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BOOK OF ABSTRACTS 4







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SUBCLINICAL HYPOTHYROIDISM IN GRAVID RATS CAUSES DELAYED OSTEOGENIC DIFFERENTIATION IN PUPS

Ivan Milosević¹, Jelena Danilović Luković², Tijana Luzajić¹, Danica Marković¹, Anita Radovanović¹, Sophie Sourice-Petit³, Jerome Guicheux³, Milica Kovacević Filipović⁴

The effects of maternal hypothyroidism on the development and function of different organs of their offspring are well known. It is unclear how its subclinical form affects some of these processes, including endochondral ossification during prenatal and early postnatal development. Our previous studies have demonstrated that hypothyroid rat pups had reduced growth plate thickness.

The aim of the study was to assess bone turnover by defining the expression of tartrate-resistant acid phosphatase (TRAP), alkaline phosphatase tissue nonspecific isozyme (ALPL) and mRNA for dentin matrix acidic phosphoprotein (DMP1) in the tibia of pups from subclinical hypothyroid dams in early postnatal development. Subclinical hypothyroidism (SHT) was induced with propylthiouracil through drinking water (1.5 mg/l) in pregnant Albino Oxford dams from the first day of gravidity and during lactation. The control group was untreated. Five, sevenday-old pups from each experimental group were euthanized. All histological examinations were performed on paraffin sections of the proximal tibial growth plate. Histochemistry was used to assess the expression of TRAP, immunohistochemistry for ALPL and *in situ* hybridization for DMP1. The area of the TRAP positive signal, optical density of ALPL immunostaining, and the number of DMP1 positive cells were evaluated using the Image J. Expression of TRAP and ALPL in the proximal tibial growth plate were lower in the hypothyroid pups, and the number of cells expressing mRNA for DMP1 was decreased.

TRAP is a marker of osteoclast activity. Osteoclasts are multinucleated cells which are necessary for bone and mineralized cartilage resorption. In osteoblasts ALPL and DMP1 are expressed and they have an important role in the process of endochondral ossification. As we have shown that TRAP, ALPL and DMP1 are decreased, we may conclude that maternal SHT in rats leads to compromised cartilage to bone transition, and delayed osteogenic differentiation in the early infantile period.

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