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Does Aspirin Like Enoxaparin Effective to Reduce Thromboembolic Disease in Patients with Total Knee Arthroplasty Surgery?

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Thromboembolic disease is a common complication among patients undergoing total hip and knee arthroplasty. There are a large number of clinical trials demonstrating the efficacy of aspirin and enoxaparin in preventing pulmonary emboli and deep venous thrombosis. This study aimed to investigate the preventive role of aspirin and enoxaparin after knee arthroplasty (TKA).
Methods: In this retrospective study, 160 patients undergoing knee arthroplasty at Imam Hossein Hospital, Tehran, Iran between January 2010 and February 2012 were studied. Patients were divided into treatment groups receiving enoxaparin and aspirin and were evaluated within 28 days after surgery. After examining demographic factors including age and sex, variables such as DVT, pulmonary embolus, infection, transfusion RBCs and mortality were evaluated.
Results: A total thrombosis rate of 0.0125% (one deep venous thrombosis) was observed. The two

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groups were not significantly different in the number of patients with complications such as DVT, pulmonary embolism, infection, average number of packed RBCs, and mortality.
Conclusion: We believe that course aspirin is as effective and safe as enoxaparin for thromboprophylaxis.

Keywords: Thromboprophylaxis; total knee arthroplasty; aspirin; enoxaparin; VTE.

1. INTRODUCTION

Venous thromboembolism (VTE) is a highly prevalent complication during and after hospitalization, as well as a serious contributor to surgery and unexpected deaths in hospitals [1]. Patients undergoing knee arthroplasty (TKA) and hip arthroplasty (THA) are at increased risk of VTE in the form of pulmonary embolism (PE) and deep vein thrombosis (DVT) [2]. An epidemiological trial showed that the prevalence of DVT after TKA, THA, and pelvic fracture surgery (HFS) without medicinal thrombopro-phylaxis was 41% in seven Asian countries [3]. Following main orthopedic surgery, increased blood coagulation may remain up to four weeks, while the risk of DVT may last for 3 months after operation [4,5].

Given the increased incidence of VTE, the Scottish Intercollegiate Guidelines Network (SIGN, 2009), the UK-based National Institute for Health and Clinical Excellence (NICE, 2018), the American Academy of Orthopaedic Surgeons (AAOS, 2011), and the American College of Clinical Pharmacy (ACCP, 2012) suggest the consumption of low molecular weight heparin (LMWH) as a preferred factor to prevent thrombosis.

Most VTE happens in discharged patients and this has made it more important to evaluate the long-term prevention of the complication after major orthopedic surgery in patients. Preventive solutions, including compression devices and anticoagulants, are consumed to decrease the occurrence of VTE. Common anticoagulants include low molecular weight heparin (eg, enoxaparin sodium) and antiplatelets (eg, aspirin) [6].

Enoxaparin is parenteral heparin with a low molecular weight. The efficacy of enoxaparin in preventing DVT has illustrated in several clinical trials [7,8]. However, there are safety concerns about bleeding and wound complications, and the exact treatment duration is under debate [9]. Compared with Xa inhibitors, enoxaparin results in higher rates of post-op anemia. European guidelines have remarked that postoperative thromboprophylaxis is necessary for those elderly patients who are able to consume oral anticoagulation as an effective and tolerable manner [10].

Acetylsalicylic acid, known as aspirin, has been supported by a large number of researchers and is one of the agents included in the AAOS guidelines [11]. The benefits of aspirin in preventing pulmonary emboli are shown in literature and regarded as a safe and less expensive regimen [12].

However, aspirin is not recommended by the ACCP due to the concerns regarding its efficacy in preventing PDV [13]. Historical data reflects the existing concerns regarding the consumption of aspirin after arthroplasty for hip and knee [14]. More recently, studies using a combination of aspirin with new surgical techniques and multimodal protocols for thromboprophylaxis have reported considerably low rates of thromboembolic disorders [15].

According to the above, we investigated the effect of aspirin on enoxaparin over a 28-day period as an effective and safe means of chemical thromboprophylaxis.

2. MATERIALS AND METHODS

2.1 Study Population

In this retrospective study, 160 patients undergoing knee arthroplasty at Imam Hossein Hospital, Tehran, Iran between January 2010 and February 2012 were studied.

2.2 Inclusion and Exclusion Criteria

In the present study, the inclusion criteria were patients with knee fracture diagnosed by CT and/or X-ray. Exclusion criteria in this study included patients consuming warfarin or those undergoing simultaneous bilateral arthroplasty procedures, patients who are diagnosed with malignancies, and those with a history of a bleeding disorder or major bleeding

episodes such as intracranial or gastrointestinal bleeding, who require transfusion.

2.3 Treatment Protocol

All surgeries operations were conducted at a dedicated orthopedic hospital by an experienced arthroplasty surgeon. All patients were treated using mechanical calf compression devices. Physical therapy of patients was initiated on the day of surgery or one day after the operation in the afternoon. The general postoperative protocol was otherwise similar in all patients. Patient demographics are included in Table 1. Patients randomly divided into two groups. In group 1 Enoxaparin was begun on postoperative day 1 and 40 mg once daily and followed for 28 days. In the other group, patients received enteric-coated aspirin with a higher dose of aspirin (325 mg twice a day) for a period of 28 days. Follow-up care was carried out at 6 weeks and 6 months. Only symptomatic patients were investigated for pulmonary emboli or deep venous thrombosis. The records of patients were reviewed for any symptoms of infections, post-op transfusion requirements, pulmonary emboli, deep venous thrombosis, and re-admission during 6 months. Patients with possible symptoms of pulmonary embolus or deep vein thrombosis were further investigated using a computed tomographic pulmonary embolus protocol scan or a duplex ultrasound of the symptomatic extremity. Patients who required antibiotic treatment or debridement without component exchange were defined as patients with superficial infections. On the other side, Patients with a need for irrigation or debridement with component exchange were defined as patients with deep infections.

2.4 Statistical Analysis

Data were analyzed using independent samples t-test and Fisher exact test in SPSS 19.0 software and presented as mean ± standard deviation. P-values less than 0.05 ($P < 0.05$) were regarded to be statistically significant.

3. RESULTS

The results of the present study were evaluated in 2 groups. In group 1, 80 cases were reviewed contain 57 men and 33 women with average of age 67.4±8.4 years. Only 1 case (0.0125%) of deep venous thrombosis was documented. In the other 7 evaluated patients, no sign of pulmonary emboli or DVT was found. Moreover, 16 patients (20 %) were transfused packed red blood cells (RBCs).

In group 2, 80 cases were reviewed contain 54 men and 36 women with an average of age 63.1±6.9. Patient demographics are included in Table 1. In group 2 there were 1 (0.012%) deep venous thrombosis. 15(18.7%) patients were transfused packed RBCs. There were no infection and no deaths in two groups. Table 2 summarises the obtained data for each group and shows the resulted P values from the Fisher exact test. No significant difference was found in the range of DVT between the two groups ($P = 0.07$). Similarly, no significant difference was found between the two groups in terms of the number of patients having complications such as infection, pulmonary embolism, the average number of packed RBCs, and mortality.

Table 1. The demographic patient's data

Variable	Group 1	Group2	P-value
Age	67.4±8.4 (52-82)	63.1±6.9 (59-79)	0.087
Gender	57 (71.25%)men	54 (67.5%)men	0.092

Table 2. Comparison of two groups in terms of variables of bleeding, embolism and death

Variable	Group 1(N)	Group 2(N)	P-value
DVT	1	1	0.07
Pulmonary embolus	0	0	1
Infection	0	0	1
Transfusion RBCs	16	15	0.55
Death	0	0	1

4. DISCUSSION

Thromboembolic disease is a common complication among patients undergoing total hip and knee arthroplasty. There is controversy in the exact prevalence of pulmonary emboli and deep venous thrombosis. Prevalence rates over 50% are reported in the absence of prophylaxis [13]. This rate has significantly decreased with the aid of new joint protocols that use early mobilization, modified anesthetic techniques, and mechanical compression devices [16]. Recently, Dorr et al. [17] performed a review of 1179 cases in which they used a multimodal approach to prevent thrombosis. They reported an incidence rate of 0.25% for pulmonary emboli and 5.2% for deep venous thrombosis of which only 0.4% were clinically symptomatic. Even non-chemical prophylaxis protocols have resulted in thrombosis rates below 5% [18,19].

Oster et al by reviewing data recorded in US databases stated that 2.2% of patients undergoing major orthopedic surgeries, develop thromboembolism within the first 90 days after being hospitalized. They reported that 60% of these patients had this problem after discharge [20]. Thus, the use of a suitable thromboprophylaxis method seems necessary. Despite the numerous drugs that have been introduced for this purpose, there is still controversy over the choice of a drug with higher efficacy and fewer side effects [21].

In the present study, the safety and efficacy of enoxaparin and aspirin were evaluated in prevention of VTE after TKA. Our results showed that there was no difference between the two drugs mentioned in reducing DVT, pulmonary embolism, infection, blood transfusion, and mortality.

Enoxaparin is an LMWH with rapid antithrombotic action, linear pharmacokinetics, and limited variable effects [22]. Both of the AAOS and ACCP have supported enoxaparin to be used as chemical thromboprophylaxis after arthroplasty of hip and knee [13]. The use of enoxaparin is also approved by almost all oversight groups including the Surgical Care Improvement Project [23]. However, there are concerns about the safety of this drug, and some complications such as bleeding and wounds have increasingly been noticed by some centers attempting to adhere the ACCP guidelines [24]. Furthermore, there is controversy regarding the exact treatment duration with enoxaparin. While the AAOS has suggested a treatment course of 7 to 10 days, the ACCP recommends a longer course of 28 to 35 days. It is shown that prolonged dose treatment results in reduced rate of geographically documented thromboembolism. However, it remained unclear if this produces any clinical improvements or cost-reducing [25,26].

Using LMWH for prevention of VTE can be equiponderant regarding the weight, and reduce the bleeding after operation. Although more cases of VTE occurred, no mortal pulmonary embolism happened in this study, which is comparable with the results by Fisher [27] and Eriksson [28] and is more desirable than the results by Anderson with one fatal PE. The prophylaxis anticoagulation project delivered in this study was both the safe and effective.

Aspirin has numerous advantages, particularly in outpatient settings. It is such a well-tolerated and inexpensive drug and has a few side effects. The efficacy of aspirin has been demonstrated, especially when used as a part of a multimodal approach [11]. Isolated use of aspirin is not suggested by the ACCP, as a high rate of thromboembolic conditions have been reported in the older literature [13,14].

The use of a short-term aggressive inpatient-only anticoagulation regimen is well documented in previous literature, where the average length of stay with such regimens has declared to be 7 to 10 days [29]. These protocols must be adapted since they decrease the length of stay. In this study, no difference was found in terms of post-op complications. Both the pulmonary emboli and symptomatic deep venous thrombosis were noted only in one patient (0.012%). The results for the rates of infection, bleeding, and symptomatic thrombosis was similar to another group with a 28-days aspirin course. This pilot study was performed to evaluate our thromboprophylaxis protocol. Given the fact that this study is a retrospective review, criticisms toward such a study design are possible. There was no routine monitoring for venous thrombosis, but symptomatic patients were investigated for possible thromboembolic conditions [30]. Owing to the low cases of fatal pulmonary embolus in patients after arthroplasty, it is not possible to compare the mortality rates from pulmonary emboli between the groups. According to AAOS, a demonstration of 50% reduction in the mortality of pulmonary embolus among two groups requires the randomization of 30000 patients. Performing such a study would be cost-prohibitive [31]. The strength points of the present study are that it was unfunded, and addresses the major concerns of arthroplasty surgeons regarding symptomatic thrombosis, bleeding and infection.

Overall, the protocol proposed in this study was effective and safe in patients with a normal risk after arthroplasty of the knee. Moreover, it resulted in low rates of symptomatic thromboembolic cases when combined with early mobilization and mechanical compression devices. Its use resulted in a significant low complication rate and considerable cost savings.

5. CONCLUSION

Our results show that both aspirin and enoxaparin are effective in reducing venous thrombosis in TKA patients. We found that aspirin may be a safe, inexpensive, convenient, and effective alternative to long-term prevention

after TKA. We recommend randomized controlled trials with large-sample, prospective, double-blind in order to perform aspirin efficacy and safety.

CONSENT

As per international standard or university standard written patient consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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