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LETTER

Fondaparinux Monitoring: Need for a Local Fondaparinux-Calibrated Anti–F actor Xa Assay

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Fondaparinux is a pentasaccharide synthetic derivative of unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH). It possesses increased affinity to inhibit factor Xa compared with UFH and LMWHs.[1] Monitoring is not generally recommended except in special patient populations (e.g., pediatric, obese, or pregnant patients or patients with renal failure).[1]

We faced a significant challenge in determining the appropriate fondaparinux dose for our 9-year-old obese child with a history of renal failure, heparin-induced thrombocytopenia, and thrombosis. Beginning on the first day of therapy, concentrations were sent to a reference laboratory to monitor fondaparinux therapy. However, there was a 24-hour lag time until these concentrations were returned. A decision was made to assess anti–factor Xa concentrations based on local existing LMWH curves to adjust the patient's dosing until a fondaparinux-specific curve could be established. Several dosage adjustments were made based on the anti–factor Xa curves of LMWHs.

However, use of anti–factor Xa curves for LMWH is not accurate when monitoring fondaparinux therapy. Although the mechanism of action of fondaparinux is similar to those of UFH and LMWH, the differences in affinity, molecular size, and affinity for factor Xa produce variance in monitoring fondaparinux versus the anti–factor Xa standard LMWHs. The assay methodology with appropriate fondaparinux calibrators is very similar to the standard anti–factor Xa assay for LMWH or UFH, but the anti–factor Xa for LMWH and fondaparinux assays are not equivalent.

After consultation with laboratory personnel, it was determined that the best course of action would be to establish a local fondaparinux-specific assay. A fondaparinux-specific assay was created using commercial calibrator standards (Arixtra Calibrators, BIOPHEN, West Chester, OH) with an anti–factor Xa heparin assay method (STA Rotachrom Heparin Assay Kit, Diagnostica Stago, Mt. Olive, NJ).[2] On hospital day 69, an anti–factor Xa concentration based on the fondaparinux curve was found to be 0.62 mg/L. To assess differences between the assays, anti–factor Xa concentrations based on the fondaparinux assay and LMWHs assay were analyzed on hospital day 71 and were 0.86 mg/L and 1.02 mg/L, respectively. Based on this established assay, at lower concentrations of fondaparinux, there was a 20% difference in the anti–factor Xa concentrations between the fondaparinux and LMWH curves and a difference of up to 40% at the higher concentrations of fondaparinux (Figure).

If monitoring of fondaparinux is necessary, then an accurate anti–factor Xa value must be determined. To determine an accurate value, an anti–factor Xa assay must be validated using fondaparinux calibrators. If fondaparinux

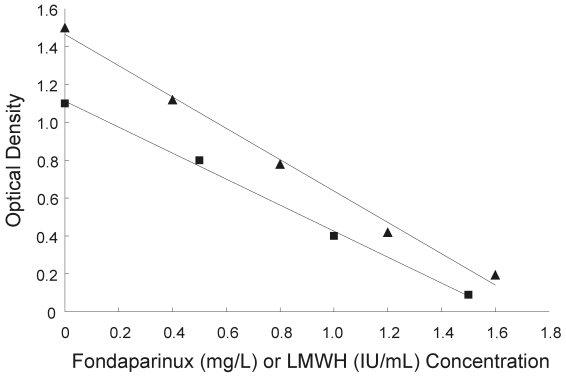

Figure. Comparison of fondaparinux anti–factor Xa curve to LMWH anti–factor Xa curve.
■ = fondaparinux curve; concentrations reported in mg/mL; ▲= Low-molecular-weight heparin curve; concentrations reported in units/mL.

concentrations are determined using the UFH or LMWH curves, the concentrations will be overestimated. This may prompt a prescriber to decrease the fondaparinux dose, when in fact the concentration may be within the desired goal range. Therefore, if fondaparinux is used in children and other special populations, clinicians must utilize a fondaparinux-specific anti–factor Xa assay for monitoring. These considerations also apply to any other anticoagulant used in special populations, such as pediatric patients, for which the appropriate calibrators must be used to establish the validated assay.

Fondparinux anti–Xa standards are commercially available, and fondaparinux factor Xa assays can be found at a reference lab. However, this would be a send-out laboratory test for most institutions, and there is often at least a 24-hour lag time until the results are reported to the referring institution. Patients with renal failure may be at increased risk of adverse events due to accumulation of fondaparinux.[3] Our patient developed acute kidney injury during his hospital stay that resolved while on fondaparinux. He continued to require multiple abdominal surgeries due to his intestinal pathology. He experienced frequent bleeding episodes, which made it impossible to wait for the samples to return from the reference laboratory before making adjustments in his therapy. To perform proper monitoring for these patients in a timely manner, we recommend that clinicians consider working with pathologists and laboratory staff to develop a local fondaparinux-specific anti–factor Xa assay.

Fondaparinux is an alternative agent for patients with contraindications for UFH and LMWH. It has the advantage of no routine monitoring in adult patients and once- or twice-daily administration. However, in special populations, monitoring is necessary. Based on the evidence presented in this case, fondaparinux monitoring must be performed rapidly and with a validated anti–factor Xa assay using fondaparinux calibrators. The use of anti–factor Xa assays with other calibrators may result in an overestimation of the dose with an increased risk of bleeding.

ABBREVIATIONS LMWH, low-molecular-weight heparin; UFH, unfractionated heparin

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