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Low Molecular Weight Heparin (LMWH)

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Indications

Low-molecular-weight heparins (LMWHs), for example, dalteparin, enoxaparin, among others are anticoagulants. These drugs are used in the prophylaxis of venous thromboembolic disease (VTE) on acute or elective admission to hospital, and they are used in the treatment of deep vein thromboses (DVT) and pulmonary embolism (PE).[1] The British National Formulary (BNF) and National Institute for Health and Care Excellence (NICE) have stated the use of LMWHs are licensed for:

- DVT prophylaxis in medium and high-risk groups (surgical, orthopedic and medical patients)
- Treatment of venous thromboembolism in pregnancy
- Treatment of DVT and PE in nonpregnant women (those with both high and low risk of recurrence)
- Treatment of STEMI (in both those undergoing percutaneous coronary intervention and those not)
- Unstable angina
- Prevention of clotting in extracorporeal circuits

LMWHs are not the sole medications that can be used for these purposes; therefore, a thorough understanding of the variously available anticoagulants and their pros and cons is necessary for an appropriate prescription.

Mechanism of Action

LMWHs are anticoagulants, acting by inhibition of the final common pathway of the coagulation cascade.[2] The coagulation cascade's goal is to fluid blood into a clot, thus preventing bleeding. The final common pathway is the conversion of fibrinogen into fibrin by the activity of thrombin. LMWH inhibits coagulation by activating antithrombin III. Antithrombin III binds to and inhibits factor Xa. In doing so it prevents activation of the final common path; Xa inactivation means that prothrombin is not activated to thrombin, thereby not converting fibrinogen into fibrin for the formation of a clot. LMHW is a small fragment of a larger mucopolysaccharide, heparin.[2] Heparin works similarly, by binding antithrombin III and activating it. Heparin also has a binding site for thrombin, so thrombin can interact with antithrombin III and heparin, thus inhibiting coagulation. Heparin this has a faster onset of anticoagulant action as it will inhibit not only Xa but also thrombin, while LMWH acts only on Xa inhibition.[2]

Administration

LMWH is administered via subcutaneous injection. This has long-term implications on the choice of anticoagulant for prophylaxis, for example, in orthopedic patients recovering from joint replacement surgery, or in the treatment of

DVT/PE. Patients often express a dislike of injections, especially self-administered ones,[3] complaining of pain or bleeding with injection, and they prefer an oral alternative. There are oral options for anticoagulation in the non-pregnant population, which often prefers this option. The oral option poses fewer needle and sharps-related risk. Outside of pregnancy, these oral options are not suitable because of transport over the placenta and risks to the embryo/fetus. Compared to heparin, LMWHs have a longer half-life, so dosing is more predictable and can be less frequent, most commonly once per day. However, patients with a high body weight will need higher doses and sometimes 2 doses daily, depending on local administration policy.[2]

Adverse Effects

As an anticoagulant, the main risk of LMWH will be bleeding. Treatment of bleeding associated with LMWH is stopping the drug and administering protamine sulfate, a strong half-life protein forming a strong bond with the heparin producing an inactive complex.[2] Other, less common, adverse effects include heparin-induced thrombocytopaenia,[4] osteoporosis and spontaneous fractures,[5] hypoaldosteronism,[6] and hypersensitivity reactions.[7] On an assessment of the needs for anticoagulant medication, there needs to be a risk-benefit analysis of the risks posed by bleeding versus the risks of clotting.

Contraindications

NICE and the BNF suggest that contraindications to all heparins include trauma, epidural half-life, hemorrhagic disorders, peptic ulcer disease, recent cerebral hemorrhage, severe hypertension, and recent surgery to the eye or nervous system. In these cases, risk-benefit the risks of anticoagulation and bleeding outweighs the potential benefit from LMWH acting as a VTE prophylaxis or at treatment doses. As LMWHs are self-administered, it is important to consider dosing in cases of chronic kidney disease, where there is a risk of accumulation and thus, higher chances of problematic bleeding.

Enhancing Healthcare Team Outcomes

Low-molecular-weight heparins are commonly used in clinical practice, especially in VTE (DVT and PE) prophylaxis. It is estimated that over half of patients admitted to hospital acutely unwell are at risk of thromboembolic disease[8] and that 5% to 10% of hospital deaths are due to VTE,[9] necessitating the need for accurate VTE risk assessment and appropriate prophylaxis. Approximately one-third of VTE-related deaths occur postoperatively,[10] but the use of LMWH postoperatively in general surgery has been shown to reduce VTE-related mortality by 70%, but it also increased the risk of bleeding and wound hematomas.[11][12] Risk assessment for VTE prophylaxis takes into account the reason for hospital admission, potential benefits, and risks of prophylaxis using pharmacologically measured such as LMWH. NICE Guideline NG89 (Venous thromboembolism in over 16s) discusses the need for VTE assessment on admission to hospital that a National Tool for VTE risk assessment was implemented in 2010, and since then, over 90% of patients admitted to hospital have a VTE risk assessment completed. This guideline describes other VTE prophylaxis measures including; anti-embolism stockings, foot, and calf pump devices, LMWH and other oral anticoagulants such as warfarin and direct Xa inhibitors (direct oral anticoagulants [DOACs], rivaroxaban). It is estimated that prophylaxis, with appropriate risk assessment, has reduced the incidence of DVT by 70%.[9] Multiple reviews have shown that VTE prophylaxis is appropriate in trauma,[13], medical,[14] and surgical[15][16][17] [15] situations, and that LMWH is suitable for this purpose.

For all healthcare professionals, it is important to understand the risks posed by VTE and that appropriate risk assessment and pharmacological or mechanical prophylaxis is given. When the interprofessional approach is taken to this, it has shown benefits in VTE prophylaxis prescription rates[18]. VTE prophylaxis and the use of not only LMWH has been shown to be a key consideration in patient care in a hospital setting and on discharge for both trauma and elective orthopedic surgical patients, for example. The interprofessional approach to minimizing VTE is key; it

involves correct and timely assessment and reassessment of pharmacological and mechanical prophylaxis needs, early and appropriate mobilization of patients, education of staff and patients regarding risks, signs, and symptoms of VTE, and understanding the importance of prophylaxis. Clinically, the use of low-molecular-weight heparins is diverse, both in treatment and in prophylaxis. The pros and cons of LMWH, as compared with other anticoagulants and mechanical VTE prophylaxis measures, are numerous. However, the key factor is assessing the patient, discussing options with them, and ultimately, making a decision that will promote compliance with their VTE prophylaxis or anticoagulation and understanding of the clinical need for them. The nurse and the pharmacist play a vital role in ensuring that the patient is prescribed an LMWH before and after most surgical procedures. In addition, before discharge, the patient needs to be educated on how to administer the LMWH and the benefits of compliance. The patient should also be taught what signs and symptoms of VTE to watch out for and when to return to the primary care provider.[19] (Level II)

Evidence-Dased Outcomes

There are dozens of randomized studies showing that a number of LMWHs can lower the risk of VTE and PE in patients with cancer, post surgery and after admission to the hospital with a medical illness. Today, the risk of bleeding from LMWH has been minimal. However, the use of LMWH in pregnancy remains debatable because there are not many good, long-term studies that have elucidated the effects of these agents on the fetus.[20][21] (Level I)

Questions

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