Category :**Hematology: Other**

A237 - ***Application of population pharmacokinetics of nadroparin for thromboprophylaxis in critically ill covid-19 patients: accurate prediction of anti-Xa levels and assessment of dosing regimens***

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Introduction:

COVID-19 ICU patients require intermediate dosing of low molecular weight heparin (LMWH) (e.g. nadroparin 5700IE b.i.d.). However, the optimal dose regimen (reaching anti-Xa target levels) is unknown. Respecting stringent sample timing (t=4h) can also be challenging. This study aimed to assess which dose is adequate for critically ill COVID-19 patients and whether a population pharmacokinetic (PK) model can predict anti-Xa levels accurately irrespective of sample timing.

Methods:

Retrospective data of 65 ICU patients with ≥1 positive SARS-CoV-2 PCR were included. At ICU admission, patients started with b.i.d. 5700 IU nadroparin. Using anti-Xa level vs. time, a population PK model was constructed with NONMEM v7.4.1. Monte Carlo simulations (10,000 patients) provided individual anti-Xa versus time curves to allow evaluation of the accuracy of sample timing with Bayesian analysis. Accuracy was described by the relative mean prediction error (rMPE) for bias (<15%) and relative root mean squared error (rRMSE) for imprecision (<25%).

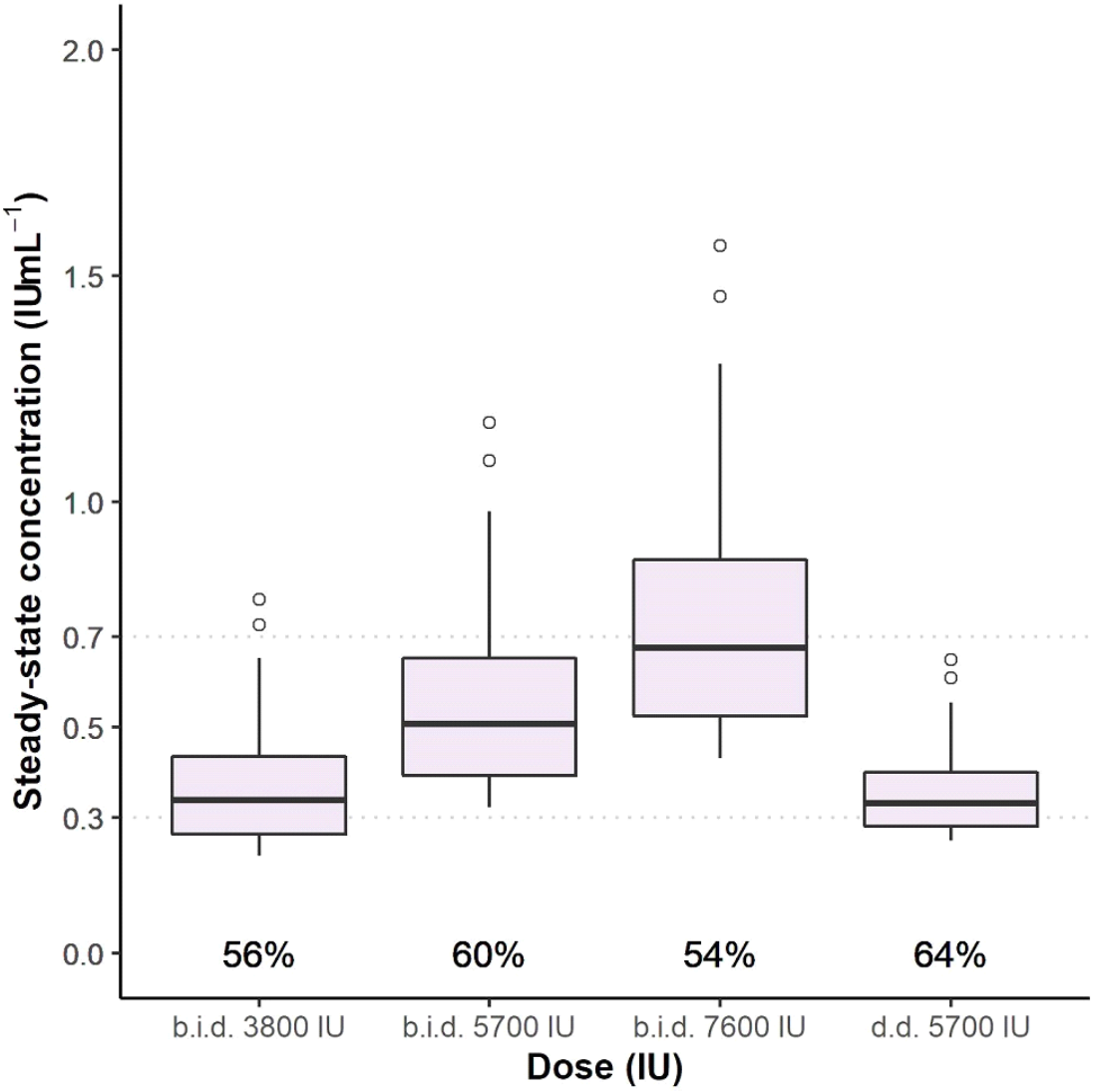
Results:

Anti-Xa levels versus time profiles were adequately described using a 2-compartment model with following covariates associated to clearance (CL): CRP, D-dimer, CKD-EPI-eGFR, corticosteroid and vasopressor use. Target level (0.3 IU - 0.7 IU/ml) achievement was most optimal for b.i.d. 5700 IU (Figure 1). Using 1 sample, t=3h allowed to estimate the anti-Xa level (rMPE: 1.8%; rRMSE: 19.1%) and CL of nadroparin (rMPE: 1.9%; rRMSE: 22.4%) most optimally. Using 2 samples, a first t=4h and second after a subsequent dose between t=2h to t=10h allowed to adequately predict anti-Xa levels (range rMPE: 0.94%-3.36%; rRMSE: 15.1%-23.7%) and CL (range rMPE:0.79%-1.49%; rRMSE: 16.6%-18.2%), respectively.

Conclusion:

Anti-Xa levels were most optimal within target using an intermediate dose (b.i.d. 5700IU). An evaluation of limited sampling strategies demonstrated the accuracy of less stringent sample timing.

Image :



Boxplots of estimated anti-Xa target levels at t = 4 hours after respective nadroparin dose regimen in the modeling (n=65) cohort. The amount of patients on target (anti-Xa 0.3 - 0.7 IU/ml) is specified with the percentage below the boxplot.