Dosing of therapeutic enoxaparin in mild to moderate renal impairment

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Introduction

- Optimal dosing of therapeutic enoxaparin in mild to moderate renal impairment is unclear
- Product information advises dosage reduction only when creatinine clearance (CrCl) is <30mL/min
- Some evidence advocates dosage reduction in mild to moderate renal impairment when CrCl is <60mL/min
- Plasma anti-factor Xa levels indirectly measure the activity of enoxaparin[1]
- The therapeutic range for twice daily therapeutic enoxaparin dosing is a peak anti Xa level level (3-5 hours post dose) between 0.5-1.0 IU/mL[1].
- Analysis of anti Xa levels may help
    - guide optimal dosing strategies AND
    - determine the extent of variability within this cohort and thus whether routine anti Xa level monitoring is required

Aim

- To identify correlations between enoxaparin dose (mg/kg), anti-factor Xa levels and CrCl in patients with a CrCl between 30-60mL/min given therapeutic doses of twice daily enoxaparin
- To use this data to comment on the current practice of dosing at 1mg/kg twice daily in CrCl 30-60mL/min

Method

Data collected retrospectively from medical records of inpatients and outpatients at eight tertiary hospitals in Queensland between 2000 and 2017 prescribed therapeutic enoxaparin

→ Enoxaparin dose and corresponding peak anti Xa level recorded for patients with a CrCl (calculated by eGFR) between 30-60mL/min prescribed twice daily enoxaparin

Data excluded:
- Doses outside the range 0.85-1.1mg/kg
- weight >100kg
- anti Xa assay not taken 3-5 hours post dose
- patients who did not receive at least 2 doses prior to anti Xa assay
- prophylactic and once daily dosing

→ **Data analysis:**
- Data assorted into CrCl ranges
- Therapeutic, sub-therapeutic and supra-therapeutic anti Xa levels categorized and compared

Results

- 65 anti Xa assays were analysed
    - Median age 76 years (range 49-91 years)
    - Median weight 74 kg (range 50-100kg)
- The majority of levels (62%) were supra-therapeutic as shown in figure 1.

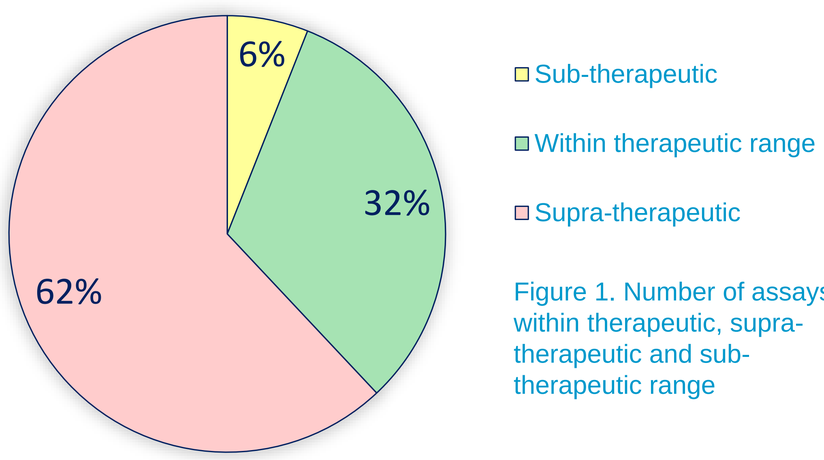

Figure 1. Number of assays within therapeutic, supra-therapeutic and sub-therapeutic range

Results continued

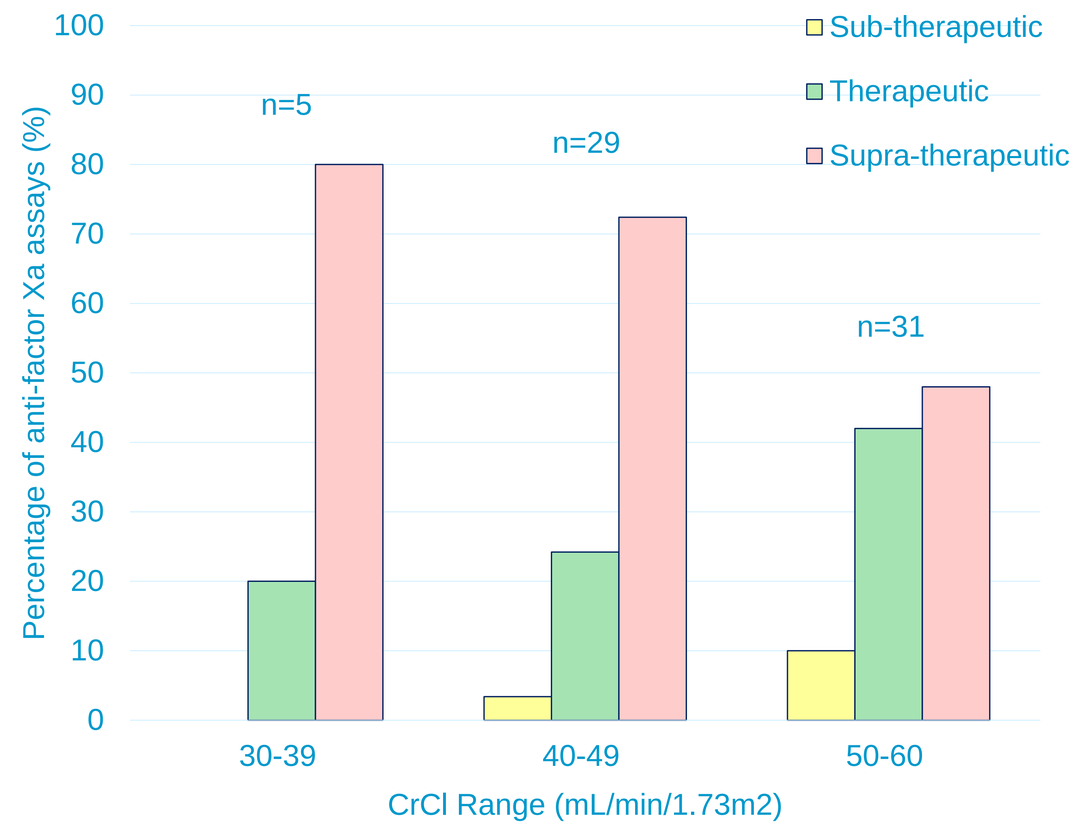

Figure 2. CrCl ranges and percentage of sub-therapeutic, therapeutic, and supra-therapeutic anti Xa levels for enoxaparin dosed between 0.85 and 1.1mg/kg twice daily

- As CrCl decreased, the percentage of supra-therapeutic levels increased, and the percentage of therapeutic levels decreased

Discussion

- Some Studies advocate for the need for dose adjustment of enoxaparin when CrCl is 30-60mL/min[1]
- Our results support this, showing an increase in supra-therapeutic levels as renal function reduced, despite dosing being within the guidelines
- Enoxaparin is largely renally excreted. Studies have shown in CrCl 50mL/min, clearance was reduced by 17%[2], and in 30-49mL/min, clearance was decreased by 31%[3] compared to normal renal function
- Several studies found that patients with a CrCl between 30-60mL/min required lower enoxaparin doses to achieve therapeutic anti Xa levels; 0.75mg/kg every 12 hours[4], and an average dose of 0.84mg/kg every 12 hours[5]
- While our study did not assess adverse outcomes there is evidence to suggest that in patients with moderate renal impairment who received 0.75mg/kg[4] or individualised dosing[6], the occurrence of bleeding is reduced
- Our research further supports the need for dose adjustment in patients with mild to moderate renal impairment

Conclusion

- Enoxaparin doses of 1mg/kg twice daily in patients with a CrCl between 30-60mL/min result in supra-therapeutic levels
- Dosage adjustment is required
- More studies are needed to evaluate and establish guidelines for individualised renal dose adjustment of therapeutic enoxaparin

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