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The DOPPS Practice Monitor for US Dialysis Care: Parathyroid Hormone Levels and Management of Mineral and Bone Disorder in U.S. Hemodialysis Patients

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Introduction

The complex entity termed as Mineral and Bone Disorder (MBD) may contribute to the development of vascular calcification and adverse clinical outcomes among patients with kidney failure¹. By the time of dialysis start, most patients have hyperplasia of the parathyroid glands² and markedly elevated parathyroid hormone (PTH) levels³; these tend to rise further with longer duration of kidney replacement therapy^{4,5}. Findings of most observational studies have described associations between high PTH levels and increased mortality in this population^{6–14}, although this association was not found in a recent meta-analysis¹⁵. Reflecting the lack of strong evidence and the heterogeneity of PTH assays, recent clinical practice guidelines published in 2009 and 2010^{16,17} suggested a PTH target level that was more liberal than what had previously been recommended¹⁸, citing 2 to 9 times the upper limit of normal for the assay used rather than 150 to 300 pg/ml. Furthermore, in the United States (US), MBD practices implemented in response to the 2011 Prospective Payment System (PPS) may have contributed to changes in PTH levels. Based on updated data from the US Dialysis Outcomes and Practice Patterns Study (DOPPS), we report trends in PTH levels and in secondary hyperparathyroidism (SHPT) therapies over the past 4 years, including differences by race.

The DOPPS Practice Monitor (DPM) was launched in 2010 to report trends in dialysis care after PPS implementation.¹⁹ The DPM is updated quarterly with the data lagged 2–4 months. DPM data here include an average of 12,334 hemodialysis patients per month in 168 facilities over a four year period from August 2010–August 2014. Sampling design for the DPM has previously been published^{20,21}. We report on levels of PTH and MBD-related treatments including oral and intravenous vitamin D agents (paricalcitol, doxercalciferol,

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calcitriol) and cinacalcet. Race was based on the patient's medical record. Data regarding facility PTH targets were answered by an average of 71 facilities in the DOPPS medical director's survey from 2010–2014. A separate analysis using the patient sample and methods described in Tentori et al.¹⁴ assessed whether the association of PTH with mortality differed by race.

Results

Trends in PTH levels and association with mortality

Among DOPPS participants in the United States¹⁴, PTH levels increased from 2010 to 2014 (Figure 1). The largest increase in PTH was observed between August 2010 and April 2011, when the median PTH increased by 32% (from 247 to 326 pg/ml) and the 90th percentile also increased by 32% (from 614 to 810 pg/ml). Between April 2011 and August 2014, however, PTH levels remained fairly constant with the median PTH levels increasing 5% (from 326 to 343 pg/ml).

The rise in PTH levels over the past 4 years was similar between blacks and nonblacks ($p = 0.26$), leading to a higher percentage of patients with very high PTH levels (> 600 pg/ml) in both groups (Figure 2). However, because black patients had higher PTH levels at the DPM baseline (416 vs. 305 pg/ml), the percentage of patients with PTH > 600 pg/ml in August 2014 was much higher among blacks vs. nonblacks (29% vs. 17%). In an analysis including US patients in DOPPS 1 – 4 (1996 – 2011)¹⁴, PTH values above 600 pg/ml were associated with increased mortality (HR=1.17 (1.05 1.32), $p=0.007$ with no effect modification identified by race).

Prescription of secondary hyperparathyroidism (SHPT)-related treatments

Overall, there was little change during the study period in the percentage of patients prescribed SHPT-related treatments, including IV vitamin D (from 79% in August 2010 to 76% in August 2014), oral vitamin D receptor agonists (~6–7% over the four year period) and cinacalcet (24–28%). A higher percentage of black patients were prescribed IV vitamin D and cinacalcet compared to nonblack patients. However, the trend in the prescription of MBD related therapies from August 2010 to August 2014 has remained stable for both black and nonblack patients (Figure 3). IV vitamin D dose by product type has not changed over the 4 year period (data not shown).

Facility-level PTH targets

From 2010 to 2014, medical directors at US DOPPS dialysis units reported targeting higher PTH levels¹⁴. The facility upper PTH target has shifted with more facilities indicating an upper target ≤ 600 pg/ml. The percentage of facilities with an upper PTH target of ≤ 300 pg/ml has sharply declined from 82% in 2010 to 22% in 2014, while the percentage of facilities indicating a PTH upper target of ≤ 600 pg/ml increased from 7% in 2010 to 62% in 2014 (Figure 4).

Summary

In the US DPM sample, median PTH levels increased 32%, from August 2010 through April 2011 and have remained relatively stable since then. Black patients carry a disproportionate burden of PTH levels above 600 pg/ml (29%; vs. 17% among nonblacks). This finding warrants particular attention, since such high PTH levels have consistently been associated with adverse outcomes^{6–14} and the association between severe hyperparathyroidism and mortality appeared consistent in both racial groups. While we had postulated that the PPS may have led to lower utilization of MBD-related intravenous drugs, vitamin D prescription remained stable over time. Rather, the increase in PTH levels seem to have been driven mainly by adoption of more liberal PTH targets, as reported in the medical director survey. However, PTH levels >600 are above any currently recommended guidelines and likely represent a modifiable risk factor for adverse outcomes. Clinicians should take this into account especially when treating black patients, since nearly a third of them presented such high levels in the US DOPPS sample.

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Figure 1.

Patient PTH levels in the prior 3 months, 2010–2014. Values at each month are based on the most recent measurement obtained within the prior 3 months; vertical lines extend from 10th to 25th (lower) and 75th to 90th (upper) percentiles; circle represents median.

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Figure 2.

Mean PTH levels and the percentage of patients with PTH > 600 pg/mL, by race, 2010–2014.

Values at each month are based on the most recent measurement obtained within the prior 3 months; vertical bars represent the percent of patients with PTH > 600 pg/mL; horizontal lines represent the mean PTH.

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Figure 3.

Prescription of MBD related therapies in the prior 3 months, by race, 2010–2014. Values for each month reflect any prescription during prior three months. Prescription of oral vitamin D (not shown) showed a similar trend in both Black and Nonblack patients.

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PTH Upper Target DOPPS Medical Director Surveys, 2010-2014

Figure 4.
PTH Upper Target DOPPS Medical Director Surveys, 2010–2014. Facility reported upper targets of PTH, 2010–2014.