Abstract


Long-term zinc deprivation accelerates rat vascular smooth muscle cell proliferation involving the down-regulation of JNK1/2 expression in MAPK signaling.


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BACKGROUND: The accelerated proliferation of vascular smooth muscle cells (VSMCs) is a contributor for atherosclerosis by thickening the vascular wall. Since zinc modulation of VSMC proliferation has not been clarified, this study investigated whether zinc affects VSMC proliferation.

METHODS AND RESULTS: Both a rat aorta origin vascular smooth muscle cell line (A7r5 VSMCs) and primary VSMCs which were collected from rat aorta (pVSMCs) were cultured with zinc (0-50 μM Zn) for short- (≤12 d) and long-term (28 d) periods under normal non-calcifying (0 or 1 mM P) or calcifying (>2 mM P) P conditions. Mouse vascular endothelial cells (MS I cells) were also cultured (under 0-50 μM Zn and 10 mM P for 20 d) to compare with VSMC cultures. While during short-term culture of VSMCs, zinc deprivation decreased cell proliferation in a zinc-concentration manner both under non-calcifying and calcifying conditions in A7r5 and pVSMCs (P < 0.05), during long-term cultures (28 d), A7r5 VSMC proliferation was inversely related to medium zinc concentration under normal physiological P conditions (regression coefficient r(2) = -0.563, P = 0.012). The anti-cell proliferative effect of zinc supplementation (>50 μM) was VSMC-specific. Long-term (35 d), low zinc treatment down-regulated JNK expression and activation, while not affecting ERK1/2 MAPK signaling in A7r5 VSMCs.

CONCLUSION: The results showed that chronic zinc deprivation accelerated VSMC proliferation, perhaps due to down-regulation of MAPK-JNK signaling, and that the anti-cell proliferative role of zinc is VSMC-specific. The findings suggested that zinc may have anti-VSMC proliferative properties in atherosclerosis.

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