

DIFFERENTIAL EFFECTS OF CALCITRIOL AND PARICALCITOL ON VASCULAR CALCIFICATION IN HIGH PHOSPHATE-FED, UREMIC MICE. Mohga El-Abbadi, Bryan Bartley, Cameron Gaskill, Carly Ingalls, and Cecilia M. Giachelli, University of Washington, Seattle, WA, USA

Purpose: The goal of this study was to examine the effects of 1,25(OH)₂D₃ (calcitriol) and 19-nor-1 α , 25(OH)₂D₂ (paricalcitol) on vascular calcification in a uremic mouse model of medial calcification.

Methods: Vascular calcification was induced in mice by partial renal ablation and the implementation of a 0.9% high phosphate diet. Two weeks after inducing uremia, mice were treated with biologically equivalent doses of either calcitriol (0.03 μ g/kg, ip, 3x/week) or paricalcitol (0.3 μ g/kg, ip, 3x/week) for 3 weeks. **Results:** Serum analyses revealed similar PTH levels for both groups (960.26 \pm 244.29 and 984.3 \pm 316 pg/ml, respectively; P = 0.96). Biochemical analysis of the aortic arches revealed a 3.7 fold lower aortic calcium content in the paricalcitol versus the calcitriol treated mice (8.99 \pm 3.13 versus 33.66 \pm 6.7 μ g calcium/mg dry wt, respectively; P = 0.003). While serum calcium levels were comparable between groups, serum phosphate levels were significantly lower in the paricalcitol versus the calcitriol treated group (10.3 \pm 0.5 and 14.4 \pm 2.0 mg/dl, respectively; P = 0.05). Although a marked increase in serum blood urea nitrogen (BUN) levels developed over the course of the treatment in the calcitriol group (58.5 \pm 7.2 posturemia/preD versus 82.0 \pm 10.9 mg/dl at termination), no such increase was observed in the paricalcitol treated mice (52.0 \pm 5.29 posturemia/preD versus 52.5 \pm 3.1 mg/dl at termination). A statistically significant difference in serum BUN levels was detected between the two groups at termination (P = 0.02). Finally, calcitriol-treated mice had lower values for body weight (17.6 \pm 0.9 and 20.4 \pm 0.53gm, respectively; P = 0.02), serum glucose (87.4 \pm 14.3 and 139.5 \pm 6.9 mg/dl, respectively; P = 0.005), and serum albumin (2.8 \pm 0.3 and 3.5 \pm 0.1 g/dl, respectively; P = 0.02) at termination when compared to the paricalcitol treated mice.

Conclusions: Paricalcitol, at a 10-fold higher dose than calcitriol, was less calcific and caused less deterioration in renal function in uremic, high phosphate-fed mice possibly by calcium- and PTH-independent mechanisms.