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CADMIUM AS A RISK FACTOR FOR OSTEOPOROSIS AND FRACTURES IN WOMEN

Av

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ABSTRACT

Cadmium is toxic and accumulates in the body, particularly in the kidneys. Cereals, vegetables and potatoes are the main sources of exposure, besides tobacco smoking. The critical effect of cadmium is considered to be renal damage. Massive exposure is known to cause osteomalacia and osteoporosis with multiple fractures. A few recent studies have indicated that the exposure in the general population is associated with osteoporosis, but the link is not clear.

The aim of this thesis was to investigate effects of long-term low-level cadmium exposure on bone health, and to explore whether these effects were mediated *via* reduced activation of 1,25(OH)₂D (vitamin D) in the kidney. Another aim was to elucidate possible combined effects of cadmium and vitamin A (retinol) on bone health. Two population-based studies were used consisting of postmenopausal women, 54 to 69 years of age, with low cadmium exposure. Cadmium exposure was assessed by measuring cadmium concentrations in urine (as a biomarker of long-term exposure) and by estimating the dietary cadmium intake *via* a food frequency questionnaire. Total-body bone mineral density (BMD) and data on fracture incidence (1997-2009) were ascertained. Circulating levels of 1,25(OH)₂D and retinol were measured in serum.

Multivariable-adjusted inverse associations were observed between both urinary and dietary cadmium and BMD at the total body, femoral neck, total hip and lumbar spine. We also observed a statistically significant 2-3 fold increased risk of osteoporosis (T-score <-2.5) per µg/g creatinine of urinary cadmium, or per 10 µg/day of dietary cadmium. Among never-smokers, a several-fold statistically significant increased risk of any first fracture, first osteoporotic fracture and first distal forearm fracture was observed for urinary cadmium. A 30-50% statistically significantly increased risk of any first fracture were observed comparing high dietary cadmium intake (≥13 µg/day, median) with lower intakes (<13 µg/day) among all women and never-smokers, respectively. Combined high dietary and high urinary cadmium (≥0.50 µg/g creatinine) as compared to low, a 3-fold statistically significantly increased risk of osteoporosis and fractures were observed among never-smokers.

Urinary cadmium was not associated with 1,25(OH)₂D and there was no association between 1,25(OH)₂D and markers of bone or kidney effects. This indicates that the negative association between low cadmium levels and BMD was not mediated *via* decreased circulating levels of active vitamin D. Serum retinol concentrations within the normal range tended to be associated with higher BMD at the distal forearm. Serum retinol concentrations in the upper normal range may counteract the negative effect of cadmium on bone.

Altogether this thesis provides important evidence that cadmium exposure at the low exposure levels found in the Swedish general population is associated with negative effects on bone, as indicated by decreased BMD and an increased risk of osteoporosis and fractures. The findings are of high public health relevance since the main dietary cadmium exposure is *via* our most important foods, there are no signs of decreasing exposure levels, and that osteoporosis and related fractures are prevalent.