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ENOXAPARIN FOR DEEP VENOUS THROMBOEMBOLISM (DVT)- REVIEW ARTICLE

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ABSTRACT

Deep vein thrombosis is thrombus formation in deep vein that dominantly occurring in lower limb and pelvis. Enoxaparin is a low molecular weight heparin that has been used widely. The aim of this review is to get evidence base of DVT treatment by enoxaparin. Study was done by search in Pub med with keywords Enoxaparin and DVT and were found 6 articles. Search by data base Science direct with keywords enoxaparin and were found 98 articles. Of these, we only use 32 articles related to this discussion. The results of this study are enoxaparin can used to phropilaxy of DVT on patients undergoing surgery especially hip or knee arthroplasty. Enoxaparin still effective to treat DVT.

Keywords: Enoxaparin, DVT, Pubmed, Science direct

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INTRODUCTION

Deep vein thrombosis (DVT), is a major cause of morbidity and mortality worldwide that prevented. This diseases was caused by thrombus formation in deep vein. Most location of DVT is pelvis and lower limb (1). The estimated DVT incidence is 2/3 of the total VTE and it is estimated to occur 1 per 1,000 people each year (2-4). About 1/3 of DVT cases can develop pulmonary embolism (PE) (5).Venous thrombosis is thrombosis in deep vein that caused by coagulation blood flow in stasis vein. (6-8). Around 10 % in patients suffer DVT was cared in ICU (9). The clinical symptoms of DVT varies depending on the area and location of the thrombus. The cardinal signs and symptoms of DVT are asymmetrical swelling, warmth, or pain in the extremities (10). Suspected Patients DVT was checked D-dimer. The D-dimer level <0.5mg/mL was not DVT. D-dimer level is sensitive but lack of spesivity (11-12). The Gold standard diagnosis is Angiografi and USG USG doppler

TREATMENT by ENOXAPARIN

The goal of DVT treatment is to prevent thrombus formation or spreading of thrombus, preventing pulmonary embolism, and post thrombotic syndrome. The combination Heparin and oral anticoagulan oral are the choose initial treatment (7,13).

Enoxaparin is a low molecular weight heparin anticoagulant. This drug was prepared by alkaline degradation of unfractionated benzylated heparin intestinal mucosa of porcine (14-16). This medicine is indicated to Prophylaxis and treatment of thromboembolism in children; management of venous thromboembolism on pregnancy; anticoagulant therapy during temporary interruption of vitamin K antagonist therapy in patients at high risk for thromboembolism; prophylaxis of DVT following moderate-risk general surgery; major gynecologic surgery and Prophylaxis following higher-risk general surgery for cancer (17).

This medicine act like as unfractionated heparin. Enoxaparin bound anti-thrombin resulting inactivation of Xa factor. The adverse event (bleeding and thrombocytopenia) of low molecular weight heparin lower than unfractionated heparin. Research by Zenáhlíková *et al*., 2010 found that in most patients with sepsis, prophylaxis with enoxaparin did not cause the necessary FXa inhibition. Inhibition of FXa by enoxaparin depends mainly anti thrombin and protein C activity (18). Enoxaparin (40mg subcutaneous daily for 2 weeks) as a low molecular weight heparin effective as prophylaxis against thromboembolism following total knee replacement surgery (19). Enoxaparin prophylactic at dose of 30-mg twice-daily is inadequate in many burn patients to prevent developing deep venous thrombosis (DVT) (20).

A meta-analysis by Patrick *et al*, found that the observed RR (enoxaparin/UFH) of VTE patients with DVT was 0.81 (95% CI, 0.52-1.26) for the intention-to-treat population (RR, 0.70; 95% CI, 0.43-1.13; for per-protocol analysis) (21). Research by Steven *et al*,

2000 that involved 263 patients who underwent total knee arthroplasty, 122 received adjusted low-dose warfarin and 141 received enoxaparin as deep vein thrombosis (DVT) prophylaxis. Three patients in the warfarin group and 3 in the enoxaparin group developed ultrasound-detectable DVT ($P > .05$). From the results, can be concluded that enoxaparin reduced DVT incidence (22).

Borris *et al.* compared use of enoxaparin with dextran 70 as a prophylaxis thrombosis in patients underwent hip arthroplasty. There were 206 consecutive patients underwent hip arthroplasty during thromboprophylaxis involved in this research. A total 6 of 102 (6%) treated by enoxaparin developed deep vein thrombosis (DVT), meanwhile 21 of 104 (20%) in dextran group patients (23).

The once-daily enoxaparin at dose of 1.5 mg/kg subcutaneously has the same effectiveness and safety as conventional treatment with continuous intravenous UFH infusion. However, once-daily enoxaparin regimens are easier to administer (subcutaneously vs intravenously), do not require monitoring of aPTT, and reduce the average hospital stay 4 days shorter (24).

Efficacy of enoxaparin higher than new drug dabigatran at dose of 150 mg, and adverse effect of bleeding from enoxaparin lower than fondaparinux (25). Research by Norwood *et al,* 2001, that covered 118 patients blunt trauma found that enoxaparin prevent venous thromboembolism in this patients. Only 2% patient developed DVT with one of which was proximal to the calf (95% CI, 0% - 6%) (26).A prospective study that designed in which 165 patients with symptomatic, unilateral, first-episode DVT were done by José A.González-Fajardo. The design wass randomized to a long-term anticoagulant treatment with coumarin or enoxaparin during at least 3 months. The results of this research were: the enoxaparin group have lesser incidence of Post-thrombotic syndrome (39.3% absent, 19.6% severe) compare by coumarin group. (29.5% absent, 29.5% severe). The accumulated recurrence rate of enoxaparin lower than coumarin (19.3% vs 36.6% with ($P = .02$) (27).

Clinical Research with animal studies (dogs) by Mooris *et al,* concluded that enoxaparin (100 units/kg (1.0 mg/kg) every 12 hours) inhibited propagation of pre-formed thrombi as effective as dalteparin ((200 units/kg every 24 hours (n=4)) (28).

Research by Riha *et al*, involved 63 patients (28 patients were treated by enoxaparin on 30 mg twice daily, 35 patients on 40 mg once daily). The results of this research were the incidence of DVT in surgical patients who receive 30 mg twice daily higher than 40 mg daily. Enoxaparin at dose of 40 mg per day results peak anti-Xa levels higher than 30 mg twice daily significantly (29).

Enoxaparin has affectivities in prevention of VTE after total knee replacement lower than rivaroxaban and apixaban (direct Xa inhibitors) (30). Research by Kurtoglu, *et al,* 2010, involved 246 patients (128 men with

mean age, 54.28 ± 16.48 vs 118 women with mean age, 50.11 ± 16.47 years old) with symptomatic lower extremity DVT. All patients were included in this open-label, single-arm, multicenter, phase IV clinical trial conducted at 14 centers in Turkey. The research resulted enoxaparin plus warfarin reduced physical symptoms, including tenderness, edema, pain ($P < .001$), and the circumference of the affected leg ($P < .001$). Enoxaparin plus warfarin is effective in improving clinical symptoms by reducing thrombus formation without a significant risk of major bleeding for the outpatient ambulatory treatment of lower-limb deep vein thrombosis (31).

Research by Nurmohamed *et al.*, 1995 involved 1427 patient's postoperative deep vein thrombosis in general surgery. The results were: DVT was detected in 58 enoxaparin-treated patients (8.1%, 95%; CI 6.2% -10.3%) and in 45 patients treated by heparin (6.3%, 95% CI 4.7% -8.4%, $P > 0.05$). Major bleeding complications occurred in 11 patients treated by enoxaparin (1.5%, 95% CI 0.8%-2.7%) and in 18 patients treated by heparin (2.5%, 95% CI 1.5%-3.9%, $P > 0.05$). A total Four patients treated by enoxaparin (0.6%) required reoperation for bleeding as compared to 13 patients in heparin group (1.8%, $P = 0.03$). Enoxaparin (low molecular weight heparin) showed as effective and safe as Heparin (32)

CONCLUSION

Enoxaparin is low molecular weight heparin. This medicine effective to reduce DVT incidence on patients undergoing surgery. Enoxaparin still effective to treat DVT with minor adverse event.

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