

A PROSPECTIVE STUDY OF PHARMACOLOGICAL PROPHYLAXIS OF DEEP VEIN THROMBOSIS IN ARTHROPLASTYK. G. Gopalakrishna¹, Diwakar T. N², K. S. Manjunath³, Annappaswamy⁴**HOW TO CITE THIS ARTICLE:**

K. G. Gopalakrishna, Diwakar T. N, K. S. Manjunath, Annappaswamy. "A Prospective Study of Pharmacological Prophylaxis of Deep Vein Thrombosis in Arthroplasty". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 17, April 28; Page: 4751-4760, DOI: 10.14260/jemds/2014/2506

ABSTRACT: BACKGROUND: Joint replacement surgeries were associated with significant risk of deep vein thrombosis further leading to complications like pulmonary embolism, a need for prevention of complications by using DVT prophylaxis among Indian patients. **OBJECTIVE:** The risk of DVT & pulmonary embolism following joint replacement surgeries were largely studied in western countries whereas the same following arthroplasty was studied to a lesser extent in India. To find out the efficacy of Pharmacological Prophylaxis against DVT (Deep Venous Thrombosis) or PE (Pulmonary Embolism). To find out incidence of DVT (Deep Venous Thrombosis) or PE (Pulmonary Embolism) Despite prophylaxis. **METHODS:** prospective study of pharmacological prophylaxis of deep venous thrombosis in arthroplasty using low molecular weight heparin and aspirin .patients were investigated pre & post operatively with Doppler study for evidence of venous thrombosis. **RESULTS:** Distal DVT was found in two patients who underwent THR; there was no case of proximal DVT with THR and TKR. No DVT was detected in any patient who had undergone TKR preoperatively or postoperatively. **CONCLUSION:** We believe that though there is enough evidence in the Western literature to advocate routine thromboprophylaxis for patients undergoing total joint replacement and surgery for fractures of lower limb, there is not yet enough evidence to justify the same for Indian patients undergoing major lower limb surgery. A duplex sonography should be preferably carried out on all the elderly and high-risk patients undergoing total joint arthroplasty, Trials involving a larger number of patients in future are required.

KEYWORDS: DVT, prophylaxis, arthroplasty.

INTRODUCTION: Total hip replacement has become a standard treatment for patients exhibiting hip joint deterioration by a number of causes, even in the third world countries. Deep vein thrombosis (DVT) is one of the most common complications of total hip arthroplasty (THA), runs high-risk and requires prophylaxis of the highest degree.

The triad of venous stasis, hyper coagulability, and endothelial injury is associated with thrombus formation. The greatest risk of femoral vein occlusion and activation of the clotting cascade occurs during the insertion of the femoral component.

The significance of DVT lies in its ability to cause pulmonary thromboembolism .Proximal DVT usually occurs as a result of local vessel wall injury or an extension of distal DVT. The majority of proximal DVTs can resolve spontaneously without any clinical sequelae, although the rest of them are more likely to result in pulmonary thromboembolism than distal DVT.

The highest risk of occurrence of DVT has been reported to be on the fourth postoperative day,¹ and the second highest, on the 13th day.² The highest incidence of fatal pulmonary embolism occurs in the second week, and the risk is supposed to exist until approximately 3 months after the surgery. The incidence of DVT in the non-operated leg is about 20%.³

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After performing THA without prophylaxis, the incidence of DVT is 40% to 70%; proximal DVT is 10% to 20%; clinical DVT is 1% to 3%; non-fatal symptomatic pulmonary thromboembolism is 1% to 2%; and fatal pulmonary thromboembolism is 0.1% to 1%.⁴ The DVT occurring above the knee level is called as proximal DVT. The popliteal vein enters a window in the adductor magnus, at which point it is termed the femoral vein, previously termed the superficial femoral vein.

The femoral vein ascends and receives venous drainage from the profunda femoris vein, or the deep femoral vein, and after this confluence, it is the common femoral vein. As the common femoral vein crosses the inguinal ligament, it becomes the external iliac vein.

The incidence of proximal DVT is low and that of fatal thromboembolism is very rare, this concerns about efficacy and side-effects of various methods used for prophylaxis & has led to wide spread differences in opinion among orthopedic surgeons in using prophylaxis for DVT. Thus, the whole issue of prophylaxis for DVT is very controversial.

The statistics on DVT are mainly based on various studies of European and American populations. Because there are some genetic differences exist between Asian populations and European and American populations, the incidence of DVT can be different in Asian populations, for example, the incidence of DVT after THA has been insignificant at our institute.

DVT can be diagnosed by using a number of diagnostic modalities. Doppler ultra sonography is a non-invasive and cost-effective modality. It can be used repeatedly, as and when required; it has no side-effects and matches the sensitivity and specificity of the venography as far as proximal DVT is concerned. Low-molecular-weight heparins (LMWHs) are commonly used to provide prophylaxis for DVT after THA. Enoxaparin is one of the most popular LMWHs used for this purpose.⁴

MATERIALS AND METHODS: This clinical study on prospective study of pharmacological prophylaxis of deep venous thrombosis in arthroplasty was conducted in department of Orthopedics, Bangalore Medical College and research institute, Victoria, Bowring & Lady Curzon Hospitals, Bangalore between October 2011 and November 2012. During this period, 50 patients selected on purposive random sampling were treated for prophylaxis of DVT in Arthroplasty. A prior consent was obtained from all the patients and the study was approved by the Ethical Committee of the Hospital.

METHODOLOGY: Required data was collected from patients admitted in Victoria Hospital, Bowring and Lady Curzon hospitals. All patients included in study were assessed pre-operatively with structured questionnaire and physical examination and screened for DVT radiologically by Doppler Ultra sound, Blood investigations like PT and a PTT, with other routine investigations.

A prospective study including 50 patients undergoing THA, TKA and HRA (hemi replacement arthroplasty of hip) was conducted at our institute between October 2011 and November 2012.

EXCLUSION CRITERIA: Patients who have got pre-operative Deep Venous Thrombosis were excluded from the study. Also all patients with risk factors were excluded. All patients undergoing the study were interviewed and comprehensive clinical history and examination was conducted on them to rule out presence of risk factors for DVT like:

1. Previous Thromboembolism
2. Cardiovascular Complications
3. Estrogen use/chronic steroids/anticoagulants

4. Cancer and its treatment
5. Pain and Swelling in the leg
6. Prolonged immobility
7. Trauma
8. Other Major Surgery
9. Stroke
10. Paralysis
11. Chronic smoking.

Preoperative assessment for DVT was done in all patients on both the lower limbs by color Doppler ultrasonography, using a Philips IU-22 ultrasound machine using a linear array high frequency probe 9-11 MHz with grey scale and color Doppler mode. Interpretation of Doppler reports was made by the same radiologist who was unaware of the pharmacological prophylaxis and the study as a deliberate attempt made to remove observer bias.

All patients undergoing for Total Hip Replacement, Total Knee Replacement and Hemi Replacement Arthroplasty in our institution were included & Patients who have got pre-operative Deep Venous Thrombosis were excluded.

Blood Investigations: The following blood investigations done:

CBC, ESR, BT, CT, PT, aPTT, D-Dimer, INR, RBS, Na⁺, K⁺, Urea, Creatinine, Venous Doppler, Chest x-ray, ECG and 2D Echo.

D-dimer assay is a useful test to detect deep vein thrombosis in post-operative patients. A negative D-dimer test rules out deep vein thrombosis & a positive test merits further evaluation.⁵

Indications of THR: Study includes 14 patients with 17 THR. The indications for THR are 5 AVN, 5 Secondary Arthritis, 4 Rheumatoid Arthritis, 2 Fracture Neck of Femur and 1 Ankylosing Spondylitis.

Indications of TKR: Study includes 13 patients with 14 TKR. The indications for TKR are 11 Osteo Arthritis and 3 Rheumatoid Arthritis.

Indications of HRA: Study includes 23 patients with 23 HRA. The indications for HRA are 21 Fracture Neck of Femur, 1 Intertrochanteric fracture and 1 Avascular Necrosis of head of femur.

Radiological Investigations: Venous Doppler done preoperatively to rule out the deep venous thrombosis and post operatively done on 7th day and 3rd week to know whether DVT developed or not, for TKR, HRA and 7th day, 3rd week and 12th week for THR.

Agarwala et al., while comparing color Doppler with venography for DVT evaluation found sensitivity and specificity of color Doppler duplex sonography as 91.6% and 100%, respectively. They recommended color Doppler as a reliable and convenient diagnostic tool for DVT evaluation.⁶

Ching-Jen Wang, MD, (2003), studied that, Ultrasound is a reasonably good alternative to venography in the diagnosis of DVT after TKA.⁷

Post-Operatively examined for symptoms/signs of DVT in the calf and thigh/PE.

Post-Operative Examinations:**Symptoms:**

1. Pain in the calf and thigh.
2. Chest Pain.
3. Breathlessness.
4. Haemoptysis.
5. Mental Status.
6. Fever.

Sign's:

1. Swelling.
2. Warmth.
3. Tachycardia.
4. Calf muscle tenderness.
5. Homan's Sign.
6. Pitting oedema.

DVT Prophylaxis with Injection Clexane 40mg.subcutaneous once a day following 8 hours of surgery for 5 days and Aspirin for 4 weeks.

Expected complication due to Prophylaxis were observed like, Wound hematoma Erythema, Erythema with fever, Wound drainage, Infection, Major bleeding.

Follow - Up: Patients who under gone TKR, HRA were followed till 4th week and who undergone THR were followed for 12th week.

During follow up patients were examined for any symptoms and signs of development of DVT

Doppler ultra sound done for both the lower limbs on 7th day and 3rd week to see the development of DVT for TKR, HRA and 7th day, 3rd week and 12th week for THR.

OBSERVATIONS:

Sex; Of the 50 patients treated surgically, 16 were male and 34 were females.

Age: All patients were in the age group between 26 and 76 years. The youngest patient was a female with fracture neck with non-union who had head and acetabular changes.

Occupation: Majority of the patients were House wives followed by those doing heavy manual labors.

Superficial varicose veins noted in one patient preoperatively. There was no problem of DVT postoperatively.

INDICATIONS FOR SURGERY: Most of the patients under gone THR were avascular necrosis and secondary arthritis, and for TKR Osteoarthritis and for HRA fracture neck of femur.

COMPLICATIONS: Wound hematomas were found in 3 patients. Local bruising found in 2 patients and one patient developed fever with local bruising, all of whom were on enoxaparin. They required prolonged Antibiotic treatment for mean of 7 days. Major hemorrhage and thrombocytopenia did not occur in any of the cases, with enoxaparin.

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Detected DVT: Distal DVT was found in two patients; there was no case of proximal DVT. One of these patients was a 57 year (Case No.7) old woman house wife, who had undergone a bilateral THR for secondary Arthritis of hip. On the 3rd week of postoperative distal asymptomatic DVT was detected on color Doppler ultrasonography.

The other patient was a 41 year old man (Case No.30) who had undergone a THR for bilateral avascular necrosis of femur. He had varicose veins on both legs. Distal asymptomatic DVT was detected on the 3rd week of postoperative color Doppler ultrasonography. There was no pulmonary thromboembolism in either of the patients. They were followed up for 12th week and 10th week respectively and no evidence of post-thrombotic symptoms.

No case of DVT was detected in any other patient who had undergone TKR, HRA in both limbs.

Patients with evidence of deep venous thrombosis underwent follow up Doppler study one week after the detection of thrombus to rule out proximal propagation of the thrombus. Both Patients with distal DVT did not show evidence of further propagation of thrombus on repeat Doppler study. In fact, there was resolution of thrombosis in both the patients. None of the patients developed clinically evident pulmonary embolism while in hospital or during the first four weeks following surgery in TKA, HRA and 12 weeks for THR.

PL Chin, et al. Concluded, in Western population the prevalence of DVT after total knee Arthroplasty has been reported to be 46 to 84%. In Asian population it is lower. But recently has been increasing. This difference may be due to a lack of prothrombotic clotting factor polymorphisms (factor V leiden and prothrombin G20210A) among the Asians⁸. Post-operative deep vein thrombosis is believed to be rare in Asians⁹

RESULTS & ANALYSIS: The average age of patients undergoing THR was 44 years and for TKR it was 61 years. The most common diagnosis in patients undergoing THR were avascular necrosis of head of femur and secondary Arthritis, in TKR it was primary osteoarthritis and in HRA, fracture neck of Femur.

Distal DVT was found in two patients; there was no case of proximal DVT. One of these patients was a 57 year old woman house wife, who had undergone a bilateral THR for secondary Arthritis of hip. On the 3rd week of postoperative distal asymptomatic DVT was detected on color Doppler ultrasonography. The other patient was a 41 year old man who had undergone a THR for bilateral a vascular necrosis of femur. He had varicose veins on both legs. Distal asymptomatic DVT was detected on the 3rd week of postoperative color Doppler ultrasonography.

No case of DVT was detected in any patient who had undergone TKR, HRA preoperatively or postoperatively in both limbs.

Patients with evidence of deep venous thrombosis underwent follow up Doppler study one week after the detection of thrombus to rule out proximal extension of the thrombus. Both Patients with distal DVT did not show evidence of further propagation of thrombus on repeat Doppler study.

In fact, there was resolution of thrombosis in both the patients. None of the patients developed clinically evident Deep venous thrombosis or pulmonary embolism while in hospital or during the first four weeks following surgery in TKA and HRA. Wound hematomas were found in 3 patients. Local bruising was found in 2 patients and one patient developed fever with local bruising, all of whom were on enoxaparin. Major hemorrhage and thrombocytopenia did not occur in any of the cases, with enoxaparin. They required prolonged antibiotic treatment for mean of 7 days.

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Age group	Frequency	Percent
20-29	1	2%
30-39	2	4%
40-49	10	20%
50-59	10	20%
60 & above	27	54%
Total	50	100%

Table 1: Age Incidence

Sex	Numbers	Percentage
Male	16	32%
Female	34	68%
Total	50	100%

Table 2: Sex Distribution

No. of patients	No. of officials	No. of Nurses	No. House wives	No. of labors
50	8	2	18	22
	16%	4%	36%	44%

Table 3: Occupation

Prophalaxis and Venous Thromboembolism Results: This study includes 50 no. of patients which has THR, TKR and HRA for 14, 13 & 23 patients respectively. All patients were investigated with pre-operative Doppler scan and blood investigations like PT and aPTT.

All patients received Thrombo prophylaxis, Injection Clexane, 40mg. subcutaneous, once a day for 5 days, 8hours following surgery & Aspirin continued for 4 weeks. Post operative follow up scan done on 7th day and 3rd week for TKR and HRA and 7th day, 3rd week and 12th week for THR patients.

Distal asymptomatic DVT was noted in 2 THR patients. No proximal or distal DVT detected in TKR and HRA. Also, no sympamatic or Fatal pulmonary embolism noted in all patients.

The study revealed 4% of asymptamatic distal DVT detected during 3rd week follow up scan. DVT resolved during follow up scan without treatment which did not propagate proximlly.

	No. of patients	No. of hip	Avg. Age
THR	14	17	44
M	6	7	45
F	8	10	42

Table 4: THR

	No. of patients	No. of knee	Avg. Age
TKR	13	14	61
M	4	4	68
F	9	10	57.6

Table 5: TKR

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	No. of patients	No. of Hip	Avg. age
HRA	23	23	65
M	6	6	64
F	17	17	66

Table 6: HRA

			THR	TKR	HRA
Total no. of Patients		50	14	13	23
Thrombo prophylaxis received		50	14	13	23
No. of DVT	Proximal		0	0	0
	Distal		2	0	0
Percentage of DVT		4%			
Symptomatic PE			0	0	0
Fatal PE			0	0	0

Table 7: Prophalaxis and Venous Thromboembolism Results

No. of patients under gone THR	No. of patients under gone TKR	No. of patients under gone HRA
14	13	23
28%	26%	46%

Table 8: Percentage of THR, TKR & HRA

Total no. cases	No DVT	With DVT
50	48	2
	96%	4%

Table 9: Percentage of DVT

Complications of Prophylaxis: Our study revealed complications of injection Clexane 40mg subcutaneous once a day for 5 days.

Agarwala et al. found the incidence of DVT to be 45.4% in patients receiving prophylaxis therapy and 71.4% in patients not receiving prophylaxis. However, they did not notice any bleeding complication following thromboprophylaxis.⁶

	No. of operations	Complications found	% of complications
Total	54	Total complications	6 11%
Total no. THR	17	Wound hematomas	3 18%
Total no. TKR	14	Local bruising	2 13%
Total no. HRA	23	Fever with local bruising	1 4%

Table 10: Complications of Prophylaxis

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DISCUSSION: There are not many Indian studies on lower limb VTE after major orthopedic surgeries like lower limb Arthroplasty, as deprived the formulation of guidelines for thrombo prophylaxis.

As per ACCP new guidelines all primary THA and TKA patients are considered “high risk” regardless of patient age, activity level, and co morbidities. The guidelines for thrombo prophylaxis assume greater importance in the face of insurance company liabilities and legal wrangles, apart from delivering a good health care system.¹⁰

The American Academy of Orthopedic Surgeons has slightly deviated to formulate a set of new guidelines for the prevention of symptomatic and fatal Pulmonary Embolism.¹⁰

The AAOS guidelines include:

1. Preoperative evaluation for a determination of “standard” and “high” risk potential.
 2. To use regional anaesthesia.
 3. Mechanical prophylaxis for all patients.
 4. Rapid postoperative mobilisation.
 5. To choose specific chemoprophylaxis agents based on the individual risk benefit profile for PE and bleeding complications.
 6. Adequate patient education.
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1. For patients at standard risk for both PE and major bleeding complications, the recommendations (Grade of B or C, level III evidence):- Aspirin, LMWH, fondaparinux (pentasaccharide), or warfarin (INR goal of 2.0 to 3.0).¹⁰
 2. For patients with standard risk of PE and elevated risk of major bleeding complications, recommendations (Grade C of level 3 evidence):- Aspirin, warfarin (INR goal of 2.0 to 3.0).¹⁰
 3. For patients with elevated risk of both PE and major bleeding complications, recommendations (Grade C of level 3 evidence):- Aspirin, warfarin (INR goal of 2.0 to 3.0).¹⁰

The most important concept in AAOS guidelines for thromboembolic prophylaxis is to assess the risk versus benefit preoperatively. However there is an inherent weakness in the AAOS guidelines to accurately assess the preoperative risk for DVT and PE.

The incidence of DVT is 40 to 60% following THR and 50 – 70% following TKR who don't receive prophylaxis for DVT. The incidence of symptomatic PE is 20% following TKR who don't receive chemo-prophylaxis. . The risk of fatal PE following primary hip or knee replacement has been consistently reported to be between 0.1% & 0.2%.¹⁰

The mortality rate of emboli in total hip arthroplasty patients who do not receive prophylactic medication is reported to be five times greater than that for abdominal and thoracic surgery in patients in the same age group.¹¹

Despite the non-availability of Level-I, studies in Indian or Asian populations, it is recommended to use pharmacological prophylaxis in the patients of THA & TKA. Ramesh K Sen et al reports that Piovela in his largest multicentric study found incident of DVT in 41% following THR and TKR has reported 10.2% of Proximal DVT.¹²

CONCLUSION: We believe that though there is enough evidence in the Western literature to advocate routine thromboprophylaxis for patients undergoing total joint replacement and surgery for

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fractures of lower limb, there is not yet enough evidence to justify the same for Indian patients undergoing major lower limb surgery. A high level of suspicion and close clinical monitoring is mandatory. More trials involving larger number of patients and at multi centres, in future, would be required to confirm the findings of our study to determine the efficacy of low molecular weight heparin.

We recommend thrombo prophylaxis to most of the patients for TJA (Total Joint Replacement)) although we agree with Gillespie et al. that the orthopedic surgeons should use pharmacological prophylaxis only for the high-risk patients (advanced age, past history of DVT, presence of varicose veins, obesity, malignancy, immobilization, etc.) in whom the potential benefits clearly appear to outweigh the risks.

However a duplex sonography should be preferably carried out on all the elderly and high-risk patients undergoing total joint arthroplasty or surgery for lower limb fractures between the seventh day and 3rd week postoperative day and a repeat ultra sonography should be performed on all the positive cases to rule out proximal propagation of thrombus. Trials involving a larger number of patients in future are required to confirm findings of this research which would help resolve the dilemma for the orthopedic surgeons in India whether or not to subject their patients undergoing lower limb surgery to chemoprophylaxis for DVT and PE.

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Date of Submission: 11/02/2014.
Date of Peer Review: 12/02/2014.
Date of Acceptance: 01/04/2014.
Date of Publishing: 28/04/2014.