Plasmatic profile and anti-secretory activity of a new immediate release formulation of esomeprazole in comparison with enteric coated tablets

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Background and Aim. H^+/K^+-ATPase inhibitors, commonly known as proton pump inhibitors (PPI), are the most potent and effective drugs indicated for the treatment of all acid-related disorders. Esomeprazole, the S-enantiomer of omeprazole, on the market since 2001, is available as enteric-coated formulations, due to its acid-lability (1). However, these preparations show delayed absorption and late anti-secretory effect unsuitable for on-demand therapy. To overcome these limits immediate-release formulations of PPI have been developed (2).
The aim of this work was to determine the plasmatic profile and the anti-secretory activity in rats of a new immediate-release formulation (IR) of esomeprazole and sodium carbonate in comparison with an enteric-coated formulation (GR).
Methods. *Plasmatic profile*: IR and GR esomeprazole tablets (diameter 2 mm) were orally administered to male Wistar rats in 1ml of water; plasmatic esomeprazole concentrations were determined by HPLC-MS analysis of blood samples collected at different time points from sublingual vein (3).
Anti-secretory activity: IR and GR esomeprazole tablets, IR sodium carbonate tablets and control (CTR) tablets (containing only excipients without sodium carbonate) were administered to rats 30 min (IR) or 120 min (GR) before pylorus ligation (4); animals were sacrificed two hours after surgery to determine gastric juice volume, acid concentration and total acid output.
Results. *Plasmatic profile*: IR esomeprazole evidently showed a more rapid absorption compared to GR tablets (t_{maxIR}=5min vs t_{maxGR}=150min), but the plasmatic peak concentrations (C_{maxIR}=0.49±0.09ug/ml vs C_{maxGR}=0.33±0.10ug/ml) and area under the curve (AUC) values (AUC_{IR}=32.81±7.86ug/ml*min vs AUC_{GR}=20.92±7.84ug/ml*min) were more favourable for the IR formulation but not significantly different.
Anti-secretory activity: IR esomeprazole significantly reduced acid concentration and total acid output with respect to CTR tablets (15.6±4.6meqH^+/ml vs 33.4±4.26meqH^+/ml; 65.2±22.96meqH^+ vs 166.2±23.55meqH^+, $P<0.05$). GR esomeprazole tablets moderately decreased acid concentration (25.3±5meqH^+/ml) and total acid output (84.3±12.51meqH^+/ml). Both IR and GR esomeprazole formulations lowered gastric juice volume compared with control tablets, although not significantly (IR: 3.9±0.3ml, GR: 3.8±1.13ml, CTR: 5.7±1.64ml). IR sodium carbonate tablets did not improve any of the evaluated parameters.
Conclusions. IR esomeprazole showed a fast absorption with an extent of bioavailability comparable to GR formulation. As consequence, IR esomeprazole reduced gastric acid secretion more quickly and efficiently than GR formulation. These preliminary results suggest a possible use of this new formulation not only for chronic therapy, as with GR proton pump formulation, but in particular for on demand therapy.

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