Supplementation of natural antioxidants such as vitamin E may thus be beneficial to all ESRD patients on MHD, even though its real benefit in the general population remains a matter for debate.

Conflict of interest statement. We have had no involvements that might raise the question of bias in the work reported or in the conclusions, implications or opinions stated.

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Clinical remission as measured by a decrease in intact parathyroid hormone levels after administration of cinacalcet in patients with severe hyperparathyroidism

Sir, By targeting the calcium-sensing receptor, cinacalcet provides a means by which intact parathyroid hormone (iPTH) secretion may be regulated, by amplifying the receptor’s sensitivity to extracellular calcium. Administration of the drug results in lower iPTH concentrations, while simultaneously lowering serum calcium (Ca), phosphorous (P) and Ca×P product [1–7]. Although a large number of studies have been done in dialysis patients using cinacalcet, most include patients with mild to moderate elevations in their serum iPTH (average baseline iPTH in patients starting cinacalcet 73 pmol/L) [1–7]. For the clinician, however, it is important to understand whether cinacalcet is also effective in patients with severe hyperparathyroidism. We report on a case series of dialysis patients, who were started on cinacalcet when they had exceedingly high baseline iPTH values (defined as >100 pmol/L). We have described the efficacy of cinacalcet in reducing iPTH levels; documented serum Ca, P, Ca×P product and alkaline phosphatase (ALP) levels at monthly intervals and have reported prescribing practices for the concurrent use of vitamin D analogues and phosphate binders. Dosing of cinacalcet and of concurrent phosphate binders, calcitriol and dialysate calcium concentrations were left to the discretion of the medical team.

A total of 33 dialysis patients [peritoneal (PD), haemodialysis (HD) and nocturnal home haemodialysis (NHD)], who were started on cinacalcet during the period October 2004 to the end of June 2006 at our institution, were identified from pharmacy records. Patients were followed until the end of June 2007. Of the study subjects (12 PD, 14 HD and 7 NHD), the average age was 54 ± 14.9 years, with 45% of the patients being female. Patients had received dialysis therapy for 7.25 ± 5.22 years. Four patients had previously undergone partial parathyroidectomy. The median baseline iPTH for all patients was 208 pmol/L (range 106–641 pmol/L). Fifty percent of patients were on calcitriol and 80% were on phosphate binders at the start of cinacalcet therapy.

Over a 1-year period there was a statistically significant decrease in iPTH levels in all patients (Figure 1). Patients on PD appeared to have the smallest reduction in iPTH levels in comparison to HD and NHD patients (39% versus 83% and 71% respectively). The fractional reduction in iPTH appeared to be greater in patients with higher baseline iPTH compared with lower levels (85%, 71% and 66% respectively in those with PTH > 300 pmol/L, PTH 151–300 pmol/L and PTH 100–150 pmol/L). Four patients had a previous parathyroidectomy; their baseline iPTH was 270 pmol/L and by 12 months it had fallen by 67% to 89 pmol/L. Mean serum calcium and Ca×P product decreased significantly over the 12-month study period; phosphorous levels also decreased over this time period, while the median ALP did not change over the study period (Table 1). Over a 1-year period, cinacalcet dose and the use of calcitriol increased significantly. Although the use of calcium carbonate increased over the study period, this was not statistically significant. The use of sevelamer and the number of patients who used no phosphate binders remained constant throughout the study period (Table 1). Sixty-four percent (nine patients) of the IHD patients switched to higher dialysate calcium concentration from a mean of 1.27 mmol/L to a baseline of 1.46 mmol/L at 12 months. Dialysate calcium concentration remained constant in all PD and NHD patients over the 12-month study period, with a mean dialysate calcium concentration of 1.25 mmol/L and 1.44 mmol/L respectively.

Our data suggest that, despite high baseline iPTH levels, cinacalcet is very effective at reducing iPTH values, as well as decreasing serum calcium and the Ca×P product. In comparison to published trials, in which the mean iPTH value was 73 pmol/L [1–7] our data are applicable to patients with extreme hyperparathyroidism (mean iPTH 240 pmol/L). In the first randomized placebo controlled study with cinacalcet, the mean baseline iPTH was 70 pmol/L, with 95% of the patients having a baseline iPTH of <72 pmol/L. [3] In another randomized, double-blind, multi-centre trial,
cinacalcet was assessed in both HD and PD patients, in which the mean baseline iPTH was 93.3 pmol/L [4]. Our study is therefore unique, in that all patients treated with cinacalcet had a baseline iPTH > 100 pmol/L and had a median reduction in iPTH of 71% by 12 months. Hypocalcaemia occurred in five patients and required an increase in vitamin D therapy and/or dialysis calcium concentration; however, none was symptomatic. These data are important because of the well-recognized consequences of hypercalcaemia and hyperphosphataemia.

We speculate that PD patients may have a reduced rate or degree of response to cinacalcet; however, we have insufficient power to evaluate this statistically. As PD patients are seen less often by their nephrologists, it is also plausible that they had less frequent dose adjustments and therefore a slower response. Rigorous study would be required to elucidate this further.

In summary, our findings suggest that cinacalcet may be an effective treatment for dialysis patients with markedly elevated baseline iPTH levels. While we have shown that cinacalcet reduced the biochemical evidence for HPT without adversely affecting mineral metabolism, further studies in much larger numbers of patients are needed to determine the long-term effect on morbidity and mortality.

Conflict of interest statement. M Battistella and SV Jassal have no conflict of interest with respect to this article. SV is currently acting as a consult for the Amgen funded study looking at Anaemia Correction and HRQoL Outcomes in Elderly CKD Patients (STIMULATE). She has held investigator-funded funding from OrthoBiotec, received speaker fees from Pfizer, Amgen, OrthoBiotec and Bristol-Myers Squibb in the past 5 years. M Battistella has attended advisory board meetings for OrthoBiotec, Roche, Amgen and Genzyme in the past 5 years.

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Table 1. Biological and therapeutic changes over the 12-month study period

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median iPTH (pmol/L)</td>
<td>208</td>
<td>127</td>
<td>121</td>
<td>59*</td>
</tr>
<tr>
<td>Mean Ca (mmol/L)</td>
<td>2.51</td>
<td>2.34</td>
<td>2.28</td>
<td>2.30*</td>
</tr>
<tr>
<td>Mean P (mmol/L)</td>
<td>1.66</td>
<td>1.59</td>
<td>1.47</td>
<td>1.48</td>
</tr>
<tr>
<td>Ca × P product (mmol²/L²)</td>
<td>4.19</td>
<td>3.72</td>
<td>3.36</td>
<td>3.40*</td>
</tr>
<tr>
<td>Median ALP (U/L)</td>
<td>202</td>
<td>233</td>
<td>223</td>
<td>212</td>
</tr>
<tr>
<td>Mean daily cinacalcet dose (mg)</td>
<td>29</td>
<td>37</td>
<td>48</td>
<td>64*</td>
</tr>
<tr>
<td>Use of calcitriol (%)</td>
<td>49</td>
<td>55</td>
<td>61</td>
<td>64*</td>
</tr>
<tr>
<td>Use of calcium carbonate (%)</td>
<td>48</td>
<td>48</td>
<td>58</td>
<td>64</td>
</tr>
<tr>
<td>Use of sevelamer (%)</td>
<td>49</td>
<td>48</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>No binders used (%)</td>
<td>21</td>
<td>21</td>
<td>30</td>
<td>27</td>
</tr>
</tbody>
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*Baseline versus 12 month P < 0.05.


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