INFLUENCE OF LEPTIN ON THE EARLY PHASES OF BONE FORMATION DURING MOUSE SKELETON ORGANOGENESIS

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Leptin is a 16-kDa hormone, primarily secreted by adipose tissue, which controls body weight through its effects on food intake and energy expenditure by negative feedback at the hypothalamic nuclei. Leptin is now known to have actions in the immune system, reproduction, development, haemopoiesis, angiogenesis and, most recently, in bone metabolism (1). Concerning the skeleton, it seems to be involved in the regulation of bone formation by two opposite mechanisms: a central control, via a neuronal pathway, exerting an inhibitory effect on bone formation and a peripheral control, via a local pathway, stimulating osteogenesis.

Notwithstanding the huge amount of data about the positive peripheral effect of leptin on growing and adult skeleton, very few observations are reported in the literature concerning leptin function during skeleton organogenesis. The aim of the present study was to investigate leptin peripheral effect on the early phases of bone histogenesis.

Ten pregnant mice were divided into two groups: five treated with over-physiological doses (2 mg/Kg) of leptin (hypodermic injected at the 7^{th}, 9^{th} and 11^{th} days of pregnancy) and five controls treated with physiological solution. The newborn mice were sacrificed one day after birth and primary ossification centers were stained with Alizarin Red S. The size of the ossification centers of long bones and hips were measured by an Image Analyzer under the light microscope.

The results showed that the ossification centers of mice born from mothers treated with leptin were more developed in lenght (statistical significance $p<0.002$) with respect to those born from the control ones; thus leptin seems to have a positive effect on ossification center growth.

We do not know as yet whether, during the early phases of endochondral ossification, leptin positive effect acts on bone cells and/or cartilage cells. The fact that leptin could positively activate both types of cells is not surprising, considering that they share common staminal progenitors.

(1) Morroni M., De Matteis R., Palumbo C., Ferretti M., Villa I., Rubinacci A., Cinti S. and Marotti G. (2004) *In vivo* leptin expression in cartilage and bone cells of growing rats and adult humans. J. Anat. 205: 291–296.