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Original Research Article

Assessment of Final Outcome of Ambulation and Exercise in the Management of Patients with Deep Vein Thrombosis in a Tertiary Care Hospital of Andhra Pradesh

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Abstract

Background: Deep vein thrombosis (DVT) was reported as the third commonest cardiovascular disease and a major cause of hospital morbidity and mortality due to its propensity to cause pulmonary embolism and post thrombotic syndrome. Bed rest has been advised historically as the main anchor of its treatment. However early ambulation has its beneficial effects.

Aim of the Study: To study the effects of ambulation and exercise in patients with Deep Vein Thrombosis in its progression and improving limb pain and preventing the risk of thromboembolism.

Materials: 56 patients with different types of DVT were included after confirmation with laboratory and radiological investigations. Patients were divided into two groups; Group A patients were subjected to a fixed protocol of ambulation and exercise. Group B patients were restricted to bed rest. Both the groups received same line of medical treatment containing anticoagulants, DOAC drugs and LMWH. VAS score, Villalta score and limb measurements of patients were used to assess the final outcome. All the data was analyzed using standard statistical methods.

Results: Among the 56 subjects selected for the study, there were 19 (67.85%) males and 09 females (32.14%). The mean age was 49.34±4.10 years in group A and 51.27±4.25 in group B. The mean values of VAS score, Villalta score and limb measurements of patients were similar in both the groups. The p value was 0.461 and there was no difference in the final outcome in both groups; p taken as significant at 0.05. There was no incidence of pulmonary embolism in both the groups. The number of recurrences was 02 in the group A and 08 in the group B. There were no deaths in both groups.

Conclusions: Ambulation and exercises in patients with Deep Vein Thrombosis reduced pain, swelling of the limbs better and earlier than in patients on bed rest. It does not increase the incidence of pulmonary embolism or mortality. It prevents recurrences of DVT.

Keywords: Embolism, Pulmonary Embolism, Mortality, Blood Clots and Ambulation.

Background

Deep Vein Thrombosis is commonly encountered in the medical wards with a prevalence of 0.5/1000 person/ year [1]. The recurrence rate within 6 months of primary diagnosis was 9–10% of patients and 30% of the patients will have recurrence up to 8 to 10 years [1]. Because of its high incidence and potentiality to result in pulmonary embolism, the treating physicians' concern was to provide definite treatment and prevent complications [2]. Confinement to bed was practiced over many years in the treatment of DVT with an intention to prevent dislodgement of the clot in the deep veins and to infuse 24 hour unfractionated heparin [3]. But this treatment was not evidence based and many physicians started to recognize the risk of blood stasis during bed rest [4]. After the invention of low molecular weight Heparin preparations (LMWH) since 1990, DVT patients are now treated as outpatients [5]. In February 2021 the European Society for Vascular Surgery (ESVS) in the European Journal of Vascular & Endovascular Surgery classified the DVT into Unprovoked DVT, Provoked DVT, Proximal DVT, Upper extremity DVT, lower extremity DVT and DVT in special populations [6]. Accordingly, the society also recommended the guidelines to use Direct oral anticoagulant therapy (DOAC), Low molecular weight Heparin (LMWH) dosage schedules [6]. The clinical spectrum of DVT ranges from clinically unsuspected and unimportant status to massive pulmonary embolism resulting in sudden deaths [7]. The clinical presentation of DVT consists of sudden breathlessness, Pleuritic chest pain, and cough, with or without hemoptysis, Syncope especially with massive pulmonary embolism, feeling of impending collapse, associated with apprehension and / or anxiety. The complaints related to the lower extremity DVT are swelling of lower limbs, warm and tender to touch. Tachypnea (Respiratory rate > 20), Tachycardia, loud second heart sound, fever, cyanosis are other common features. There are several publications reporting the management of DVT, pulmonary embolism and progressive DVT patients by many randomized controlled trials (RCTs) and registries of prospective studies which have mentioned early ambulation, exercise and also bed rest [8,9]. Early ambulation and exercise under practical circumstances was suggested in the "9th guideline" of antithrombotic therapy by American College of Chest Physicians (ACCP) [10]. DVT may also arise from splanchnic vein and other atypical locations [11]. Recently cancer related DVT (Cancer associated Venous Thrombosis- CAT) is increasing being added to the literature as the prevalence of cancer is increasing [12]. Both Anticoagulants and thrombolytic agents can be used to treat DVT. The former prevents further clot formation and the later allows the natural fibrinolytic mechanisms of the patients to lyse the existing clot [13]. Heparin and LMWH form the main stay of anticoagulant therapy. DOAC drugs include Coumarin derivative; the prime derivative was warfarin sodium [14]. Both these medicines act by acting upon the clotting factors and co-factors of clotting saccade [15]. Other DOAC drugs used are oral factor Xa inhibitors like rivaroxaban and fondaparinux [15]. As the initial period in patients with acute massive pulmonary embolism (PE) is associated with hemodynamic instability, it is treated by using thrombolytic agent like tissue plasminogen activator [t-PA]. Sometimes surgical intervention may be required in DVT patients to include thrombectomy and/or venous interruption [16]. Early ambulation and exercise are underutilized in the patients with DVT which actually help in preventing the risk of PE and recurrence of DVT [17]. Review of literature showed that an immediate resume of daily movement as compared to complete bed rest, did not exacerbate the post-thrombotic syndrome or subsequent

PE [18]. The present study was conducted in a tertiary care Hospital to study the efficacy of ambulation and exercise in addition to regular treatment of DVT.

Materials

56 patients diagnosed with different types of DVT belonging to both genders were included in this study. The study was conducted over a period of 18 months from May 2016 to November 2018 at Viswabharathi Medical College Hospital, Kurnool, Andhra Pradesh. An institutional ethics committee clearance was obtained and an ethic committee approved consent form was used to conduct the study. Inclusion Criteria: Patients aged above 18 years and below 78 years were included. Patients with all types of DVT including acute and established DVT with or without pulmonary embolism were included. Patients already on therapeutic doses of DOAC drugs were included. Patients willing to participate in early ambulation and exercise regularly were included. Patients without musculoskeletal abnormalities were included. Exclusion Criteria: Patients having DVT with malignancy were excluded. Patients with musculoskeletal diseases interfering with ambulation were excluded. Patients with gross hemodynamic imbalances like right heart failure (RHF), demonstrated on 2D Echo were excluded. Patients with resting hypoxia < 92% were excluded. Patients developing hypoxia on exercise <92% were excluded. Patients developing cardio-pulmonary symptoms like dyspnea, sinus tachycardia, sinus bradycardia, extra systoles and discomfort in the chest were excluded. 56 patients were divided into two groups: Group A: consisted of 28 patients who were allotted to a fixed protocol of early ambulation and exercise and Group B: consisted of 28 patients who were not willing to participate in a fixed protocol of early ambulation and exercise. Both the patients received the similar anticoagulant drugs and DOAC drugs with similar dosage schedules. A random number obtained from "random number generator" from the internet was used to allot the patients to the different groups. Primary outcomes were measurement of weight, height, calculating BMI, physical activity and cardio-respiratory fitness. Laboratory tests: D-dimer test, Compression ultrasonography were used. Other imaging tests: MRI and CT scan (wherever necessary) were undertaken. Medical Treatment schedule: Regimen I: For acute DVT patients the following regimen was used: 1. unfractionated heparin infusion: 18IU/Kg/hour (26 to 30 thousand units/in 24 hours) followed for 5 to 7 days. (APTT values were monitored every 6^{th} hourly for initial 24 hours followed by daily once. The APTT was aimed at 1.52 to 2.5x normal. Platelet counts checked daily. Heparin discontinued when INR was more than '2' for more than 48 hours). 2. Tab Warfarin sodium 2 to 5mg daily; dose adjusted s per INR values (target INR was 2 to 3) for 3 months. Regimen II: For not acute DVT patients the following regimen was used: 1. LMWH was given at 1mg/Kg body weight (average 40mg) every 12 hours (APTT monitored weekly) 2. 2. Tab Warfarin sodium 2 to 5mg daily; dose adjusted s per INR values (target INR was 2 to 3) for 3 months. Exercise schedule: The exercise schedule was depicted in the Table1.

Table 1: Shows the exercise schedule adopted in the study.

Type	Duration- Physical Activity
Warm-up	10 minutes- Easy light movements of legs and arms to prepare muscles for the aerobic and weigh training
Aerobic Exercise	15 to 20 minutes continuous exercise; includes walking or tread mill walking using large muscles in the body, most days in a week.
Weight Training exercise	10-20 minutes of Walking

Cool Down	5-10 minutes Light movements to bring back the heart rate to normal. Stretching to decreases muscle soreness and increases flexibility
Stretching	Up to 5 minutes of light stretching: Hold stretch, keep breathing.

Throughout the exercise schedule the heart rate, respiratory rate, were monitored and in case of discomfort in the chest the exercise was stopped and patient connected to monitor with ECG. BORG Rating of perceived exertion (RPE); (Having scores from 0 to 20) was used to find the intensity level of exercise achieved by the patients; expressed as, Very- Very light: 6 7 8. Very Light: 9 10. Fairly Light: 11 12. Somewhat Hard: 13. Hard: 14 15 16. Very Hard: 17. Very, Very Hard: 18 19 20. A rating of 11-13 was taken as an ideal score. An in house physiotherapist conducted a tolerance test for exercise to all the patients with an invidualized exercise orientation session. The patients were given an option to choose a supervised programme at the cardiac rehabilitation department of Hospital or at home environment. The logs of exercise programmes were reviewed weekly one by the physiotherapist. The final outcome and clinical success was estimated by using the variable like: The final outcome was measured by analyzing the remission of pain in the limb measured using a visual analogue scale (VAS) during the study period in both the A and B groups. As VAS was a subjective and continuous live value an inverse variance method was employed and classified as 4 grades: 0 to 3: poor. 4 to 6: fair. 7 to 10: good. The standard mean difference (SMD) between the group A and B was taken as an effective measure. A 'T' test was used to know the statistical significance using the difference of means in both the groups (p taken as 0.05 was considered significant). Similarly to assess the symptomatic improvement following the treatment a Villalta [19] score was used to assess the post thrombotic syndrome evaluation which grades all the symptoms with a given score; from 0-none, 1-mild, 2-moderate and 3-severe scores. All the data was analyzed using Excel computation sheet. Statistical methods: Mean, standard deviation and percentages were used to describe the variables.

Results

Among the 56 subjects selected for the study, there were 19 (67.85%) males and 09 females (32.14%). The mean age was 49.34±4.10 years in group A and 51.27±4.25 in group B. The age group distribution and other demographic data were tabulated in Table 2. Both the groups were similar and there was no significant difference in variables of the two groups (Table 2). (p value >0.05)

Table 2: Shows the demographic details of the study groups (n-58; A group-28, B group-28).

Observations	Group A (Ambulation and exercise)-28	Group B (Control group)-28	p value
Age			
18 to 27	01 (03.57%)	02 (07.14%)	
28 to 38	04 (14.28%)	04 (14.28%)	
37 to 48	06 (21.42%)	05 (17.85%)	0.977
47 to 58	07 (25.00%)	06 (21.42%)	
57 to 68	06 (21.42%)	07 (25.00%)	
67 to 78	04 (14.28%)	04 (14.28%)	
Mean Age (Yrs), SD	49.35±4.10	51.27±4.25	
Gender			

Male Female	19 (67.85%) 09 (32.14%)	17 (60.71%) 11 (39.28%)	0.146
BMI (Kg m^2), mean, SD	30.55±2.85	31.65±4.75	0.128
Vo_{2max} (mL Kg^{-1} min^{-1}), mean, SD	27.35±2.55	28.45±1.95	0.861
Education < 10^{th} class Pre graduation Graduation and above	 10 (35.71%) 12 (42.85%) 07 (25.00%)	 11 (39.28%) 11 (39.28%) 06 (21.42%)	 0.165
Hypertension Yes No	 11 (39.28%) 17 (60.71%)	 13 (46.42%) 15 (53.57%)	0.854
Diabetes Mellitus Yes No	 07 (25.00%) 21 (75.00%)	 09 (32.41%) 19 (67.85%)	 0.723
Smoker Yes No	 10 (35.71%) 18 (64.28%)	 12 (42.85%) 16 (57.14%)	 0.744
Employment Labourer Officegoer House wife	 12 (42.85%) 09 (32.41%) 07 (25.00%)	 13 (46.42%) 07 (25.00%) 08 (28.57%)	 0.664

Table 3 showed the types of DVT diagnosed and treated in the subjects of the study and the incidence of types of DVT were similar in both the groups and there was no significant difference between the two groups; the p value was >0.05.

Table 3: Shows the types of DVT observed in the study (n-56; Group A-28, Group-B-28)

Type of DVT	Group A- 28	Group B- 28	P value
Unprovoked DVT	08 (28.57%)	07 (25.00%)	0.156
Provoked DVT	03 (10.71%)	04 (14.28%)	
Proximal DVT	06 (21.42%)	05 (17.85%)	
lower extremity DVT	07 (25.00%)	09 (32.14%)	
Upper extremity DVT	02 (07.14%)	01 (03.57%)	
DVT in special populations	02 (07.14%)	02 (07.14%)	

The Table 4 depicted the incidence of different symptoms noticed in the subjects. The symptomatology in both the groups was similar and there was no statistical significant difference among the (p value more than 0.05).

Table 4: Showed the symptoms observed in the subjects ((n-56; Group A-28, Group-B-28)

Symptoms and signs	Group A- 28	Group B- 28
Breathlessness	11 (39.28%)	12 (42.85%)
Pleuritic chest pain	05 (17.85%)	07 (25.00%)
Cough, with or without hemoptysis	06 (21.42%)	07 (25.00%)
Syncope	10 (35.71%)	11 (39.28%)
Feeling of impending collapse	05 (17.85%)	06 (21.42%)
Apprehension and/ or anxiety	14 (50.00%)	15 (53.57%)
Swelling of lower limbs	18 (64.28%)	14 (50.00%)
Limbs warm and tender to touch	21 (75.00%)	19 (67.85%)

Sinus tachycardia	14 (50.00%)	16 (21.42%)
Tachypnea	16 (57.14%)	17 (60.71%)
Loud second heart sound	08 (28.57%)	09 (32.14%)
Fever	22 (78.57%)	21 (75.00%)
Cyanosis	03 (10.71%)	04 (14.28%)

Laboratory investigations were tabulated in Table 5 showed the laboratory values of various tests undertaken in the study, in both the group of patients and it was observed that there was no statistical difference between the values in two groups. P was greater than 0.05; p taken as significant at <0.05.

Table 5: Shows the Lab investigations and Radiological signs noted in the subjects (n-58; A group-28, B group-28)

Lab Investigations	Group A- 28	Group B- 28	P value
Complete Blood Picture			
Normal	06 (21.42%)	09 (32.14%)	
Neutrophilia	12 (42.25%)	11 (39.28%)	
Lymphocytosis	10 (35.71%)	08 (28.57%)	
ESR			
Normal	09 (32.14%)	10 (35.71%)	
Abnormal	19 (67.85%)	18 (64.28%)	0.425
Platelet count			
Normal	22 (78.57%)	24 (85.21%)	
Low counts	06 (21.42%)	04 (14.28%)	
Hb%			
Normal	10 (35.71%)	12 (42.25%)	
<10Gm%	09 (32.14%)	08 (28.57%)	
>10Gms%	09 (32.14%)	08 (28.57%)	
D-Dimer, Mean, SD	6.14 ± 5.35 μg/ml	5.83 ± 6.72 μg/ml	
Compressed Ultra sonogram			
Iliac vein	01 (03.57%)	01 (03.75%)	
Common femoral vein	02 (07.14%)	01 (03.75%)	0.512
Superficial vein	03 (10.71%)	04 (14.28%)	
Popliteal vein	09 (32.14%)	08 (24.75%)	
Calf veins	07 (25.00%)	06 21.42(%)	
No signs	06 (21.42%)	08 (24.75%)	
X-Ray chest PA view			
Normal	23 (82.14%)	25 (89.28%)	--
Abnormal	05 (17.85%)	03 (10.71%)	
CT scan chest/ abdomen/ limbs			
Positive signs	14 (50.00%)	16 (57.14%)	--
Negative signs	14 (50.00%)	12 (42.85%)	
MRI scan chest/ abdomen/ limbs			
Positive signs	13 (46.42%)	15 (53.57%)	--
Negative signs	15 (53.57%)	13 (46.42%)	

The medical treatment regimens used in the subjects of two groups was tabulated in Table 6 and it was observe that there was no difference in allotment of regimens to the two groups in the study; both were similar in adoption of treatment schedules. P value was more than 0.05.

Table 6: Shows the medical treatment given and ambulatory exercises adopted and its quality in the subjects (n-58; A group-28, B group-28)

Type of DVT	Group A- 28	Group B- 28	P value
Unprovoked DVT			
Regimen I	02 (07.14%)	03 (10.71%)	
Regimen II	06 (21.42%)	04 (14.28%)	
Provoked DVT			
Regimen I	01 (03.57%)	01 (03.57%)	
Regimen II	02 (07.14%)	03 (10.71%)	
Proximal DVT			
Regimen I	02 (07.14%)	03 (10.71%)	0.793
Regimen II	04 (%)	02 (%)	
lower extremity DVT			
Regimen I	02 (07.14%)	03 (10.71%)	
Regimen II	05 (17.85%)	06 (21.42%)	
Upper extremity DVT			
Regimen I	01 (03.57%)	00 (00%)	
Regimen II	01 (03.57%)	01 (03.57%)	
DVT in special populations			
Regimen I	01 (03.57%)	01 (03.57%)	
Regimen II	01 (03.57%)	01 (03.57%)	

The ambulatory and exercise schedules adopted in the patients of this study were shown in the Table 7 below. Only group A participated in exercise protocol and group B patients were in bed rest.

Table 7: Shows the BORG PRE- (Perceived Rating of Effort) in the subjects and its effect on clinical improvement of DVT in the subjects (n-58; A group-28, B group-28)

BORG- RPE	Group A- 28	Group B- 28	P value
Very -very light 0 to 5	--	28 (1005)	
Fairly Light [11,12]	05 (17.85%)		0.0001
Somewhat Hard [16,17]	17 (60.71%)	--	--
Hard [18,19]	06 (21.42%)	--	--

The final outcome of the study was assessed using the mean values of VAS score, Villalta score and limb measurements. The p value was 0.461 and there was no difference in the final outcome in both groups; p taken as significant at 0.05. There was no incidence of pulmonary embolism in both the groups. The number of recurrences was 02 in the group A and 08 in the group B. There were no deaths in both groups.

Table 8: Shows the assessment of final outcome of ambulation and exercise in post DVT treatment in the subjects

Parameters for assessment	Group A- 28		Group B- 28		P value
	Before	After	Before	After	
VAS: Mean, SD	4.85±0.75	2.10±0.55	4.60±0.25	3.15±0.65	
Villalta score, Mean, SD	2.55±0.10	1.35±0.10	2.40±0.35	1.95±0.50	
Limb measurement, Mean, SD	86.55±11.35	61.25±8.85	87.50±9.15	77.25±6.45	0.461
Pulmonary embolism	00		00		
Recurrences	02		08		
Deaths	00		00		

(n-58; A group-28 B group-28) Applying T test for significance t value was 0.796566 and p was 0.461 (there was no significant difference between the two groups as p was >0.05)

Discussion

In the present study an attempt was made to study the effects of ambulation and exercise in patients with Deep Vein Thrombosis, in its progression, improving limb pain and preventing the risk of thromboembolism. The hypothesis was that here would be some benefit was possible when patients with DVT were ambulated and exercise was prescribed. The inclusion criteria were chosen to attempt prescribed intervention among a group of patients and accordingly the study was designed. There was no attempt to specify the inclusion criteria for specific outcomes which could have resulted in selected reporting of outcomes. The primary endpoints in the study were measurement of weight, height, calculating BMI, physical activity and cardio-respiratory fitness, D-dimer test, Compression ultrasonography, MRI and CT scan. In a meta-analysis conducted by Zhenlei Liu, Xixi Tao and Yuexin Chen, [19,20]; in their study of "Bed rest versus early ambulation with standard anticoagulation in the management of deep vein thrombosis; a meta-analysis" they pointed out beneficial effects of ambulation over bed rest. They did not take progression of DVT, related deaths and recurrences as end points. They pointed out that exercise did not have any deleterious effects like pulmonary embolism or deaths in DVT patients. Though their results were significant statistically they failed to point out the clinical significance of these results. The authors also concluded that patients on early ambulation though had initial increase in pain but had better pain relief at the end of the exercise schedules. Nadia Aissaoui , Edith Martins , Simon Weber *et al* [19] in a meta-analysis of five studies, concluded that patients with DVT alone or with pulmonary embolism or with both were not associated with higher incidence of pulmonary embolism, recurrence or progression of DVT or death. They did not recommend bed rest as part of early treatment of DVT patients. Hugo Partsch, Werner Blättler *et al* [21] in a study, showed that in Acute DVT patients who were mobile and administered with LMWH were advised early ambulation and exercise with compression bandages were found to have rapid relief of pain and decrease in the limb edema. But there was increase in the risk of pulmonary embolism. In this study there was no increase in the incidence of pulmonary embolism and deaths but had good relief of pain and decrease in the limb edema. Cathy M. Anderson, Tom J. Overend *et al* [22] concluded that their study would make the physicians confident to advise in advising early ambulation as their study did not show any risk in promoting pulmonary embolism by advising ambulation. Partsch, Hugo *et al* [23] concluded that early ambulation and exercise helped in early relief of pain and reduction in the dimensions of limb girth than in patients under bed rest. The progression of size of the thrombus was found to be greater in patients with bed rest. In the present study the final outcome was assessed using the mean values of VAS score, Villalta score and limb measurements. There was no statistical difference in the results of both groups. (p value was 0.461; p taken as significant at <0.05) There was no incidence of pulmonary embolism in both the groups. The number of recurrences was 02 in the group A and 08 in the group B. There were no deaths in both groups.

Conclusions

Ambulation and exercises in patients with Deep Vein Thrombosis reduced pain, swelling of the limbs better and earlier than in patients on bed rest. It does not increase the incidence of pulmonary embolism or mortality. It prevents

recurrences of DVT. The present study provided statistical evidence but the clinical significance in both the groups was similar. Studies with larger number of subjects are necessary to validate the benefits and final outcome to prove ambulation and exercise are beneficial in DVT.

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