FOREWORD

Gastric secretion of hydrochloric acid is a critical component in a number of rather common diseases of the upper gastrointestinal tract. Gastroduodenal peptic ulcer disease and gastro-oesophageal reflux disease (GORD) are paradigms of such conditions. The gastric acid is important both in itself directly and also indirectly, as a gastric pH less than 4.0 is essential for the activation of pepsin.

In GORD, the gastric acid is involved in the pathogenesis both of the symptoms and of the oesophagitis, the latter being the more severe the greater the exposure of the oesophagus to acid. The presence of gastric acid in the oesophagus is also relevant for the development of intestinal metaplasia, which is characteristic of Barrett's oesophagus, as the magnitude of gastro-oesophageal reflux is directly related to the extent of metaplasia.

Gastric acid inhibition, first achieved with true clinical efficacy with the histamine$_2$ (H_2) receptor antagonists and later optimised with the proton pump inhibitors (PPIs), has been the cornerstone of medical treatment for gastroduodenal peptic ulcer disease. The discovery of *Helicobacter pylori* and the unequivocal demonstration that its eradication causes a change in the natural history of the disease that is equivalent to clinical cure – in view of the disappearance of relapses – has detracted from neither the importance of acid nor the need for effective acid inhibition in the design of eradication therapy.

Gastric acid is also important in gastroduodenal ulcer disease related to the use of drugs liable to induce gastric lesions, particularly the NSAIDs and acetylsalicylic acid. Antisecretory treatment is effective in achieving healing in ulcers related to these drugs, even during their continued, long-term use, and prevention of such lesions may be achieved through concomitant administration of PPIs.

It is thus quite understandable that the discovery of PPIs has displaced the H_2 receptor antagonists from the therapeutic scenario in GORD, despite the latter being excellent drugs. The proven efficacy and safety of PPIs in the treatment of all forms of GORD has rendered them drugs of first choice, both for achieving remission of symptoms and healing of oesophagitis, and for preventing relapses (long-term treatment). Yet, even though the therapeutic efficacy of PPIs is very high, this does not mean that aims and targets for improvement cannot be proposed. Such improvements may include agents with greater inhibitory potency, more rapid onset of action, or both, or the optimisation of the performance of agents that are already available through the implementation of therapeutic models with improved results in terms of co-effectiveness, cost-utility, patient satisfaction and convenience of use by the patient.

The incorporation of esomeprazole into the therapeutic armamentarium has meant that a new PPI is now available that differs from the previous ones in its slightly greater inhibitory potency, which translates into a therapeutic gain in the healing rates and the rapidity of relief of symptoms in oesophagitis. This gain is important, at least because of the qualitative change it represents, although its

magnitude in absolute quantitative terms is also not negligible. When the healing of oesophagitis is assessed, the magnitude of the therapeutic gain achieved increases in proportion to the increasing severity of the original oesophagitis.

In contrast, the availability of such effective and safe drugs as the PPIs, which have unquestionably become the drugs of first choice in the medical treatment of GORD, has in recent years focused interest on the search for new therapeutic strategies that might increase their efficiency. The most outstanding of these strategies is that of long-term medical treatment, first in the intermittent and later in the on-demand modality, which we have learned from the patients themselves who have demonstrated its efficacy in daily life and use.

These innovations have prompted and warranted a review of the clinical significance of potent acid inhibition and of its applications in daily practice, particularly in GORD, and also of the clinical value of new therapeutic and diagnostic strategies based on the administration of PPIs.

The following papers address potent acid inhibition from a number of different perspectives and in a number of situations, taking advantage of the ability for critical analysis, personal involvement with the topics addressed and personal experience of the various authors, to whom gratitude for their cooperation is due. These papers also have the added advantage, as a guarantee of their validity, that the statements made and the conclusions drawn are based on scientific evidence whenever it is available. In categorising the level of evidence and the grade of recommendation (and results) in the literature, we have chosen the methodology proposed and established by the Oxford Centre for Evidence-Based Medicine (http://www.cebm.net/levels_of_evidence.asp#levels). However, there remain situations in which uncertainty persists or in which there is no accepted or defined position. In such cases, the authors were requested to state their own positions and attitudes, guided by their own experience and with no conditions restricting their freedom to express their opinion. In all cases, the guiding principle has been to analyse the existing knowledge in order, whenever possible, to draw conclusions applicable to clinical practice. This principle has warranted a final summarising chapter in which concrete questions that may arise in daily clinical practice are answered on the basis of the information from the various topic-related papers.

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