

22-Oxa-Calcitriol (Maxicalcitol) does not have the Same Suppressive Actions on 1-84 PTH and Large C Terminal PTH Fragments

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Maxicalcitol (22-oxa-calcitriol) is a newly developed vitamin D analog for treatment of secondary hyperparathyroidism. So-called "intact" PTH (iPTH) assays have been used to study the suppressive actions of vitamin D analogs. The utility of iPTH assays, however is limited, in that they do not measure iPTH or 1-84 PTH, exclusively. For roughly five years it has been known that these iPTH assays measure both 1-84 PTH and 7-84 PTH. The purpose of this study was to determine the effects of Maxicalcitol on both 1-84 PTH and C terminal PTH fragments (likely 7-84 PTH).

For the study, the unique Scantibodies DUO PTH assay method was used, which was developed and validated for quantitative determination of both 1-84 PTH and 7-84 PTH and 13 patients (pts) with iPTH levels >300 pg/mL were enrolled. The pts' previous vitamin D treatment was halted prior to the administration of the first Maxicalcitol dose: pts with iPTH >500pg/mL received 10 mcg IV; pts with iPTH levels 300-500pg/mL received 5 mcg (thrice weekly after each dialysis session). Maxicalcitol was administered for 12 wks and the 1-84 PTH and 7-84 PTH levels studied.

The most dramatic decrease in 1-84 PTH, 7-84 PTH, and 1-84 PTH/7-84 PTH ratio were observed after 12 wks of Maxicalcitol administration. The decreases in 1-84 PTH and 7-84 PTH correlated negatively with changes in serum Ca ($r^2=0.54, 0.37$, respectively), but the change in the 1-84 PTH/7-84 PTH ratio was not related to serum Ca changes.

It has been reported that acute Ca changes control the relative proportions of the secretion of 1-84 PTH and large C terminal fragments (CTF; which is likely 7-84 PTH) from the parathyroid gland such that the ratio of 1-84 PTH/C terminal fragments decreases with an increase in Ca. Thus, Ca does not cause a parallel decrease in both 1-84 PTH and CTF. As the chronic suppressive effects of vitamin D analogs have only focused on the sum of 1-84 PTH and CTF, important actions of vitamin D have been overlooked. Our observations with one vitamin D analog indicate that the effects on 1-84 PTH and 7-84 PTH are not equal. As 7-84 PTH has been demonstrated to lower bone turnover, further studies are required to determine the effect of vitamin D analogs on both 1-84 PTH and 7-84 PTH.

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