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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Use of LMWH in patients with advanced liver cirrhosis

Low molecular weight heparins (LMWH) are commonly used in the prophylaxis and treatment of venous thromboembolic (VTE) diseases. However, there is limited evidence to guide the use of LMWH in patients with advanced liver cirrhosis.

It is well known that patients with advanced liver disease are affected by haemostatic alterations that can create a hypocoagulable state. The mechanisms that create this issue are firstly, decreased synthesis of vitamin K clotting factors II, V, VII, IX, X and XI, and secondly, decreased platelet production. These abnormalities are reflected through routine laboratory tests showing a deficiency in procoagulants - i.e. decreased platelet count and elevated prothrombin time, international normalised ratio and partial thromboplastin time. It was once thought that this deficiency in procoagulants resulted in protection against VTE and an increased bleeding risk. However, patients with advanced liver disease also have increased levels of procoagulants (factor VIII and von Willebrand factor) which all lead to a hypercoagulable state. Routine laboratory tests do not reflect this. The complex haemostatic alterations in the patient with advanced liver disease implies they have an increased propensity to bleed during procedures and from varices but are also at increased risk of thrombosis, namely portal vein thrombosis.

A recent literature review published in the *Annals of Pharmacotherapy* assessed the risk of VTE in patients with chronic liver disease (CLD). The review included six retrospective studies that assessed the incidence of VTE in this patient group: the overall findings of these studies suggested that the incidence varied in the range of 0.5 – 6.3%. Population-based studies have reported VTE relative risks of 1.74 – 2.10 in patients with CLD compared to controls.

To date, there is no data comparing the efficacy or risks of using pharmacological prophylaxis in patients with CLD with other hospitalized patients. Further studies are needed to determine if patients with CLD would benefit from receiving pharmacological VTE prophylaxis. There is one study assessing the efficacy and usefulness of anti-Xa monitoring of LMWH under prophylactic doses of enoxaparin (20mg or 40mg once daily) and therapeutic doses of enoxaparin (1mg/kg twice daily) in 84 patients with advanced liver cirrhosis. The study found that anti-Xa activity was negatively correlated with the severity of liver disease – using standard doses of enoxaparin, cirrhotic patients failed to reach recommended anti-Xa levels, implying that lower anti-Xa levels might be an optimal target in patients with CLD, or that the acquired deficiency of antithrombin (AT) in cirrhotic patients leads to reduced efficacy of LMWH. Adjusting doses to achieve recommended anti-Xa levels may be inappropriate in patients with CLD, and may actually result in an increased incidence of bleeding.

In summary, it would appear that the risks and benefits of VTE prophylaxis in patients with CLD are yet to be clearly determined. The use of anti-Xa monitoring for patients with CLD also warrants further investigation and at this stage should be used with caution. Alternative novel monitoring methods may prove to provide better monitoring options in the future.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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