Sex steroid deficiency alters renal calcium transporter expression independently of its effect on bone resorption

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It is well established that sex steroid deficiency induces bone loss, resulting in osteoporosis. Consequently, global androgen receptor knock out (ARKO) mice have trabecular and cortical osteopenia. Bone cell-specific ARKO mice however, have a much less pronounced bone phenotype, suggesting that androgens have an influence on processes in other systems or organs which in turn have an impact on bone metabolism. The kidney is a likely candidate, as it plays an important role in calcium homeostasis, through reabsorption/excretion and synthesis of vitamin D. Therefore, we hypothesize that androgens regulate renal calcium homeostasis, hereby indirectly affecting bone resorption. To test this hypothesis, adult male C57BL/6J mice were orchidectomized (ORX vs SHAM) and treated with the antiresorptive drug risedronate (RIS vs vehicle), in order to study the effects of sex steroid depletion on renal calcium homeostasis independent of bone resorption. Orchidectomy resulted in a decreased kidney weight (2 weeks post-ORX), hypercalciuria (1 week post-ORX) which was normalized 2 weeks post-ORX along with normal serum levels of calcium, 1.25(OH)2D3, PTH, and FGF23. Orchidectomy combined with prior bone antiresorptive treatment abolished the early hypercalciuric phase and even resulted in transiently decreased serum calcium levels 1 week post-ORX. Compared to control mice, a significant upregulation of renal calcium transporters (TRPV5, PMCA, NCX1, CaBP9K and CaBP28K) was observed in both the ORX and ORX+RIS group, while intestinal calcium transporters (TRPV5, TRPV6, PMCA, CaBP9K) remained unchanged, suggesting that sex steroid deficiency might impact renal calcium homeostasis independent of its effect on bone resorption.

Conflict of interests

None

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