

Safety and efficacy of fondaparinux in renal insufficiency utilizing anti-Xa monitoring

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OBJECTIVE: Fondaparinux (FX) is a synthetic anticoagulant that prevents thrombin formation and thrombus development through selective inhibition of factor Xa. FX can be used for therapeutic anticoagulation and venous thromboembolism (VTE) prophylaxis in patients with heparin-induced thrombocytopenia (HIT) and heparin/porcine product limitation or allergy. FX has a labeled contraindication in patients with impaired renal function ($\text{CrCl} < 30 \text{ mL/min}$), yet small reports exist suggesting predictable outcomes of an extended interval dosing regimen for VTE prophylaxis. The goal of this study is to evaluate the safety and efficacy of a health-system anti-Xa monitoring protocol for extended interval FX dosing for VTE prophylaxis in renal insufficiency.

METHODS: Medical records of adult patients admitted to a YNHHS hospital between January 1, 2017 and December 31, 2019 who received at least one dose of FX 2.5 mg every 48 hours with renal impairment [$\text{CrCl} < 30 \text{ mL/min}$, acute kidney injury (AKI), or renal replacement therapy (RRT)] and at least one appropriately timed anti-Xa level (peak or trough) were included. The primary outcome evaluated was efficacy defined as anti-Xa peak measured 3-5 hours post-dose between 0.39 and 0.5 mg/L and/or trough measured 47-49 hours post-dose of $< 0.27 \text{ mg/L}$. The duration of FX exposure and level frequency were assessed as secondary outcomes. Safety outcomes evaluated in this study included the incidence of bleeding events or thrombosis within 14 days post-FX administration.

RESULTS: Forty-two patients were screened for inclusion ($n=17$) with a total of 47 anti-Xa levels. Only 51.1% ($n=24$) of anti-Xa levels were drawn appropriately and included for analysis, 75% ($n=18$) peaks and 25% ($n=6$) troughs. Chronic kidney disease was the most frequent renal function at therapy initiation (41.2%) followed by AKI (35.3%) and RRT (23.5%). HIT (52.9%) and heparin allergy or porcine limitation (35.3%) were the primary indications for VTE prophylaxis with FX. The primary outcome of anti-Xa level within goal range was observed in 41.7% of levels ($n=10$), encompassing 22.2% ($n=4$) of included peak levels and all included trough levels ($n=6$). Ten anti-Xa peak levels (55.6%) were below goal range and 4 (22.2%) were above goal range. Median [IQR] peak anti-Xa was 0.44 mg/L [0.27-0.58] and trough 0.14 mg/L [0.13-0.21]. Patients received a median [IQR] 3 doses [2-10] of FX correlating with 6 days [4-13] of therapy. The safety endpoint of bleeding events occurred in 17.6% ($n=3$) while there were no thrombotic events.

CONCLUSION: This study suggests extended interval FX for VTE prophylaxis in renal insufficiency is potentially effective at preventing thrombosis but further studies are warranted to determine optimal dosing balanced with a risk of bleeding.