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MEETING ABSTRACT

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Effects of alendronate on carbohydrate metabolism and behavior in young healthy rats

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Background: Osteocalcin is a vitamin K-dependent protein that is synthesized by osteoblasts and incorporated in the bone matrix in its carboxylated form (cOC). During the process of bone resorption, osteocalcin undergoes a decarboxylation reaction and is released in the circulation in its un(der)carboxylated form (ucOC). Experimental studies performed on osteocalcin-deficient mice revealed that ucOC functions as a hormone regulating energy homeostasis [1] and controlling behavior [2].

Alendronate is a bisphosphonate used for treatment and prophylaxis of osteoporosis. It increases bone mineral density by inhibiting bone resorption. As a result, alendronate impairs the release of ucOC in the circulation and decreases its plasma concentration [3].

Objective: The aim of the present study was to estimate the effect of alendronate on carbohydrate metabolism and behavior in young healthy rats.

Methods: 24 male Wistar rats were divided in two groups: an experimental group, receiving alendronate subcutaneously three times weekly in a dose of 50 µg/kg body weight, and a control group receiving saline. The rats had free access to food and water. The duration of the study was 15 weeks. At the end of the experiment biochemical and behavioral tests were performed. Carbohydrate metabolism was evaluated by measuring the fasting blood glucose level (FBG) and performing an insulin tolerance test (ITT). The area under the BG–time curve (AUC) was calculated. To evaluate the locomotor activity, we used the open field test (OFT); we assessed anxiety by the social interaction test (SIT) and depression-like behavior by the forced swimming test (FST). Student's *t*-test was used for analysis.

Results: The FBG was higher in alendronate treated animals, as was the AUC from the ITT. Alendronate had no effect on locomotion in the OFT and on the immobility time in the FST. However, the time of social interaction in the SIT was significantly reduced in the alendronate-treated group indicating an anxiety-like behavior.

Conclusion: Alendronate treatment impaired carbohydrate metabolism and caused an anxiety-like behavior in rats. We are tempted to speculate that alendronate produced the observed effects by reducing the plasma level of un(der)carboxylated osteocalcin thus impairing its physiological role as a regulator of energy homeostasis and behavior.

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Keywords: alendronate – fasting blood glucose – insulin tolerance test – anxiety

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