Effect of water fluoridation on the development of medial vascular calcification in uremic rats.

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Abstract

Public water fluoridation is a common policy for improving dental health. Fluoride replaces the hydroxyls of hydroxyapatite, thereby improving the strength of tooth enamel, but this process can also occur in other active calcifications. This paper studies the effects of water fluoridation during the course of vascular calcification in renal disease. The effect of fluoride was studied in vitro and in vivo. Rat aortic smooth muscle cells were calcified with 2mM Pi for 5 days. Fluoride concentrations of 5-10 μM--similar to those found in people who drink fluoridated water--partially prevented calcification, death, and osteogene expression in vitro. The anticalcifying mechanism was independent of cell activity, matrix Gla protein, and fetuin A expressions, and it exhibited an IC50 of 8.7 μM fluoride. In vivo, however, fluoridation of drinking water at 1.5mg/L (concentration recommended by the WHO) and 15 mg/L dramatically increased the incipient aortic calcification observed in rats with experimental chronic kidney disease (CKD, 5/6-nephrectomy), fed a Pi-rich fodder (1.2% Pi). Fluoride further declined the remaining renal function of the CKD animals, an effect that most likely overwhelmed the positive effect of fluoride on calcification in vitro. Ultrastructural analysis revealed that fluoride did not modify the Ca/P atomic ratio, but it was incorporated into the lattice of in vivo deposits. Fluoride also converted the crystallization pattern from plate to rode-like structures. In conclusion, while fluoride prevents calcification in vitro, the WHO's recommended concentrations in drinking water become nephrotoxic to CKD rats, thereby aggravating renal disease and making media vascular calcification significant.

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KEYWORDS:

Chronic kidney disease; Fluoridation; Fluoride; Mönckeberg’s sclerosis; Nephrotoxicity; Vascular calcification
