PHARMACIST-NURSES RESPONSIBILITY IN MONITORING ENOXAPARIN LEVEL AND DOSE ADJUSTMENT; REVIEW

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Abstract:
Pharmacists suggested how to monitor and alter the dose of enoxaparin for trauma patients in the Surgical Intensive Care Unit (SICU). Medical practitioners frequently approved pharmacist suggestions, leading to trauma patients often reaching the desired AFXa-TR level after pharmacist-recommended dosage adjustments. Additional study is needed to determine the most effective enoxaparin dosage for preventing VTE in trauma patients. Enoxaparin anti-Xa levels are commonly measured inaccurately, leading to dosage modifications being made without proper support from these levels. This might pose a risk to patient safety.

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Introduction:

Venous thromboembolism (VTE) is a frequent and avoidable source of illness and death associated to hospital stays. Thromboprophylaxis dosing strategies using low molecular weight heparins (LMWHs) are well understood for patients with normal kidney function but are less defined for those with renal impairment due to limited available literature. These patients were excluded from many important clinical trials. Adjusting the dosage or monitoring of preventative doses of LMWHs is advised in specific clinical situations, including renal impairment, by the use of the chromogenic test anti-Xa. Patients with renal insufficiency are more susceptible to thrombosis and bleeding. Elderly individuals with both renal impairment and other conditions are not well represented in clinical trials, making thromboprophylaxis hard for this group.

There is a lack of research on the effectiveness and safety of various preventive dosages of LMWHs in cases of severe renal impairment with creatinine clearance (CrCl) below 30 mL/min. Tinzaparin and dalteparin can be safely used in renal impairment at prophylactic dosages, but enoxaparin has shown drug buildup. Pharmacokinetic investigations have shown an inverse correlation between CrCl and LMWH anti-Xa levels, particularly with enoxaparin, in individuals with severe renal impairment. In older individuals with renal failure who were given prophylactic enoxaparin 40 mg, there was an increase in anti-Xa levels, particularly in those with severe renal impairment. Enoxaparin has been shown to build up in senior people with kidney problems, yet it is often used and has been researched in medically unwell elderly patients.

Currently, there is no definitive guidance on the optimal dosage of enoxaparin for older individuals with renal dysfunction. Unfractionated heparin is the preferable choice over low molecular weight heparin in this patient population. Heparin is preferable, however it has a greater risk of bleeding compared to LMWH. Furthermore, healthcare professionals may choose LMWH over heparin due to its less frequent dosing schedule. Enoxaparin is often recommended, however manufacturers do not provide a consistent prescription for adjusting the dosage in cases of renal impairment. Either 20 mg or 30 mg doses are administered subcutaneously once day, depending on the region of usage. Prescribers typically choose institution-specific tactics or decide to prescribe the dose provided in a prefilled syringe. In Lebanon, a prefilled syringe containing 20 mg of enoxaparin is available, leading many clinicians to use this administration method. A recent research in Lebanon found that using enoxaparin 20 mg for thromboprophylaxis in patients with renal impairment led to satisfactory rates of both thrombosis and bleeding.

Clinical pharmacy services have been shown to enhance patient outcomes. 1 Pharmacists in acute care settings support patient care by offering medication information and recommendations to healthcare teams and patients, conducting medication reconciliation and collecting medication histories, evaluating the cost-effectiveness of medications, and guaranteeing patient safety through medication monitoring and review. Enoxaparin shows consistent pharmacokinetics and pharmacodynamics in most clinically stable people, therefore regular monitoring of anti-Xa levels to assess anticoagulation effects is often unnecessary. Anti-Xa monitoring may be necessary for some patient groups to guarantee safe and efficient anticoagulation in cases when the ideal dosage is not easily anticipated. These patient features include of renal or hepatic failure, extreme body weight (≤ 40 kg or ≥150 kg), neonates, children, pregnancy, extended treatment (≥7–10 days), and old age [7]. Moreover, there is insufficient data to justify the use of anti-Xa monitoring in most patients who are prescribed enoxaparin, save for specific patient groups. Monitoring Enoxaparin anti-Xa levels can be challenging and frequently inaccurate in practical practice. Therefore, it is crucial to use anti-Xa monitoring effectively for certain patient groups to avoid needless monitoring of these costly laboratory markers [7].

One of the primary and crucial components of therapeutic drug monitoring (TDM) is the precise and correct quantification of drug levels in clinical settings. An accurately timed peak anti-Xa level should be taken around 4 hours after the dosage and once the medication has achieved steady-state concentrations. Using samples that are collected either too early or too late should be avoided when trying to predict the activity of enoxaparin. This is because these samples are less likely to provide an accurate measure of anticoagulation when compared to established target anti-Xa concentrations. As a result, a healthcare provider might make unnecessary adjustments to the enoxaparin dosage, which could lead to increased risk of thrombosis or bleeding.

Review:

Trauma patients admitted to the surgical intensive care unit (SICU) commonly use subcutaneous enoxaparin 30 mg twice daily (BID) for venous thromboembolism (VTE) prophylaxis.1 This

regimen is based on limited evidence and there are at least three studies suggesting similar VTE rates when compared to once daily enoxaparin or three times daily unfractionated heparin [6]. Interestingly, recent evidence has identified rare achievement of target anti-factor Xa trough concentrations (AFXa-TR) and significant VTE reduction when adjusting enoxaparin dose to achieve AFXa-TRs of 0.11 - 0.20 IU/mL. Some experts, therefore, recommend adjusting enoxaparin in trauma patients based on AFXa-TR [7].

In June 2017, Upstate University Hospital started adjusting enoxaparin VTE prophylaxis based on AFXa-TR in trauma patients admitted to the SICU based on discussion between pharmacy and attending trauma physicians about the above noted literature. Upstate University Hospital has a multidisciplinary SICU team that includes an attending surgical physician who specializes in trauma care, three surgical residents, a pharmacist who specializes in critical care, and nurses certified in the treatment of trauma patients. A critical care pharmacist, who has been an active member of the trauma team for approximately five years, rounds with the team five days a week. Additionally, rotating staff pharmacists with critical care experience provide operational support and clinical advisement 24 hours a day. At any one time the SICU team cares for 5-10 patients with a variety of traumatic injuries including but not limited to motor vehicle accidents (MVA), penetrating traumas, and burns. All treatment decisions are at the discretion of the attending physician including the initiation of enoxaparin VTE prophylaxis, ordering of AFXa-TR, and dose adjustments based on resultant AFXa-TR; as currently there is no official protocol at our institution describing this process. All patients receiving enoxaparin for VTE prophylaxis are initiated on enoxaparin 30 mg BID and after discussion with the treatment team, doses are adjusted up or down in 10 mg/dose increments to achieve an AFXa-TR of 0.11 – 0.20 IU/mL. AFXa levels are routinely used at our institution and our laboratory services run AFXa assays 24 hours a day [8,9].

Pharmacists utilize the renal dose adjustment policy daily to improve patient care and prevent adverse drug events or other effects from incorrect medication dosage, including readjusting doses in patients with fluctuating renal function. Despite its frequent utilization, compliance with the policy is not routinely assessed and has not been officially evaluated. This study evaluates pharmacist compliance with the renal dose adjustment policy, establishing a baseline for a clinical service that is utilized frequently within the acute care setting [10].

Adjusting medication doses for renal function is arguably one of the most important interventions a clinical pharmacist can make. According to the National Institute of Diabetes and Digestive and Kidney Diseases, approximately 14% of the population has chronic kidney disease. The high prevalence has remained steady since the early 2000s, and the risks associated with chronic kidney disease, including cardiovascular disease, hyperlipidemia, anemia, and metabolic bone disease, are well established. It is also widely believed that pharmacists can make a difference in patient outcomes by performing renal dose adjustments for patients with chronic kidney disease; however, there is not much existing literature regarding the quality of these adjustments. A study evaluated the appropriateness of renal dose adjustments made in a single hospital, examining heart failure patients upon hospital discharge and found that 12.6% of eligible prescriptions were inappropriately prescribed based on the estimated glomerular filtration rate (eGFR). Sheen and Choi looked at rates of medication "overdoses," defined as medications that should have been given at a lower dose based on a patient's renal function. They found an overall overdose rate of 5.3% over 4 years; however, the role of the pharmacist in renal dosing at this institution was not discussed. One study found a decrease in physician noncompliance with dosing guidelines from 53% to 27.5% with the addition of a pharmacist attending medical rounds and offering dose recommendations. A 2019 study from Lebanon also examined the appropriateness of medication doses for renal dysfunction ordered by prescribers, finding high rates of inappropriate doses, and further emphasizing the need for pharmacist involvement to improve patient care and prevent prescribing errors [11,12,13].

An additional aspect to evaluating the compliance of renal dose adjustments performed by pharmacists during hospitalization is ensuring these adjustments are appropriately carried over to a patient's discharge orders. Michaelsen et al explored the importance of performing medication reconciliation upon discharge from the hospital and discovered that a large portion of discrepancies relate to a prescription's route, dose, or frequency. This is an important consideration for many clinical service evaluations; if interventions are not carried out at discharge, the impact on patient outcomes may be significantly less [13].

One of the most essential aspects to TDM in clinical practice is the appropriate obtainment of drug or drug target serum concentrations.

Incorrectly drawn anti-Xa levels have several important clinical implications. First, clinicians may be unaware that these are drawn inappropriately and interpret these levels as is. This has the potential to lead to patient harm with either a higher or lower subsequent dose adjustment then needed, thus compromising the anticoagulation efficacy and safety of enoxaparin [14].

Conclusion:

Assessing the impact of clinical pharmacy is challenging due to the multifaceted influence of many members of multidisciplinary teams on patient outcomes. It is challenging to isolate the effects of pharmaceutical services from those of other fields. Assessing clinical pharmacy services to evaluate compliance helps identify if policies are being optimized. Enhancing policies that enable pharmacists to perform at their highest capacity leads to better patient outcomes, cost savings, and stronger multidisciplinary interaction. The assessment of the renal dosage adjustment policy highlighted potential policy enhancements and educational prospects, as well as aided in preparing for future evaluations of pharmacist clinical services.

All pharmacists, both staff and clinical, received training and were required to offer suggestions, analyze, and modify enoxaparin dosage according to AFXA-TRs in trauma patients. Our study aimed to analyze pharmacist involvement in monitoring prophylactic enoxaparin in the Surgical Intensive Care Unit (SICU). We sought to characterize pharmacist recommendations for enoxaparin monitoring in trauma patients in the SICU and describe how often medical providers accept these recommendations.

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