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Poster presentation

The role of cGMP-cGKI-signaling for duodenal bicarbonate secretion

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Background

The duodenal mucosa protects itself from gastric acid injury by the secretion of bicarbonate from epithelial cells. We determined a possible role of the cGMP-cGKI pathway for the duodenal bicarbonate secretion by studying conventional cGKI knockouts (cGKI-KOs) and rescue mice (RM) that express either the cGKIα or Iβ isoform in SM22α positive smooth muscle cells [1].

Results

The basal secretion rate of bicarbonate was strongly reduced in the different gene-targeted cGKI mice. Moreover, the H^+ induced bicarbonate secretion was significantly increased in controls but nearly absent in all cGKI mutants, whereas invasive pH measurements in fasted animals demonstrated that the gastric acid production of all genotypes was similar. The dysfunction of the duodenal bicarbonate secretion of RM and cGKI-KO animals was associated with severe gastrointestinal bleedings, which were caused by the age-dependent aggravation of an epithelial ulceration that localized to the papilla Vateri.

Conclusion

The analysis of cGKI-KO and RM indicates that a cGMP-cGKI-dependent pathway is present in non-smooth muscle cells of the duodenum that is involved in the basal and acid-induced secretion of bicarbonate. The inability to secrete adequate amounts of bicarbonate ultimately leads to duodenal ulceration. We postulate that the continuous blood loss accounts for the chronic anemia of cGKI mutant mice and causes the premature death of the cGKI-KOs and RM.

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