Abstract

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Zinc modulation of insulin-like growth factor's effect in osteoblastic MC3T3-E1 cells.

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OBJECTIVE: Whether the anabolic effect of insulin-like growth factor-I (IGF-I) in osteoblastic MC3T3-E1 cells is modulated by zinc, an activator of bone formation, was investigated in vitro.

METHODS: After subculture for 3 days, the cells were cultured for 72 h with IGF-I (10(-8) M).

RESULTS: The peptide produced a significant increase of protein concentration, deoxyribonucleic acid (DNA) content, and cell number in the cells. These increases were markedly enhanced by the presence of zinc sulfate (10(-5) M), but not zinc-chelating dipeptide (beta-alanyl-L-histidinato zinc; 10(-5) M). Also, the cellular alkaline phosphatase activity was synergistically increased by the presence of both IGF-I and zinc sulfate. Thus, effect was not seen in the presence of both insulin (10(-8) M) and zinc sulfate (10(-5) M). The effect of zinc sulfate to enhance the IGF-I-increased alkaline phosphatase activity and protein concentration in the cells was clearly prevented by the presence of cycloheximide (10(-6) M), staurosporin (10(-8) M), or okadaic acid (10(-7) M) with an effective concentration. However, staurosporin had a partial inhibiting effect on the IGF-I or the IGF-I plus zinc-induced increases in cellular protein, although okadaic acid entirely blocked the IGF-I or the IGF-I plus zinc effect.

CONCLUSIONS: The present study demonstrates that the anabolic effect of IGF-I in osteoblastic cells is enhanced by zinc ion. The enhancement by zinc may be mediated through the signaling pathway of protein kinase C and protein phosphatase in the cells.

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