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
- The therapeutic range for twice daily therapeutic enoxaparin dosing is a peak anti Xa level between 0.5-1.0 IU/mL
- 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 2007 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.

Discussion

- Some Studies advocate for the need for dose adjustment of enoxaparin when CrCl is 30-60mL/min
- 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%, and in 30-49mL/min, clearance was decreased by 31% 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, and an average dose of 0.84mg/kg every 12 hours
- 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* or individualised dosing, 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

References


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