Mechanism of colchicine-induced steroidogenesis in rat adrenocortical cells

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摘要

Abstract

Conflicting data for the effects of colchicine on cholesterol transport and steroidogenesis raise the question of the role of microtubules in cholesterol transport from the lipid droplet to mitochondria in steroidogenic cells. In this study, using corticosterone radioimmunoassay and immunofluorescence microscopy, we re-evaluated the effects of colchicine on hormone production and morphological changes of lipid droplets' and studied the signaling pathway involved in colchicine-induced steroidogenesis. Colchicine stimulated steroid production in a dose- and time-dependent manner. The structural integrity of both the microtubules and the lipid droplet capsule was destroyed by colchicine treatment. Disruption of the lipid droplet capsule occurred later than microtubule depolymerization. After cessation of colchicine treatment and a 3 h recovery in fresh medium, capsular protein relocated to the droplet surface before the cytoplasmic microtubule network was re-established. beta-lumicolchicine, an inactive analogue of colchicine, disrupted the capsule and increased hormone production without affecting microtubular structure. Thus, microtubule depolymerization is not required for the increase in steroid production and capsular disruption. To explore the signaling pathway involved in colchicine-induced steroidogenesis, we measured intracellular cAMP levels. Unlike ACTH, colchicine did not increase cAMP levels, suggesting that the cAMP-PKA system is not involved. Colchicine and ACTH had additive effects on corticosterone production, whereas colchicine and PMA did not, implying that part of the PKC signaling mechanism may be involved in colchicine-induced steroidogenesis. Cycloheximide, a protein synthesis inhibitor, completely inhibited colchicine-induced steroidogenesis and capsular disruption. These results demonstrate that the steroid production and lipid droplet capsule detachment induced by colchicine are both protein neosynthesis-dependent and microtubule-independent.