The Gold Standard Anticoagulation Therapy for Post-Op Total Knee/Hip Replacement

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Abstract

Venous thromboembolism (VTE) is seen as an immediate threat to clients experiencing major orthopedic surgeries like total knee arthroplasty (TKA) and total hip arthroplasty (THA). Considering the recognized risks of VTE, arthroplasty surgeons are thoughtful of the requirement for VTE thromboprophylaxis. For instance, it is reported that the occurrence of deep venous thrombosis without the administration of prophylaxis is up to 57 percent with total hip arthroplasty while, with total knee arthroplasty, the proportion is up to 85 percent. Nonetheless, the methods of therapies of thromboprophylaxis applied in the reduction of the dangers to patients have been changing. Clinical practice procedures have been produced by many professional bodies, as some healthcare systems have also set their guidelines. The appropriateness of the anticoagulant used is shaped by the equilibrium between its effectiveness and safety concerning the bleeding risks of the drug. Nevertheless, it is essential to consider a multimodal methodology that emphasizes on early postoperative awareness and the utilization of both anticoagulants and mechanical options.

Keywords: Pulmonary embolism (PE), Prophylaxis, Venous thromboembolism (VTE), Thromboprophylaxis, Deep vein thrombosis (DVT)

Introduction

Venous thromboembolism (VTE) relates to one pathological process that includes the thrombosis of a peripheral vein (DVT or deep venous thrombosis), embolization, and a branch of the pulmonary artery thrombosis (PE or pulmonary embolism) (Budhiparama, Abdel, Ifran & Parratte, 2014). The need for systematic thromboprophylaxis especially for patients with certain high-risk factors is significantly high. Especially amongst patient who undergo surgeries that high risks of postoperative deep vein thrombosis (DVT) or pulmonary embolism (PE). DVT and PE are essential issues of concern regarding public health. The issuance of prevention to those who seem at risk is an essential initiative for the prevention of postoperative wounds and infections. There is increased recognition and orthopedic practice challenge concerning the increased chance of venous thromboembolism and its attendant problems and mortality following major orthopedic procedures, surgical procedures for hip joint ruptures, and arthroplasty of knee and hip joint. The occurrence of deep venous thrombosis without the administration of prophylaxis is up to 57 percent with total hip arthroplasty while, with total knee arthroplasty, the proportion is up to 85 percent (Budhiparama et al. 2014). The rate of pulmonary embolism (PE) is 2 percent of patients following total hip arthroplasty and 1.7 percent of the total knee arthroplasty clients.

It is established that symptomatic venous thromboembolism takes place in nearly 4 percent of clients, implying that it is more common than the problems like luxation and other postoperative diseases like respiratory failure, pneumonia, and bronchospasm. The statistics shown above imply that a safe and useful thromboprophylaxis is needed. Anticoagulant prophylaxis that was used initially, including the unfractionated heparin and then low molecular weight heparins in major orthopedic operation, was prevalent in the final quarter of the 20th

century (Gali, 2017). Nevertheless, research findings have indicated that there are new and improved anticoagulants that are safer and more useful than the initially used interventions. Nevertheless, the focus of this paper is on whether the hospital unit, which uses Lovenox, should replace it with Eliquis, based on the effectiveness, safety, cost-effectiveness of the drugs, and the need for blood draws from the laboratory, among other properties.

Problem Statement

Annually, about 600,000 patients develop venous thromboembolism, while more than 50,000 patients die from blood clots (pulmonary embolism), which block blood circulation to their lungs (Budhiparama et al. 2014). Applying prophylaxis for DVT is not expensive and complicated. Indeed, many studies demonstrate that preventing DVT is more cost-effective as compared to treating its impacts (Gali, 2017). The application of drugs like Lovenox in people who are in danger should be a routine procedure in the orthopedic practice. It is salient to note that the methodology to DVT/PE prevention is similar to preventing postoperative wound diseases like bronchospasm, pneumonia, and respiratory failure. It is essential to know the risks associated with the anticoagulants used in preventing DVT/PE, when to use the preventive procedure, and utilizing the suitable mechanisms when a permanent solution is to be found in regards to the prevention of PE/DVT.

Background

The chances of developing a DVT can increase if individuals have certain risk elements. These include clots, extended periods of immobility like bed rest or traveling on air, trauma, and estrogens (Budovich, Zargarova & Nogid, 2013). The confirmation of a DVT is followed by medication with an anticoagulant. These drugs prevent further blood clots from developing. Examples of anticoagulant used for the prevention include heparin, apixaban, enoxaparin (Kinov,

Tanchev, Ellis & Volpin, 2014). Lovenox, one of the LMWHs, has been authorized for application in the DVT prevention after total hip replacement procedure (Solayar & Shannon, 2014). Clinical tests have indicated Lovenox to be superior to many other blood thinners like dextran, placebo, and unfractionated heparin in DVT prophylaxis. Various published studies have tried to contrast the effectiveness of Lovenox with that of other blood thinners or anticoagulants like Eliquis (Gali, 2017). Finally, economic suitability and sustainability of the health care system should be a criterion for selection of the anticoagulants to be used in preventing DVT/PE. This implies that hospitals have to evaluate the efficiency of the system in regards to the cost of the anticoagulant and balance it against other aspects of effectiveness and safety of the selected drug.

Purpose

The purpose of this project is to evaluate the different anticoagulants therapies for preventing PE/DVT for post-op total knee and hip replacement. It evaluates these drugs with the view of choosing the gold standard anticoagulation between them, i.e., Eliquis and Lovenox. Various recent evidence and sources are utilized to achieve this task. Further, the information and finding obtained from these sources will be significant for the nursing practice, the healthcare systems as a whole, as well as the leadership of the drug production and application. Concerning the nursing practice, the findings will be useful in the orthopedic practice as they will guide the nurses on the best anticoagulant and timing of prevention. The healthcare system and leaders in the drug production and use will also benefit from this project as they will recognize the need to rethink their treatment administration and drug manufacturing processes, respectively.

The Nature of the Project

The project utilized the evaluative research design to accomplish its purpose. It involved the review of various anticoagulant therapies available, including Lovenox, Eliquis, and Aspirin, to determine the best therapy, with the focus on the factors such as the cost of the intervention and effectiveness. Different case studies were accessed in various literature and sources to determine the experiences of these classes of therapies in patients who have undergone hip or knee surgery. It is a cross-sectional project that acquires the information from various sources for evaluation to determine the best intervention concerning the prophylaxis. The research design and approach is more appropriate than other available approaches because it allows the researcher to discern through the cases of blood clots after knee or hip replacement in the orthopedic surgery and reports of the effectiveness of the drugs used during the prophylaxis to understand and evaluate the best anticoagulant.

Research Question(s)

The research question entails, which is the gold standard anticoagulation therapy, between Eliquis and Lovenox, to be used to prevent PE/DVT for post-op total knee/hip replacement?

P= population (sample)/problem

The population is the patients who have undergone total knee/hip replacement or surgery.

I= intervention

The intervention is the anticoagulation therapy, namely, Eliquis vs. Lovenox

C= comparison group

The comparison is the effectiveness of the use of each of the two anticoagulants, that is, Eliquis vs. Lovenox.

O= outcome(s)

The outcome is the selection of either Lovenox or Eliquis.

Summary

This chapter has described the overview of the paper, including the problem statement, research design, background of the topic, research question, and most importantly, the purpose of the project. Both deep venous thrombosis and pulmonary embolism have been seen to cause loss of lives for several clients who have not been offered proper prophylaxis. Besides, the anticoagulant therapy can assist in preventing post-op total knee/hip replacement blood clots from forming if the most efficient anticoagulant therapy is chosen and administered at an appropriate time after knee/hip surgery. The evaluation of the most effective therapy is facilitated through the evaluative research approach in conjunction with the analysis of various case studies presented in different research studies.

LITERATURE REVIEW

Introduction

This chapter intends to offer a review of the literature that will provide the direction for the paper. Different journal articles and previous research conducted will be reviewed to gain an understanding of the topic of focus and help evaluate the various classes of anticoagulant therapies, including the use of Aspirin, Lovenox, and Eliquis.

Historical Overview

Prevention of PE by the vein ligation over the thrombosis region was explained firstly by Homans in 1934. Bilateral ligation of the femoral vein was the most recognized means for prophylaxis of VTE since at that moment there were no drugs for the prevention of the VTE (Budovich, Zargarova & Nogid, 2013). Next, there was an introduction of ligation of inferior vena cava. These two methods diminished sharply given the invention of oral anticoagulants and heparin. The attachment of a filter in the inferior vena cava was later invented in the 1970s. Besides, the indications for its application are VTE with concomitant active hemorrhage or other contraindications for anticoagulant treatment (Gali, 2017). Solayar and Shannon (2014) identified that intravenous heparin was effective in the postoperative VTE prevention.

Further, in the 1980s, the low molecular weight heparins (LMWHs), such as Enoxaparin (Lovenox), were introduced. These drugs have more reduced antithrombin function than anti-factor activity, implying that they can effectively regulate blood clot formation and, therefore, protect the patient from DVT and PE, which may enhance their safety quality. They are also administered in fixed doses as opposed to unfractionated heparin by daily subcutaneous injection and do not need routine laboratory checking (Gali, 2017). This makes them more appropriate for application following the hospital discharge, which is advantageous after the significant joint

arthroplasty. Finally, because of its anti-aggregant property, Aspirin was proposed for prevention of DVT in 1968. Aspirin has a relatively low thromboprophylactic impact. Also, its insignificant decrease of the chance of VTE in clients with ruptures of the hip is followed by problems like surgical wounds bleeding, gastrointestinal hemorrhage, and the urge for red blood cell transfusion when applied in stopping the clotting (Budovich, Zargarova & Nogid, 2013). Moveover, Stacy (2017) added non-steroidal anti-inflammatory drugs (NSAIDs) to the contraindications before administering blood thinning agents as in the pan-Canadian Oncology Symptom Triage and Support (COSTaRS) (p. 94). The risk for bleeding, even fatally, increases with the administration of NSAIDs together with levonox or eliquis post-operatively. Therefore, the drug was not universally suggested for VTE prophylaxis, as per the 2001 and 2006 procedures.

Current Findings

Eliquis/apixaban (one of the factor Xa inhibitors) has been found to be very effective in decreasing the chance of stroke in persons with clotting diseases (Kinov et al. 2014). It is administered in two daily doses of 2.5 mg 12 to 24 hours postoperative (Pineo et al., 2013). The drug does not call for regular blood examinations and no diet regulation as in other blood thinners. Eliquis can reduce the chance of clots forming again around the lung or leg regions. After elective knee-replacement surgery, Bauer (2013) reiterates the findings of other researchers that eliquis has far better efficacy than Lovenox and presents a similar or lower risk of bleeding (p. 2488).

Eliquis is considered as one of the most recent additions to the modern generation of anticoagulants. The drug variety has been instrumental in ensuring that the populace has access to relevant blood thinners. Its superiority in preventing blood clots and internal bleeding is

evidence of the efficiency of the drug. In fact, the research by Knesek, Peterson, and Markel (2012) agree that the drug is the safest amongst the new generation of anticoagulants. The components used in Eliquis have been found to offer reliable protection against the inhibition of coagulation thus ensures that the blood remains thin. Therefore, there is consistent evidence that the drug is an ideal selection for the prevention of clotting. It provides a qualitative measurement for factor Xa inhibitors thereby eliminating incidences of side effects.

The use of anticoagulants plays instrumental roles in ensuring that blood clots are efficiently managed in the body. In DVT, the clots form in the large veins of the body or thighs. In PE, the clot forms in one part of the body then travel to other body parts through the bloodstream. The condition is more prominent when blood clots form in the legs dues to DVT, and then its effects spread to the lungs. The nature of the two clotting situations implies that a reliable anticoagulant will help address the challenge and ensure that the body returns to normalcy.

A major challenge on the use of Lovenox as described by Messerschmidt and Friedman (2015), is that ample tests must be conducted on the victim's blood to identify its efficiency on a patient. The situation may not be favorable especially in times of emergencies. Also, users ought to be aware of the common side effects that may occur when they use the drug. For instance, taking the drug when using aspirin is bound to reduce safety and thus increase bleeding. The process of managing DVT and PE requires the use of drug options that would be useful blood thinners to enhance the safety of the patients and reduce incidences of recurrence. Compared to other forms of anticoagulants, the efficiency of Lovenox for patients who have undergone hip replacement is higher compared to that of Eliquis. In the study by Messerschmidt and Friedman (2015), it was identified that Lovenox has a high oral availability of about 52%. Moreover, it metabolized through cytochrome enzymes and reached a peak efficiency within 3 to 4 hours just

after its administration. Series of clinical trials support the use of Lovenox for the reduction of VTE.

Maniscalco et al. (2014) noted apixaban, among other new oral anticoagulants (NOACs), was developed to outmaneuver the limitations of preexisting anticoagulants. Previous anticoagulants like LMWHs and fondaparinux had the disadvantage of parenteral administration while apixaban requires merely oral administration. Heparin-induced thrombocytopenia by LMWHs and drug-food interactions were also evident with other anticoagulants. Frequent follow-up blood work for patients administered with anticoagulants for dose adjustment is also a thing of the past with apixaban. It enables effective patient-centered care after discharge from hospital with limited incidences of readmission.

Apixaban's pharmacodynamics and pharmacokinetics allow it to function optimally as an anticoagulant. Apixaban's/ Eliquis' remains direct and potent in its mechanism of action with an oral bioavailability of about 52%, peaking in concentration 3 to 4 hours after administration. Its half-life stands at a comfortable 8 to 15 hours allowing the drug to exert its action for durable periods. Metabolic action and other non-renal means are the primary modes of elimination of the drug. Moreover, its elimination rarely leads to the formation of reactive metabolites or even drug-drug interactions. It remains a pharmacologically favorable as a thromboprophylactic after total hip or total knee replacement.

The notable adverse drug-drug interaction for apixaban followed its concomitant administration with aspirin. This regimen would increase the risk of bleeding events (Budovich et al., 2013, p. 211). However, co-administration with aspirin or enoxaparin had a combined effect of increasing the anti-Factor Xa activity by a margin of 50 to 60% (Scaglione, 2013; Budovich et al., 2013, p 211). Moreover, co-administration with drugs that affect the CYP3A4

system and P-glycoprotein would affect the pharmacology of the drug. Ketoconazole is one such drug that affects both these systems interfering with the elimination of the drug. Co-administration with Diltiazem and naproxen has similar effects due to the inhibition of P-glycoprotein. Alternatively, rifampin, phenytoin, phenobarbital, carbamazepine or St. John's wort cause a decrease in eliquis concentration as they are inducers of CYP3A4 and P-glycoprotein that rump up its elimination.

Adverse effects related to thromboprophylactics are primarily bleeding events. Bleeding events with apixaban are mostly within the gastrointestinal tract. With a 5mg BID regimen, Budovich et al. (2013) estimate a maximum of 2.13% rate of major bleeding (p. 212). Other side effects include nasopharyngitis, constipation, nausea, and vomiting. Allergic reactions to the drug have an incidence of less than 1% of patients administered with apixaban (Budovich et al., 2013, p. 212).

Apixaban is contraindicated in patients with severe hepatic dysfunction and patients with a creatinine clearance of less than 15 mL per minute (Budovich et al., 2013). For patients aged above 80 years or weighing below 60 kg, the doses should be reduced to 2.5 mg BID (Budovich et al., 2013). Moreover, co-administration with CYP3A4 and P-glycoprotein inhibitors requires a similar reduction in the dosing.

Budovich et al. (2013) denote the average wholesale price (AWP) of apixaban at $5 per tablet. Given the recommended period of administration of thromboprophylaxis to avoid VTE is around 10 to 14 days after knee arthroplasty, these costs would amount to at least $50 to $70 (Maniscalco et al., 2014, p. 1; Gali, 2017, p. 4). For hip replacement, around 35 days of administration of apixaban are recommended (Gali, 2017, p. 4) This figure is well above the AWP of warfarin ($0.58 to $0.99) even over its 30-day period of administration; however, the

cost-effectiveness of liquids presents with the mostly eliminated need for laboratory analysis and relatively lower incidences of systemic embolism or strokes (Budovich et al., 2013, p. 212).

On the other hand, concerning Lovenox (enoxaparin), one of the LMWHs, there is a more reduced chance of clots coming again, with the same rates of major bleeding and death than other blood thinners. Besides, with this therapy, a patient does not have to go for laboratory examinations to identify whether it is functioning, unlike other drugs like warfarin, which call for regular blood tests. Lovenox is available in generic form and, therefore, it can be cheaper (lowest price is $78) than other anticoagulant therapies (Solayar & Shannon, 2014). It is also a better alternative for pregnant women or cancer patients. Nonetheless, it does not function well for the overweight, underweight or patients with kidney infections.

Administration begins pre-operatively around 12 to 24 hours before surgery (Pineo et al., 2013). This event adds pressure to surgeons and anesthetists alike during surgery as there is a potential risk of hemorrhaging. Empirically, administration of Lovenox pre-operatively diminishes the reputation of the drug as it increases the count of bleeding events that lead to other choices of drugs other than Lovenox.

Relative to warfarin, it does not impose as much laboratory evaluation. However, its parenteral administration makes it challenging to administer in patient-centered care. However, its efficacy in a various study has been a measure of its intended purpose against the risk of bleeding. A benefit-risk analysis conducted by Levitan et al. (2014) compared severity nonfatal major bleeding to symptomatic VTE and all-cause mortality to note that enoxaparin is as good a thromboprophylactic as the Factor Xa inhibitor, rivaroxaban (p. 165). Fuji et al. (2015) also recommend edoxaban instead of subcutaneous enoxaparin citing the risk for significant bleeding.

These studies evaluate NOACs and LMWHs on an efficacy-to-safety scale that ensures the drugs' beneficial effect would be to the long-term benefit of the patient.

Topfer (2016) and Revankar et al. (2013) noted that eliquis was a more cost-effective relative to Lovenox. The decision-tree model utilized by Revankar et al. (2013) covered the 90 days after surgery considering incidences of VTE, bleeding, and mortality. Resultantly, eliquis came out as the most effective and least expensive with savings ranging from 180 to 270 dollars relative to Lovenox. This study served as the novel economic valuation of the use of thrombo-prophylactic drugs.

Other quality assessments of the efficacies of the drugs assessed by Huang, Cao, Liao, Wu, and Gao (2013), illuminated that Eliquis is the ideal alternative for anticoagulation rather than Lovenox. The study emphasized that Eliquis is more effective in decreasing the risks of proximal DVT. While few statistical differences were identified, inherent differences with regards to liver function and patient safety especially for significant bleeding. Accordingly, patients who were on Eliquis showed remarkable signs of improvement compared to those on Lovenox. Besides, the risks of the drugs on the liver function were found to be more reliable for those under Eliquis. When used for the same time duration, the efficiency of Eliquis is far much superior. By taking into account the clinical circumstances and the economic advantages that the drugs have to offer, eliquis stands a higher chance of ensuring the recuperation of patients after surgeries.

The efficacy of both Eliquis and Lovenox indicated that DVT was less prominent amongst patients compared to those using Lovenox. Similarly, high rates of recovery for PE were exhibited amongst those administered with Eloquis (Huang et al., 2013). The meta-analysis assessments indicated that all patients were at risk of mortality. However, the incidences in the

study stood at 0.65% for Lovenox and 0.13 for Eliquis (Huang et al., 2013). The outcomes are evidence of the efficiency of the latter in treating DVT and PE incidences. However, other inherent differences in the trial designs and subgroup analyses support the uses of Eliquis over Lovenox for the same duration especially in times of emergency.

Some studies were consistent with their results in noting the efficacy-to-safety balance that is in favor of apixaban rather than enoxaparin. With the mortality rates of active cancer patients, 3 months after the commencement of the administration of enoxaparin at 7.7% relative to 6.0% in the apixaban group, the distinction of the two drugs can be set apart (Huang et al., 201). Apixaban presents a clinically lighter burden on the patient and personnel that culminates in a favorable prognosis more times than not.

Aspirin, is comparatively cheaper, has an ease of use and administration, and, like Lovenox, does not require laboratory monitoring and is in general well tolerated (Budovich, Zargarova & Nogid, 2013). Lovenox remains inferior to Eliquis in efficacy owing to its dose-related effectiveness and related risks of bleeding. This distinction was illustrated by Levitan et al. (2014) as they did a double-blind, double-dummy study where 2.5 mg of eliquis daily proved more efficient than a 40 mg daily Lovenox regimen over 35 days with similar bleeding profiles (p. 594). Nevertheless, in agreement with the previous findings, Aspirin is not suggested because of its complications like the need for red blood cell transfusion and surgical wound bleeding when used to prevent the clotting.

The Selected Anticoagulant Therapy

Evidence-based practice opts for eliquis as the best drug for the control against clotting complications (Gali, 2017; Levitan et al., 2014). Comparatively, Lovenox has several advantages, including reduced frequent dosing, a reduced occurrence of adverse impacts like

bleeding, and reduced urge for blood draws for laboratory monitoring. However, considering the risk of bleeding during surgery due to pre-operative administration and the empirical evidence citing it for relatively more bleeding events, eliquis stands out as the proper choice of thromboprophylactic at the moment. Over the shelf, the anticoagulant is also comparatively cheaper as compared to Eliquis; however, considering its effect on the prognosis, future readmissions and mortality, eliquis is a far cheaper option (Revankar, 2013). Thus, looking at the elements like the cost, safety, and ability to stop bleeding and clot, the gold standard anticoagulant therapy between the two anticoagulants, namely, Lovenox and Eliquis, for preventing PE/DVT for post-op total knee/hip replacement is eliquis, which should be continued in the hospital unit.

Conclusion

There is an increased number of arthroplasties undertaken each year globally. VTE is still a clinical problem because of the risk of symptomatic VTE and mortal PE. The focus today is on the symptomatic episodes and risks of bleeding when attempting to prevent blood clotting associated with the THA and TKA. It is essential to create a balance between the effectiveness and safety since inadequate anticoagulation leads to excessive bleeding. Besides, there is a need for more advanced research on the people at risk of bleeding and VTE. The ultimate judgment on perfect thromboprophylaxis rests with the treating doctor, who is most well-conversant with each client's unique medical records and history. This piece has suggested the gold standard anticoagulant therapy between Lovenox and Eliquis for preventing PE/DVT for post-op total knee/hip replacement, selecting eliquis as the cost-effective anticoagulant. This is based on the cost-effectiveness, safety, and ability to reduce bleeding and clotting.

Summary

The literature review has discussed the historical overview of the pharmaceutical agents used in stopping VTE after knee/hip replacement. It has also offered the current findings concerning the used drugs, focusing on the pros and cons of the different drugs available. A conclusion has been given concerning the gold standard anticoagulant therapy selected among Lovenox and Eliquis. Especially, eliquis has been selected as the most effective, safest, and comparatively cheaper therapy based on the cost, functionality, and safety aspects. Consequently, according to the finding, it is recommended that the orthopedic unit of the hospital should switch to eliquis for prevention as the gold standard anticoagulant therapy for post-op total knee/hip replacement. Further, early examination for the VTE is recommended for proper intervention. The hospital unit should also engage a multimodal intervention where drugs and mechanical prophylaxis like Anti-embolism stockings are applied. Besides, even though the use of eloquis should be continued in the unit, Lovenox maybe considered because it can be effective for some patients unless the chance of bleeding outweighs the gains from the use of this drug. Finally, patients need to be assessed for the chance of bleeding and thromboembolism before the start of VTE prophylaxis.

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