The National Kidney Foundation

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A Retrospective Clinical Audit to Evaluate Low Dose vs. Standard Dose Intravenous Etelcalcetide Treatment in Haemodialysis Patients

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Background

- Etelcalcetide is an intravenous calcimimetic agent that has been approved for managing secondary hyperparathyroidism (sHPT) in adult haemodialysis(HD) patients.
- The recommended starting dose of etelcalcetide is 5mg three times a week.[1] However, observational studies indicated that a lower initial dose can effectively manage sHPT. [2,3]
- This clinical audit aimed to evaluate the effectiveness of low accumulated etelcalcetide dose (LD) compared to standard dose (SD) within the first six months of initiation in managing sHPT among HD patients in Singapore.

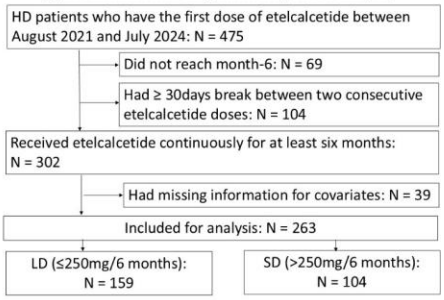
Method

- The retrospective clinical audit included HD patients managed by community dialysis centers in Singapore who received intravenous etelcalcetide continuously for six months, from August 2021 to July 2024.
- Patients were categorised into LD (≤250mg/6 months) and SD(>250mg/6 months) groups.
- The primary outcome was absolute and percent change in serum parathyroid hormone (PTH) at six months.
- Secondary outcomes were absolute and percent changes in serum calcium, phosphate and alkaline phosphatase (SAP) levels at six months.
- Three regression models were constructed: Model 1 was unadjusted, Model 2 adjusted for baseline demographic and laboratory parameters, dialysis vintage, vascular access type, accumulated alfacalcidol dose and comorbidity. In Model 3, all variables in Model 2 were used to calculate the propensity score for inverse probability weighting (IPW) and these variables were also adjusted.

Results

- Patients who have received etelcalcetide continuously for six months from August 2021 to July 2024 and without missing information (N = 263) were included.
- Patients were selected based on Figure 1 below.

Figure 1: Selection of HD patients eligible for analysis



- Hundred and fifty-nine patients (60.5%) received LD and 104 (39.5%) received SD.
- Patients' baseline characteristics are summarised in Table 1.

Table 1: Baseline characteristics of eligible patients

Variables	LD (N=159)	SD (N=104)	p-value	p-value (after weighting)
Etelcalcetide dose (mg/6mths)	185 (155-195)	344 (298-388)	<0.001	NA
Age (Year)	63.0 (54.0-72.0)	60.5 (53.0-68.0)	0.103	0.656
Gender (Female)	78 (49.1%)	37 (35.6%)	0.042	0.939
Ethnicity				
Chinese	91 (57.2%)	59 (56.7%)		
Malay	50 (31.4%)	39 (37.5%)	0.251	0.966
Others	18 (11.3%)	6 (5.8%)		
Dialysis vintage (Year)	6.00 (4.00-9.00)	8.00 (5.00-11.0)	0.004	0.906
Alfacalcidol dose (mcg/6mths)	58.0 (32.0-91.5)	71.0 (38.8-114)	0.033	0.869
Baseline PTH (pmol/L)	119 ± 41.1	150 ± 67.1	<0.001	0.810
Baseline SAP (u/L)	174 ± 134	240 ± 248	0.006	0.381

Categorical variables were summarised as count (proportion) and compared using Fisher's exact test. Continuous variables were summarised as either median (interquartile range) or mean ± standard deviation and compared using either Wilcoxon rank-sum test or Student's t-test.

- There were more females in the LD group than the SD group (LD: 78 (49.1%), SD: 37 (35.6%)).
- Mean baseline PTH levels were higher in the SD group (LD: 119±41.1pmol/L, SD: 150±67.1pmol/L).SD patients also had more alfacalcidol over six months, longer dialysis vintage and higher baseline SAP.
- After inverse probability weighting, the two groups were comparable for all baseline characteristics.

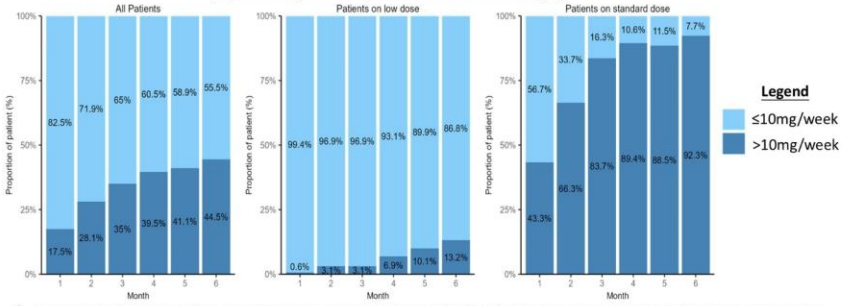
Table 2: Difference in reduction in laboratory parameters between two patient groups *(reference group:LD)*

Outcomes	Model 1 (Unadjusted)	Model 2 (Adjusted)	Model 3 (Weighted and Adjusted)
Absolute reduction in PTH (pmol/L)	11.5 (-3.43, 26.43)	-1.81 (-15.58, 11.95)	0.79 (-11.23, 12.82)
Percent reduction in PTH (%)	6.7 (-10.01, 23.4)	-2.49 (-19.11, 14.14)	1.42 (-11.57, 14.42)
Absolute reduction in Ca (mg/dL)	0.28 (0.1, 0.46)*	0.29 (0.15, 0.43)**	0.27 (0.14, 0.4)**
Percent reduction in Ca (%)	2.71 (0.88, 4.55)*	2.86 (1.37, 4.34)**	2.65 (1.23, 4.06)**
Absolute reduction in SAP (u/L)	0.05 (-0.27, 0.38)	0.1 (-0.24, 0.44)	0.11 (-0.19, 0.41)
Percent reduction in SAP (%)	0.8 (-5.58, 7.18)	1.91 (-4.86, 8.68)	2.63 (-3.38, 8.64)
Absolute reduction in PO4 (mg/dL)	18.78 (-10.58, 48.14)	4.16 (-23.37, 31.69)	11.47 (-10.06, 33.01)
Percent reduction in PO4 (mg/dL)	4.68 (-4.25, 13.61)	2.23 (-6.23, 10.68)	3.97 (-3.42, 11.36)

*p-value<0.05, **p-value<0.001. Results are summarised as estimate (95% confidence interval). Change in lab parameters were analysed using linear regression

- Over the 6-month period, there were no significant differences between the groups in reducing PTH, SAP and serum phosphate (Table 2).
- However, SD patients showed higher absolute (0.27, 95% Confidence Interval (CI) 0.14-0.4mg/dL) and percent reduction (2.65, 95% CI 1.23-4.06%) in calcium than LD.
- Findings were consistent in unadjusted, adjusted and weighted models.

Figure 2: Proportion of patients in each dose category



- Dose trajectory over the months were examined graphically. Patients were separated into two categories based on average weekly dose in each months as shown in Figure 2.
- The SD patients were receiving higher doses than LD patients since the first month. And they also had higher baseline PTH. The extent of calcium reduction tend to be higher among patients with high baseline PTH.[4] Both factors can potentially put these patients at a higher risk of hypocalcemia.

Conclusion

- The audit demonstrated that low and standard etelcalcetide doses had comparable effects on PTH levels in patients undergoing HD. Based on specific patient characteristics, such as dialysis vintage, baseline PTH and SAP levels, and clinical assessment, initiating doses lower than the recommended amount can be considered. Findings from the audit were consistent with other observational studies.
- Patients receiving standard dose and have high baseline PTH should be closely monitored for signs and symptoms of hypocalcemia.
- Clinical trials on etelcalcetide have been adopting the recommended starting dose, leaving room for future studies to investigate the impact of the low dose approach.

References

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