laser therapy. In Uanai medicine the intervention of Hirudotherapy proves highly efficacious in varicose vein. Leeches not only sucks blood locally over the varicose veins but also inject the bioactive substances like hirudin, hyaluronidase, acetylcholine, hirudin, decorsin, calin, tryptase inhibitors and natural steroids, which is observed to regulate the venous flow and improve the venous valvular function and thus preventing the backflow.

Result

From the ANOVA and the Tukey's test thereafter, it is evident that there is a significant difference between the base line parameters and the successive follow up parameters which means that Vascular lumen goes on increasing while as thrombus formations goes on decreasing indicating that the treatment is clinically effective.

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Conflict of interest

There is no any conflict of interest exists.

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