Efficacy of Lansoprazole in the Short- and Long-Term Treatment of Gastro-Oesophageal Reflux Disease
A Systematic Overview

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Summary

The aim of this survey was to systematically overview clinical studies, published in the English literature, regarding the treatment of reflux oesophagitis with the newly developed proton pump inhibitor (PPI) lansoprazole, compared with other acid suppressant drugs. A total of 11 studies were identified in the literature and included in the overview; of these, four studies compared lansoprazole with ranitidine, one with famotidine and four with the PPI omeprazole. Two studies focused exclusively on the comparison of different dosages of lansoprazole. This overview showed that, with regard to healing rate and symptomatic relief, lansoprazole was superior to H₂ receptor antagonists. Regarding healing rates and symptom response, lansoprazole was equal to omeprazole. The few data concerning long-term treatment indicated similar efficacy for the two PPIs. The tolerability of lansoprazole did not appear to be different to H₂ receptor antagonists and omeprazole.

Gastro-oesophageal reflux disease (GORD) is a common disease, at least in the Western world. Epidemiological data indicate a prevalence of symptoms of between 11.6%[1] and 36%[2] in the general population, whilst endoscopic prevalence of GORD (defined as erosive or ulcerative oesophagitis) varies in different studies between 1.1%[3] and 22.8%,[4] depending upon the type of patients assessed at each specific centre. Oesophagitis, however, presents a temporal trend that has constantly increased over the last 20 years, linked only in part to improved diagnostic procedures. At several European endoscopy centres, this disease has become one of the most frequently encountered diseases at gastroenteric endoscopic examination.[5]

From a pathophysiological point of view, GORD is considered a multifactorial disease, in which the aggressive factors that lead to reflux and the defensive factors, such as the anatomical and functional antireflux barrier, oppose one another.[6] Among the different factors that contribute to GORD, motility factors certainly represent a major cause and, within these, a central role is played by an inappropriate release of the lower oesophageal sphincter.[7]

Gastric acid secretion, which is significantly and markedly increased in only a moderate number
of cases,\[8\] plays a critical role from a therapeutic point of view. In fact, it has been documented that the incidence of acute healing of reflux oesophagitis is linearly correlated with the level of inhibition of gastric acid secretion; healing is mediated by a reduction in the level of exposure of the oesophagus to acid within a 24-hour period.[9] Thus, it is not surprising to observe that in the literature, the best data regarding healing of lesions and symptoms are those obtained with proton pump inhibitors (PPIs) such as omeprazole, pantoprazole or lansoprazole.[10-14]

In many cases, these data refer not only to the short-term healing of oesophagitis, but also to the prevention of relapses.[10] The prevention of relapses is probably the most critical point for therapy. In fact, since oesophagitis is a chronic condition and, considering the increased tendency to relapse after withdrawal of acute treatment (up to 80% after 6 months[15]), therapy is fundamental in the majority of cases.

The aim of the present study was to re-evaluate, by performing a systematic overview of the literature, the short- and long-term data regarding the efficacy of lansoprazole, a PPI that has recently been introduced to the market.

**Materials and Methods**

The articles taken into consideration in this review were randomised, controlled clinical studies, published in the English language between 1991 and 1996, which evaluated the effectiveness of lansoprazole in the treatment of GORD and in the prevention of relapses. These articles were selected on the basis of references on the topic and with a manual and computerised Medline search of the literature. Specifically, those randomised and controlled clinical studies that evaluated the efficacy of lansoprazole alone, or in comparison with H2 receptor antagonists (H2-RA), or with other PPIs, were considered.

A total of 10 studies[16-25] were identified, of which eight were comparative trials[16-23] and two were focused exclusively on a comparison of two dosages of lansoprazole.[24,25] The study by Bardhan et al.[18] included both a comparison with an H2-RA (ranitidine) and a comparison of two different dosages of lansoprazole. Furthermore, two of these studies[16,17] included an efficacy analysis of maintenance treatment.[26,27] For those clinical studies that were the topic of several publications, only the most recent have been considered.

For each study, the following data were considered, where available: patient numbers, gender, age, study design, treatment scheme (this information is presented in detail), percentage of healing at the end of treatment, and percentage of relapse at 6 to 12 months.

The definition of therapeutic efficacy has been considered to be as indicated in the single articles.

**Data Analysis**

For the analysis, standard methods for calculating the odds ratio (OR) and confidence limits (CI) at 95% were employed from 2 x 2 tables.[28,29] The expected number of events in the cases treated and those not treated with lansoprazole and the variance between observed (\(O\)) and expected (\(A\)) cases were calculated using the Mantel-Haenszel procedure.[28] It was assumed that if the treatment did not demonstrate efficacy, the value (\(O-A\)) with variance, \(V\) (or the standard deviation, \(\sqrt{V}\)), would differ from \(O\) only by random variability.

However, if the treatment of lansoprazole was active, the value (\(O-A\)) would be positive and, although in the single studies this trend could be limited or not evident based on the random effect, this should become evident whenever the grand total (GT) of the differences (\(O-A\)) obtained in the single studies was analysed.

Conversely, if the treatment was not effective, the grand total would differ from zero only for the random effect, with the variance equal to the sum of the variances of the single studies (SSV) and standard deviation, \(\sqrt{SSV}\). Furthermore, assuming that the effect of the treatment was not heterogeneous among single studies, then the OR of the treatment effect was calculated in the following way: \(\text{exp}(\text{GT/SSV})\) with confidence limits (CI) of 95% = exponential (GT/SSV ± 1.96\(\sqrt{SSV}\)).