

Effect of Epinephrine on 14C- α -methyl-D-glucopyranoside (α -MG) Uptake in Renal Proximal Tubule Cells

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Background: Epinephrine is known to be a very important factor in the regulation of renal sodium excretion. However, the effects of epinephrine on Na⁺/glucose cotransporter have not been elucidated in primary cultured renal proximal tubule cells (PTCs). Thus we investigated that effect of epinephrine on 14C- α -methyl-D-glucopyranoside(α -MG) uptake and its related signal pathways in the PTCs.

Methods: Male New Zealand White rabbits(1.5-2.0kg) were used for these experiments. PTCs were grown in D-MEM/F12 supplemented with insulin, transferrin and hydrocortisone. α -MG uptake, AA release, PGE2 assay, cAMP assay and Western blotting were performed.

Results: Epinephrine(>4hr, 10⁻⁶M) inhibited α -MG uptake in time- and dose- dependent manner. Phentolamine(α antagonist, 10⁻⁹M), prazosin(α 1 antagonist, 10⁻⁹M), yohimbine α 2 antagonist, 10⁻⁹M), propranolol(β antagonist, 10⁻⁹M) were used in order to to examine the adrenergic receptor subtype that mediates inhibition of α -MG uptake in response to epinephrine. Adrenoceptor antagonists significantly inhibited α -MG uptake and AA release. The Effects of epinephrine on α -MG uptake and AA release were also blocked by staurosporine and bisindolymaleimide I (PKC inhibitors), SQ 22536 and PKI(PKA inhibitors), 8-Br-cAMP, mepacrine and AACOCF3 (PLA2 inhibitors). Indeed, epinephrine increased PGE2 productions and intracellular cAMP content. We also examined the involvement mitogen activated protein kinase(MAPK) pathway in epinephrine induced inhibition of α -MG uptake. Epinephrine activated phosphorylation of p44/42 MAPK over 60 min. PD 98059(a p44/42 MAPK inhibitor), but not by SB 203580(p38 MAPK inhibitor) blocked the effect of epinephrine on α -MG uptake.

Conclusion: Epinephrine inhibited Na⁺/glucose cotransporter via PKA/PKC, PLA2, p44/42 MAPK signaling pathway in primary cultured rabbit renal proximal tubule cells.