

Effect of Lead Nanoparticles Inhalation on Bone Calcium Sensing Receptor, Hydroxyapatite Crystal and Receptor Activator of Nuclear Factor-Kappa B in Rats

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ABSTRACT

This study aimed to investigate whether Pb nanoparticle exposure affects the bone calcium sensing receptor (CaSR), hydroxyapatite crystal, and receptor activator of nuclear factor-kappa B (RANK) in rats exposed to subchronic and chronic inhalation. Thirty two rats were randomly divided into eight groups. One group is a non-exposed group. While three groups were exposed to nanoparticles Pb at the following doses 6.25; 12.5; or 25 mg/m³ an hour daily for 28 days. Another three groups were exposed to nanoparticles Pb at following doses 6.25; 12.5; and 25 mg/m³ one hour daily for 6 months. The expression of trabecular CaSR was significantly decreased at the all doses subchronic exposure compared to the control group (P < 0.05). The CaSR expression significantly decreased in second and third doses subchronic exposure groups compared to the control groups (P < 0.05). With subchronic exposure, the crystal size was increased in second dose group and decreased in lowest and highest doses compared to the control (untreated) group. The crystal size and c-axis were decreased in all dose chronic exposures compared to the control (untreated) group. The expression of cortical RANK was significantly lower at the two lowest dose chronic exposures compared to the control group (P < 0.05). In conclusion, Pb nanoparticle inhibit hydroxyapatite crystal growth at least a part via down regulation of CaSR and RANK.

Key words: inhalation; crystal; calcium sensing receptor; trabecular; cortical.

1. INTRODUCTION

Lead (Pb) is a heavy metal that is more widespread than any other metal. Pb can enter the human body through the respiratory and digestive tract (1). Pb has been postulated to be stored in the three parts of the body, including blood, soft tissue, and bone. Pb which located in the bone with a half-life of 30-40 years. Pb follow the path of calcium to enter the cells of the body (2). Modeling using the crystal marker indicates that the incorporation of Pb into trabecular bone hydroxyapatite crystals will increase density and decrease in bone porosity. This indicates that exposure to Pb will improve the quality of trabecular bone. Pb competes with divalent ions when the absorption of nutrients. Some examples of the divalent ions are calcium and zinc. Pb competes with calcium, disrupt the regulation of cell metabolism by binding to receptors, second-messenger calcium, calcium transport blocking the calcium channels and calcium-sodium pump, as well as competing in the calci-

um-binding protein (3).

The calcium-sensing receptor (CaR) is a member of the superfamily of G protein-coupled receptors (4). The calcium-sensing receptor (CaR) is a seven transmembrane domain G-protein coupled receptor that was initially characterized as the sensor responsible for modulating parathormone and calcitonin release in response to changes in blood calcium levels (5). However, the CaR is more than just a calcium sensor; it is a fairly broad spectrum sensor of small cationic molecules, capable of transducing signals in response to changes in the concentration of heavy metals, including lead and cadmium (6), as well as cationic amino acids (7). Receptor activator of NF-κB, alternately identified as TNF-related activation-induced cytokine receptor (TRANICE-R) or osteoclast differentiation and activation receptor (ODAR) is the signaling receptor for RANKL. RANK has been designated TNFRSF11A, and is a type I 616 amino acid homo-trimerizing transmembrane