

Effect of Extracellular ATP on PTH-dependent Regulation of Phosphate Transport in Rabbit Proximal Tubule Cells

부산대학교 의과대학 생리학교실

권지혜, 송선욱, 정진섭, 김용근, 우재석

Purpose: This study was undertaken to evaluate the effect of P2 receptor activation on the PTH-dependent regulation of phosphate transport in the renal proximal tubules.

Method: Proximal tubule cells were isolated from the rabbit kidney and cultured in hormonally-defined media. Effects of different nucleotides on the PTH-dependent generation of cAMP and inhibition of phosphate transport were examined.

Results: ATP exerted differential effects. In the absence of PTH, it inhibited phosphate uptake and stimulated cAMP generation. However, in the presence of PTH, it attenuated the effect of PTH to stimulate cAMP generation and inhibit phosphate uptake. The effect of ATP in the absence of PTH to stimulate basal cAMP production and inhibit phosphate transport might be mediated by cyclooxygenase-dependent metabolism of arachidonic acid, because those effects were abolished in the presence of indomethacin. Forskolin and dibutyryl-cAMP (DiBu-cAMP), as well as PTH, inhibited phosphate uptake. However, in contrast to the effect on PTH-induced inhibition, ATP did not affect the forskolin- or DiBu-cAMP-induced inhibition. Likewise, ATP did not affect the forskolin-induced stimulation of cAMP production. Agonist profile of the effects of different nucleotides suggested that P2Y1- and P2Y2-like receptors are involved in the effect of ATP. The effect of ATP to attenuate the PTH action was significantly blocked by calphostin C or PKC-depletion. Similar results were observed in pertussis toxin-treated cells.

Conclusion: These results suggested that PKC-dependent modification of the Gi protein and, subsequently, reduced responsiveness of the adenylate cyclase is responsible for the attenuating effect of ATP on the PTH-dependent regulation of phosphate transport in rabbit proximal tubule cells.