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Editorial

Side Effects of Proton-pump Inhibitors: Another Reason to Indicate Anti-reflux Surgery for Barrett's Esophagus?☆

Efectos secundarios de los inhibidores de la bomba de protones, ¿una razón más para indicar la cirugía antirreflujo en el esófago de Barrett?

Gastroesophageal reflux disease (GERD), which is very prevalent in our setting, encompasses a wide spectrum of scenarios that combine different clinical, endoscopic, radiological, manometric and pH conditions. Barrett's esophagus (BE), the final stage of the disease and a consequence of continuous severe reflux (acid or bile) in the esophagus, is very important as it is the only known lesion that can lead to the development of adenocarcinoma of the esophagus. The treatment of BE requires controlling its cause, which currently involves the life-long use of antisecretory medications or anti-reflux surgery. The debate about which of the two options is better does not seem to have a clear winner, at least based on objectively assessable points. Both have been demonstrated to be equally effective to control symptoms as well as associated acute endoscopic lesions.[1] As for preventing neoplastic degeneration, there does not seem to be significant differences, although there are several indications that lead one to suspect that anti-reflux surgery has a greater protective effect compared with pharmacological treatment.[2]

It would also be important to analyze the costs and side effects of each treatment in order to resolve this dilemma. With regards to the former, Faria et al.[3] demonstrated that laparoscopic Nissen fundoplication is a cost-effective alternative to continuous drug treatment for GERD in the long-term. Nonetheless, it presents a mortality rate of less than 1% and a post-operative morbidity rate that ranges between 5% and 20%. Gas/bloat syndrome (in more than 80% of cases at varying intensities), dysphagia and diarrhea are the common later complications of surgery. Most symptoms improve or disappear during the first 6 months after the intervention. The failure of anti-reflux surgery usually occurs and is observed in the first 2 years post-op, and the rate of re-operations ranges between 0% and 15%.

On the other hand, omeprazole has well-known side effects, many of which are dose-dependent, including *Clostridium difficile* infections, higher risk of pneumonia and bone fractures, thrombocytopenia, iron and vitamin B_{12} deficiencies, rhabdomyolysis and magnesium absorption disturbances.

Recently, the publication of the results of a well-designed case/control study in a large population in JAMA about the effects of continued omeprazole and H2 antagonist use has generated certain social concern. In fact, many patients, especially those under prolonged treatment with proton-pump inhibitors (BE patients, for instance), have requested information about this factor in recent weeks, both about the truth of the news and the implications in their cases in particular. In the introduction of their paper, Lam et al.[4] reported that a B_{12} deficiency that is undiagnosed, and which therefore goes untreated, can lead to neurological damage, anemia and dementia, which in some cases is irreversible. This article concludes that the risk of developing vitamin B_{12} deficiency is greater in subjects who are treated with omeprazole or H2 antagonists for two or more years, with higher risk at higher dosages. It seems that this association is more notable in women and young people treated with strong antisecretory drugs, although it diminishes when this medication is taken intermittently.

The problem that is generated is important because, although BE represents the paradigm of the chronic antacid "taker", the consumption of this type of medication is very high in the general population, not only in subjects with reflux disease without associated complications but also in others who are treated with gastro-erosive drugs. In addition, omeprazole has become part of our personal arsenal, and is often taken for any type of epigastralgia or stressful situation in our daily lives because we trust that it is innocuous.

In clinical practice, when we take into account these premises and consider young patients with BE who are

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asymptomatic with omeprazole or similar medications, a multitude of questions arise. Do we operate on these patients who, frightened by this information, demand a quick surgical solution? Should we extend the indications of anti-reflux surgery (for reflux diseases in general and BE in particular) given these reported results? In addition to periodic endoscopic examinations to rule out dysplasia and pH adjustments with the dosage of omeprazole, should we add plasma determinations of vitamin B_{12} and magnesium every so often?

In this era of defensive medicine, these are not irrelevant questions, although patient safety and the objective analysis of the information should come first. In our accumulated experience of more than 25 years with patients with BE, we have not detected any cases of serious harm caused by omeprazole, although we do not have lab analyses studying elecrolytes or certain vitamins. As it occurs in other areas of surgery, reflux disease and BE require the multidisciplinary collaboration of experts as well as discussion of each case in order to offer individualized treatment that is appropriate in the light of new information and knowledge as it becomes available to us.

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