NSW TAG NSW Therapeutic Advisory Group Inc. | Advancing quality use of medicines in NSW

Group Discussion: LMWH monitoring

Date: June 2018

Questions:

1) A member has enquired regarding local policies, protocols or guidances that hospitals are using to guide monitoring of patients prescribed therapeutic low molecular weight heparins (and danaparoid). Please provide the local policies/guidances to NSW TAG.

2) NSW TAG would like to understand the utility of anti-Xa monitoring in hospitals where there might be challenges in the accessibility to/availability of anti-Xa assays and results turn-around and hence the monitoring of patients with renal impairment, obesity etc. Please provide feedback if this is an issue at your hospital.

Background:

The recent updated version of **eTGs Cardiovascular** state:
'The anticoagulant effect of LMWH is predictable and routine anticoagulation monitoring is not required.
Measure anti-Xa levels to guide dosing in patients with kidney impairment or morbid obesity, and in pregnant women. Monitoring can also be used if bleeding or thrombosis occurs during long-term therapy. Target therapeutic ranges of anti-Xa levels vary; use local laboratory ranges.'

The **AMH** states:
'LMWH and danaparoid: Consider monitoring antifactor Xa in patients at high risk of bleeding (eg multiple trauma, renal impairment, cancer, thin or obese patients, pregnant women) or if overdose is suggested by bleeding; there is no evidence, however, that monitoring reduces bleeding risk.'

Up To Date:
Laboratory monitoring/measurement— If there is any question as to the correct dose of LMW heparin (eg, for those with obesity or renal insufficiency), measuring anti-factor Xa activity testing is sometimes used. If anti-factor Xa testing is used, it should be noted that "optimal" target ranges differ, depending not only upon the schedule of treatment (e.g. once or twice daily) but also on the preparation and assay used. Thus, institutional guidelines for the specific LMW heparin and clinical setting should be followed. Dose reduction should be considered if the anti-factor Xa activity four hours after subcutaneous injection is excessive. As an example, the therapeutic range for full-dose (treatment-dose) enoxaparin dosed twice daily is generally 0.5 to 1 anti-Xa units/mL when measured four to six hours following injection.
Of note, the aPTT is relatively insensitive to LMW heparin effect and thus is not appropriate for monitoring.
Additional testing and monitoring includes the following:
●Platelet count monitoring is appropriate for some patients receiving LMW heparin due to the potential risk of heparin induced thrombocytopenia (HIT), although this risk is very low (see 'Platelet count monitoring' above). A platelet count also should be checked if there is any concern about bleeding or thrombosis.

●Routine monitoring of the hemoglobin level generally is not needed; however, hemoglobin level should be checked if there is any concern about bleeding.
●Periodic bone density testing (e.g, annually) is appropriate for individuals receiving long-term therapy with a LMW heparin.'

Responses:
Twelve responses were received. There is variation in the availability of guidelines for use of LMW heparins across the state. There is a great deal of effort and resources required to develop and maintain anticoagulation guidelines. Given the complexity of the clinical area, there are also medico-legal issues regarding their distribution.

Responses suggest that haematologists are routinely consulted for difficult cases e.g. dosing in obese patients. However managing these patients is challenging for many rural hospitals as they don't have an on-site haematologist and can't feasibly monitor antiXa levels. They often rely on an informal arrangement with their friendly haematologist at the larger hospital who tries to give advice without seeing the patient. This same sort of issue arises with infectious diseases and paediatric patients in non-metropolitan hospitals. There is growing concern over these informal arrangements.

Bowral (SWSLHD)

1) We use the SWS area anticoagulation guideline –permission required from Liverpool to share this.

2) The pathologist provided the following information:
   a) Product specific anti-Xa test must be ordered (eg. danaparoid, or enoxaparin, or dalteparin)
   b) The blood is separated and frozen locally
   c) Frozen plasma transported to larger hospital
   d) Turn-around time is 4-12 hours depending on time of day and courier etc.

Calvary Mater Newcastle (CMN)

1) Our adult enoxaparin drug prescribing guideline (which I think may need review with respect to dosage adjustment in the obesity) includes information about anti-Xa monitoring as follows:

   'Anti-Xa concentrations are used to monitor the effect of full-dose (treatment) enoxaparin. When requesting anti-Xa concentrations, the drug being used MUST be specified.
   Where anti-Xa concentrations are recommended, use peak concentrations to check for therapeutic dosing (particularly for doses > 150 mg/day (body weight > 100 kg). Take 3–4 hours post-dose starting with the first or second dose and aim for:

• Twice daily dosing: Peak = 0.6–1.0 Units/mL
• Once daily dosing: Peak = 1.0–1.5 Units/mL

Use trough concentrations for concerns relating to drug clearance with renal impairment. Target ranges:

• Twice daily dosing: Trough = 0.3–0.5 Units/mL
• Once daily dosing: Trough = 0.0–0.3 Units/mL'

Bankstown (SWSLHD)

Anticoagulants policy where monitoring is outlined attached. (Available on request from NSW TAG).

Canterbury

1) We use Sydney LHD anticoagulation guidelines. (Available on request from NSW TAG).
2) We cap doses of enoxaparin for obese patients at 100mg bd and ask for a Haematology consult. They usually recommend anti-Xa monitoring and that does get done without much trouble, although we think they have to send the bloods across to RPA for the test.

Far West (FWLHD)

1) We don't have any local protocol for the monitoring of LMWH. We also don't have access to a VMO Haematologist, although it's usual practice to ring Royal Adelaide and try to get onto someone in their haematology team. There's no formal agreement and Medical Services are trying to find a regular VMO. Fortunately, we do have a nephrologist VMO.

2) Anti-Xa monitoring cannot be done onsite in Broken Hill. Samples are sent to Sydney on the daily commercial flight meaning a turnaround of 24-48 hours most days and up to 72 hours over the weekend (no flight between Fri afternoon and Sun afternoon). This limits the usefulness of testing/monitoring.

John Hunter Hospital (JHH) – feedback from Dr Mark Walsh, haematologist

1) We have an adult and a paediatric dosing guideline for Clexane on the LHD intranet which we hope clinicians use but in practice the on-call haematology registrars get an overwhelming number of enquiries for their advice.

   The registrars recommend the 3 sources mentioned above and in particular Up To Date for danaparoid dosing.

2) JHH provides a 24 hour AXA level testing (DRUG MUST BE WRITTEN ON REQUEST FORM) with just the practical caveat of trying to prevent non urgent samples overloading the night shift technical officer. All JHH and samples up to and including all the labs of the New England area and up the coast to the QLD border are sent to JHH laboratory (total of 14 labs with more than 500 Clexane and more than 200 NOACs

levels annually) Port Macquarie goes to private and Coffs is exploring setting up own AXA monitoring . Once they arrive at JHH, urgent samples will be dealt with expeditiously so the turn-around time is mostly dependent on local referring lab factors which vary.

Within the Hunter area, couriers come every few hours. Outside of the Hunter, samples are generally frozen at the local receiving lab then either sent directly or via bigger laboratories (eg Tamworth) in overnight couriers as frozen transport.
I have not heard of complaints from the labs (or passed on from their clinicians) but they get a chance to raise this at monthly area wide lab management meetings. Into the future with availability of anti Xa drug antidotes, the requirement for urgent / onsite testing may fall further.

Nepean Hospital

2) Our Factor Xa assays are sent to Westmead for processing and turnaround time I believe can be up to 48 hours. We occasionally have morbidly obese patients >150kg requiring therapeutic anticoagulation and the question of dose always comes up. I think we usually rely on haematology advice for those patients.

Port Macquarie & Kempsey

1) Please find our HITS guideline which gives the details of how we use danaparoid. (Available from NSW TAG upon request).

2) We don't have anti Xa here on site and we have waited something like five days to get a level back. So it's not necessarily a practical thing to get for some sites, although apparently Coffs now has it on-site. It would be nice to have it!

Royal North Shore Hospital (RNSH)

1) To my knowledge, the NSLHD/RNSH does **NOT** have any local policies or guidelines regarding the utilisation or monitoring of enoxaparin or other LWMHs. Orders would be at the discretion of the treating team and/or at the suggestion of a clinical pharmacist or Haematology.

2) From January to September 2017 at RNS, 302 anti-factor Xa levels for enoxaparin were processed by our pathology service - 230 of these were for inpatients. It is readily available at our pathology lab.

South East Sydney Local Health District (SESLHD)

1) Our danaparoid protocol contains information on monitoring of Factor Xa levels and dose adjustments. (Protocol is available on request from NSW TAG). We don't have a district protocol for enoxaparin.

2) We have a good haematology service who get involved with more complex patients and the ability to do Xa assays locally when required.

St Vincent's

We too are interested in this question as it is something we need to tackle here. We can't currently offer anything.

Westmead

We have district wide comprehensive anticoagulation guidelines but this document is currently under review.

Responses received as at 12th June 2018

Please note that all information and policies are only current at the time the response is sent and individual hospitals should be contacted to ascertain current policies and practices. The responses received are only representative of the hospitals participating in the discussion at the time and do not necessarily indicate a complete picture of current practices. Information sharing occurs on the understanding that due acknowledgement will be given to the original source and that the information will not be quoted or used out of the context of the discussion. Permission should be sought from the original source before any policy, protocol or guideline is used or applied in another setting.