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THE INFLUENCE OF CASEINPHOSPHOPEPTIDES ON INTRACELLULAR CALCIUM CHANGES IN PRIMARY HUMAN OSTEOBLASTS: A NUTRIENT DEPENDENT MODULATION OF BONE CELL METABOLISM

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Caseinphosphopeptides (CPPs) are a family of peptides originating from in vivo and in vitro hydrolysis of casein. They possess a sequence of three phosphorylated serines followed by two glutamic acids, the acidic motif, able to bind minerals such as calcium. These nutritional compounds display the ability to increase calcium solubility in the digestive tract. Thus, CPPs were hypothesized to increase the calcium absorption and retention in vivo, with potential effects on bone mineralization. Notwithstanding, there are controversial reports on CPP action. The methodological approach used by different laboratories to study calcium absorption and bone mineralization resulted unable to out light whether the peptides have a specific effect on bone metabolism besides the enhancement of calcium availability. We have therefore designed the following study to evaluate a possible direct role of CPPs in bone cell metabolism. Primary human osteoblasts were established in culture using trabecular bone samples obtained from waste materials during orthopedic surgery of patients without metabolic or malignant bone disease. Cytosolic calcium changes were measured by video-microscopy using the fura-2 method on single cells. A mixture of CPPs of commercial origin as well as pure synthetic CPPs were used. The administration of CPPs to human osteoblasts caused an immediate but transient intracellular calcium change in a dose dependent manner. This CPP-induced effect, analogous to that reported for human intestinal cells, is not cytotoxic and is triggered by an influx of the extracellular ions through the cell plasma membrane. The osteoblast pre-treatment with the active form of vitamin D, known to differentiate human osteoblast, does not affect the cell responsiveness to CPP administration. The 24 hours cell incubation with CPPs induced the increase of the activity of alkaline phosphatase, a marker of osteoblast differentiation, reaching a level similar to that produced by vitamin D. The same CPP treatment caused a small but significative reduction in cell rate proliferation and a slight increase in apoptosis activity. Taken together these results indicate that CPPs are endowed of a bone specific effect which underlying mechanism requires further evaluation. CPPs may act not only as a mere carrier for improving calcium absorption and utilization, but also as a trophyc compound for bone health by enhancing osteoblast differentiation and activity.

Conflict of Interest: none declared

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