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ARAŞTIRMA/RESEARCH

Effect of lead nanoparticles inhalation on mesostructure and the osteoprotegerin/receptor activator of nuclear factor-kappaB ligand system in rats

Sıçanlarda kurşun nanoparçacıkların inhalasyonunun mezoyapı ve nükleer faktör-kappaB ligand sisteminin aktivatör reseptörü olan osteoprotegerine etkisi

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Abstract

Purpose: This study aims to investigate whether Pb nanoparticle exposure affects the mesostructure, and osteoprotegerin/receptor activator of nuclear factor-kappaB ligand (OPG/RANKL) system in rats exposed to subchronic and chronic inhalation.

Material and Methods: Forty eight 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.

Results: Subchronic and chronic Pb nanoparticles changed trabecular mesostructure. We found that subchronic exposure significantly increased the levels of OPG at the first and second dose exposure compared to the control groups ($P < 0.05$). In the chronic exposure, we found that the levels of OPG significantly increased at the first and second dose exposure compared to the control group ($P < 0.05$). In this study significant reduction in subchronic exposure to second and third doses compared to the first dose or exposure control ($P < 0.05$) were shown. In chronic exposure, no significant differences in RANKL levels were found between groups ($P > 0.05$). In subchronic exposure, the ratio of OPG/RANKL significantly increased between the third dose exposure compared to controls ($P < 0.05$), with not significant

Öz

Amaç: Bu çalışma, subkronik ve kronik inhalasyona maruz bırakılan sıçanlarda Pb nanopartikül maruziyetinin nükleer faktör-kappaB ligand (OPG / RANKL) sisteminin mezoyapı ve osteoprotegerin / reseptör aktivatörünü etkileyip etkilemediğini araştırmayı amaçlamaktadır.

Gereç ve Yöntem: Kırk sekiz sıçan tesadüfen sekiz gruba ayrıldı. Bir grup, açıklanmamış bir gruptur. Üç grup Pb nanopartiküllere maruz bırakılmışken 6.25; 12.5; veya 28 gün boyunca günde bir saat 25 mg / m^3 uygulandı. Diğer üç grup, nanopartikül Pb'ye maruz bırakıldı; dozlar 6.25 12.5; ve 6 ay süreyle günde bir saat 25 mg / m^3 tü.

Bulgular: Subkronik ve kronik Pb nanopartikülleri trabeküler mezoyapıyı değiştirdi. Subkronik maruziyetin birinci ve ikinci dozu kontrol gruplarına kıyasla OPG düzeylerini önemli ölçüde arttırdığını bulduk ($P <0.05$). Kronik maruziyetinde, OPG düzeylerinin birinci ve ikinci dozu kontrol grubuna göre anlamlı olarak arttığını bulduk ($P <0.05$). Bu çalışmada, subkronik maruziyetinde ikinci ve üçüncü dozları, birinci doza veya kontrol grubuyla kıyaslandığında önemli bir ($P <0.05$) azalma gösterdi. Kronik maruziyette, gruplar arasında RANKL düzeylerinde anlamlı bir farklılık bulunmadı ($P> 0.05$). Subkronik maruziyette, OPG / RANKL oranı üçüncü dozla kontroller kıyaslandığında anlamlı olarak arttı ($P <0.05$) ve kronik maruziyette anlamlı farklılıklar görülmedi.

Sonuç: Osteoblastın RANKL inhibisyonu ve OPG stimülasyonunun enazından bir bölümünün aracılığıyla Pb

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differences in chronic exposure.
Conclusion: Pb nanoparticle induced trabecular bone neoformation at least a part via OPG stimulation and inhibition of RANKL by osteoblast.
Key words: Inhalation, toxicology, bone remodeling, femur.

nanopartikül trabeküler kemik neoformasyonuna indüklendi.

Anahtar kelimeler: İnhalasyon, toksikoloji, kemiğin yeniden oluşumu, femur.

INTRODUCTION

Lead (Pb) is a heavy metal that is more widespread than any other metal. Levels of Pb in the environment increased, as mining, smelting, and a variety of uses in industry. 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. Firstly, Pb can be found in the blood. As much as 95% Pb binds to erythrocytes with a half-life of 25-30 days. Secondly, Pb can be found in soft tissue, with a half-life of several months. Thirdly, Pb can be found in the bone with a half-life of 30-40 years. As much as 90% of Pb that enters the body will accumulate in the bone. Pb follow the path of calcium to enter the cells of the body[2].

Ingestion of Pb orally by mice shows that there is an accumulation of Pb in the tibia compared with those not given the Pb. Exposure to Pb can cause a decrease in somatic growth, longitudinal bone growth and bone strength at the time of puberty. In the end, Pb exposure can inhibit osteoblastogenesis in adult animals[3]. 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 compete 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 calcium-binding protein[4].

Bone remodeling occurs throughout life via synthesis of bone matrix through the action of two major cell types: osteoblasts and osteoclasts[5]. Osteoblasts are responsible for bone formation, while osteoclasts are in charge of bone resorption[6,7]. The proper functioning of these two cell types is necessary for the maintenance of bone mass as well as bone mineral density. Osteoporosis is defined as a reduction in bone mass and the disruption of bone micro-architecture, which results in a decrease in bone strength and an increase in fracture risk[8]. This study aims to investigate whether Pb nanoparticle exposures affects the mesostructure, and osteoprotegerin/receptor activator of nuclear factor-kappaB ligand (OPG/RANKL) system in rats exposed to subchronic and chronic inhalation.

MATERIAL AND METHODS

Animals

Male Wistar albino rats, 16 weeks of age, weighing 175–200 grams, were used for this study. Forty eight rats were randomly divided into eight groups. One of the group is the non-exposed group. Three groups were exposed to Pb nanoparticles at doses of 6.25; 12.5; or 25 mg/m3 an hour daily for 28 days. Another three groups were exposed to Pb nanoparticles at doses of 6.25; 12.5; and 25 mg/m3 one hour daily for 6 months. Animals were kept in a clean wire cage and maintained under standard laboratory conditions with a temperature of 25 ± 3°C and dark/light cycle 12/12 h. Standard diet and water were provided ad libitum. Animals were acclimatized to laboratory conditions for two weeks prior to the experiment. Animal care and experimental procedures were approved by the institutional ethics committee of Faculty of Medicine, Padjadjaran University, Bandung, West Java, Indonesia.

Pb Nanoparticles exposure

Pb nanopowder was purchased from Intelligent Materials Pvt. Ltd (Nanoshell LLC, Wilmington, DE, US). The concentration of nanoparticles Pb exposure was determined according to occupational exposure in upper ground coal mining areas in South Kalimantan, Indonesia9-12 and Turkey13. The exposure chamber was designed and is available in the Laboratory of Pharmacology, Faculty of Medicine, Brawijaya University. The principal work of the chamber is to provide an ambient resuspended PM10 coal dust, which can be inhaled by rats. Chamber size was 0.5 m3 and flowed by a