The Effects of Core-Binding Factor and Collagen Type II on Hyperphosphatemia-Induced Vascular Calcification in Rats with Remnant Kidneys

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Objective: We conducted a study to observe the effects of core-binding factor A1 (Cbfα1) and collagen type II (Col II) on hyperphosphatemia-induced vascular calcification in rats with remnant kidneys, and to explore the possible mechanisms of vascular calcification in chronic renal disease (CKD) of stage 5.

Methods: For the purpose of the study, we divided 40 Sprague–Dawley rats into four groups, as follows: (i) rats with remnant kidneys that were given a high-phosphorus (HP) diet (n = 10); (ii) rats with remnant kidneys that were given a normal-phosphorus (NP) diet (n = 10); (iii) rats that had a sham operation and were given an NP diet (n = 10); and (iv) rats that had a sham operation and were given an HP diet (n = 10). After 5/6 nephrectomy or sham operation, the rats were fed an HP diet (phosphate (P), 1.2%; calcium (Ca), 1.6%) or an NP diet (P, 0.9%; Ca, 1.2%) for 16 weeks. At Week 16, urine samples were collected for 24-hour urine protein measurement and a blood sample was collected for the measurement of serum phosphorus, serum creatinine (Scr), and serum urea nitrogen (UN). The animals' thoracic aorta was then harvested. Calcium deposition was determined by von kossa staining; the expression of messenger ribonucleic acid (mRNA) of thoracic aorta for Cbfα1 and Col II mRNA was determined with the reverse transcriptase–polymerase chain reaction (RT-PCR); and the expression of Cbfα1 and Col II protein was determined through immunohistochemistry and Western blot analysis.

Results: After a 16-week dietary regimen, urine protein, serum phosphorus, serum urea nitrogen, and serum creatinine levels were significantly increased in the rats with a remnant kidney that were given an HP diet as compared with the levels of these same substances in the other three study groups (P < 0.05). Von kossa staining showed that significant vascular calcification had developed in the rats with remnant kidneys given an HP diet, whereas the rats with remnant kidneys given an NP diet and the rats that underwent sham operation followed by an HP diet only occasionally developed vascular calcification, and the rats that underwent sham operation followed by an NP diet did not develop vascular calcification. The expression of both Cbfα1 and Col II increased significantly in rats with remnant kidneys that received an HP diet, as compared with their expression in the other three groups of rats (P < 0.05); the expression of mRNA for Col II increased significantly in the remnant-kidney models that received an HP or an NP diet as compared with its expression in the other two groups (P < 0.05).

Conclusion: Hyperphosphatemia can be an important contributing factor to vascular calcification in rats with remnant kidneys, and the serum level of phosphorus is positively correlated with the expression of both Cbfα1 and Col II in these animals. The increased expression of both Cbfα1 and Col II in rats with remnant kidneys may be one of the mechanisms responsible for the hyperphosphatemia-induced vascular calcification in these animals.

FUNDING

This study was supported from Fujian Province Science and Technology Key Project (No. 2009Y0040).