Inibidores da bomba de prótons inibem a via “extracellular signal-regulated protein kinase 1/2 (ERK1/2) phosphorylation” (via ERK 1 / 2) e promove a apoptose em células do câncer gástrico

Blockage of intracellular proton extrusion with proton extrusions with proton pump inhibitor induces apoptosis in gastric cancer.

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Source
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Retraction in

Abstract

Proton pump inhibitors have been used for treatment of acid-related gastroesophageal diseases and they act as potent inhibitors of gastric acid pump, H(+)/K(+)-ATPase. Since cancer cells in vivo often exist in an ischemic microenvironment with a lower pH, maintenance of cellular pH is important for cell survival. In this study, we evaluated whether blocking of proton extrusion with proton pump inhibitors could inhibit the viability of gastric cancer cells. Treatment of human gastric cancer cells with proton pump inhibitors significantly attenuated cell viability in a time- and dose-dependent manner. The pro-apoptotic activity of proton pump inhibitors was mediated by release of cytochrome c and caspases activation. Gastric cancer cells showed the resistance to acidity of culture medium, which was related with a remarkable increase of extracellular signal-regulated protein kinase 1/2 (ERK1/2) phosphorylation in the acidic condition. This ERK1/2 phosphorylation was completely inhibited by pretreatment with proton pump inhibitors, suggesting that its inhibitory action on phosphorylation of ERK1/2 might contribute to the induction of apoptosis in
gastric cancer cells. In conclusion, our results suggest novel therapeutic approaches for gastric cancer with proton pump inhibitors.

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