EFFECTS OF Helicobacter Pylori UREASE ON ENDOTHELIAL CELLS

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Introduction and Objective: Helicobacter pylori urease (HPu) is reported as a key bacterial product that enables the bacteria to colonize and survive in the stomach, favoring the occurrence of gastric ulcer and adenocarcinoma. We have demonstrated that HPu has a pro-inflammatory effect on human neutrophils. Despite H pylori effect on endothelial cells (EC) were early described, the direct involvement of HPu in vascular effects is not completely understood. We have investigated the effects of HPu on EC and the signaling pathways involved in these processes.

Material and Methods: EC (HMEC cell line) were treated for different times with HPU 10 nM. Cell viability was analyzed using MTT assay. Cell permeability was assessed by Dextran-FITC extravasation and cytoskeleton rearrangement was analyzed through cytochemistry analysis. Proteins detection were performed by western blotting and immunostaining assay. ROS and NO production were detected by DCF and DAF probes, respectively.

Results and Conclusions: The treatment of EC with HPu (10nM) did not affect cell viability. On the other hand, HPu enhanced EC permeability and reduced transendothelial resistance. Accordingly, HPu caused dissociation of cell–cell junctional cadherins, induced VE-cadherin phosphorylation and alterations in actin cytoskeleton dynamics, and increased FAK phosphorylation. Additionally, HPu promoted the production reactive oxygen species (ROS) and nitric oxide (NO) by EC, that were impaired by a PI3K-AKT pathway inhibitors. HPu also activated nuclear factor κB (NF-kB), induced neutrophil adhesion to EC and increased E-selectin expression on EC. Moreover, HPu is able to induce the EC to tubulogenesis. The effects of HPu on EC seem to be modulated by integrins, as they were attenuated in the presence of RGD peptides. In conclusion, the data indicate that HPu activates EC, probably through an integrin-associated signaling, suggesting its role as a pro-inflammatory and pro-angiogenic key molecule in H pylori-related diseases.

Keywords: Helicobacter pylori, Urease, Endothelial cells.

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