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Harmonising proton pump inhibitors treatment in the specialist setting following the SIGE recommendations

Dear Editor,

we read with great interest the position paper of the Italian Society of Gastroenterology (SIGE) on the appropriateness of prescription for proton pump inhibitor (PPI) drugs that was recently published in Digestive and Liver Disease, as we feel that the statements reported in the manuscript should actually represent a "Dos and don'ts" companion handbook in everyday clinical practice of both primary care physicians and specialists in gastroenterology [1].

As a fact, in Italy, the category of drugs used to treat gastrointestinal disorders ranks fourth in the list of categories responsible for drug-related health care costs, and within this category of drugs, PPIs embody the main item of expenditure, with a cost of 13.2 euros *per* inhabitant and 68 daily doses prescribed every 1000 inhabitants, in 2017 [2]. Thus, despite a decreasing trend in their prescription observed in the course of the last 5 years (2017–2013: −6.8%), PPIs still represent a relevant health-care associated cost, and this finding is even more crucial when considering that a significant proportion of these prescriptions – on the average approximately 40% – are not appropriate [1–5]. Indeed, the results of a survey performed ten years ago in Italy among primary care physicians, showed that even in patients where the use PPIs may be justified – such as gastro-protection in patients taking non-steroidal anti-inflammatory drugs – there was a misuse of PPIs that led to underutilization of gastro-protection in at least one out of four patients, while approximately 60% of patients received gastro-protection despite the absence of well-defined risk factors for gastrointestinal bleeding [6,7]. Lastly, beyond increased sanitary costs, chronic use of PPIs may also be associated with the onset of potentially harmful effects that may affect the respiratory and the gastrointestinal systems, and may determine bone and electrolytic disturbances, although there is still much debate on the actual cause-effect of these associations [3]. All in all, therefore, while PPIs are an effective, useful, and manageable class of drug that represents the cornerstone of treatment of acid-related disorders, they also show a "dark side" related to incongruous, prolonged, and unjustified prescriptions that may be associated with harms and increased health-care costs.

In the majority of the published reports on this issue, mainly from the United States, some of the main reasons for prolonged and inappropriate PPI treatment – besides the above-referenced over-prescription in non-steroidal anti-inflammatory drugs users – are the lack of drug withdrawal after hospital discharge, where initial prescription might have been motivated by acute illness, and the absence of adequate re-evaluation after initial prescription in patients who suffer from gastroesophageal reflux disease, where PPI intensity of prescription or actual necessity are often overlooked, and where other therapeutic means may be effective [1,5–9]. Therefore, following the statements enunciated in the SIGE position paper, and in order to critically assess the real necessity of chronic PPI prescription in patients referred to specialist gastroenterology assessment, we recently started re-evaluating the indication of these drugs in our outpatients clinic, with the aim to provide an updated picture of this phenomenon in the specialist setting in Italy. Preliminary data related to the first 40 patients on chronic PPI treatment referred to our clinic in the last 2 months show that median duration of PPI treatment before referral is 36 months, and that approximately 30% of patients are treated outside the indications contained in the SIGE position paper [1]. Moreover, in two-thirds of these patients, no previous attempt at PPI tapering or withdrawal had previously been carried out before referral, despite the absence of an evidence-based indication to chronic PPI use. Lastly, following the recently proposed strategies of how to reduce or stop PPI treatment, we already managed to discontinue or decrease the intensity of PPI treatment while controlling symptoms in 70% of these patients [10].

In conclusion, we feel that the implementation in everyday clinical practice, at both the gastroenterology specialist and primary care physician setting, of the guidelines put forward in the SIGE position paper may provide health as well as economic benefit, and should be actively pursued in order to improve the quality of care dispensed to our patients.

Conflict of interest
None declared.

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Capsule endoscopy in suspected small bowel Crohn's disease — Is it worth repeating a negative study?

Dear Editor,

Crohn's disease (CD) affects the small bowel (SB) in a significant proportion of patients, with approximately 20% having exclusively SB disease [1,2]. Therefore, various modalities have been employed to allow a less invasive assessment/diagnosis when conventional endoscopy has failed. Capsule endoscopy (CE) has a high diagnostic yield (DY) for SB inflammation when compared with alternative SB investigations [3,4]. Therefore, in patients with known CD, the use of CE can positively affect management [5]. However, less information is available for those with ongoing clinical concern of SB CD when the initial CE is negative or inconclusive. Due to patient acceptance and ease of use, repeating CE remains a plausible option. In small series, a repeat CE following an initially negative CE for occult gastrointestinal bleeding (OGIB) has been shown to increase DY, and change management in as many as 39% of patients [6]. During an acute episode, back-to-back CE has also been shown to increase the DY in OGIB [7].

Between March 2005 and March 2018, 2276 SB CE studies were performed at our tertiary centre. During this time period the method of CE video review remained unchanged; CEs were reported based on clinical impression without use of a standardised tool (e.g. Lewis score (LS) or Capsule Endoscopy Crohn's Disease Activity Index (CECDAI)) by one or more of four experienced/experts CE readers. Our prospectively maintained database of CE examinations was used to identify patients undergoing repeat CE for suspected SB CD. Any initial CEs which lead to a diagnosis of CD and those repeated because of incomplete or inadequate recording were excluded. Eventually, a case series of 18 patients was compiled with the aim of assessing the DY of repeating a CE in patients with ongoing clinical suspicion of SB CD and an initial complete negative or inconclusive study. Further clinical data was extracted from the internal hospital records system TrakCare (©Intersystems, Cambridge, MA). The median time between CEs was 598 (48–3123) days and the second CE was carried out with a different capsule model in 12/18 (66.7%) patients. Where the initial capsule video was available this was reviewed prior to writing this letter with a LS assigned retrospectively.

The cohort consisted of 15 women and 3 men, with a median age of 44.4 (15.8–64.0) years at baseline CE. All of these patients had at least one faecal calprotectin (FC) result recorded, with between 1 and 10 (median of 2.5) samples analysed; overall median FC 142.5 (0–1045) μg/g. For the purpose of analysis, FC < 20 μg/g, which is the lower limit of detection by the laboratory (Launch Diagnostic Systems, Longfield, UK), were recorded as 0 μg/g. Median FC results are presented in Table 1 and the FC levels are compared to the CE outcome in Fig. 1.

1. Repeat CE when initial CE is normal or reveals non-IBD diagnosis

Of the five patients with a 'normal' initial CE none had repeat CE suggestive of SB CD (DY: 0%). The median time interval between CEs was 462 (91–1984) days. 4/5 (80%) of the repeats were normal, with 1/5 (20%) showing non-specific SB appearances suggestive of portal hypertensive enteropathy (PHE). The median FC value in this group was 270 (0–667) μg/g. Baseline CE was re-reviewed in 2 of these cases and LS was calculated (both LS = 0); supporting the clinical report for 'normal' issued at the time. Patients with positive initial CE, but non-IBD findings (n = 5), i.e. NSAIDs enteropathy (n = 1; LS = 112), angioectasia (n = 1; LS = 196), appearances suggestive of lymphoproliferative disease (n = 1; LS = 3593) and gastritis (n = 1), had similar findings on repeat CE and one patient with a duodenal ulcer had a normal repeat 3123 days (8.6 years) later; summarised in Table 1. Overall, these patients as a group with a complete initial CE showing no evidence of SB CD had a DY of 0/10 (0%) for SB CD on repeating the CE.

2. Initial CE showing non-specific inflammation

The initial CEs showing inflammation were divided into those which were, on balance felt suggested CD (n = 2), and those which likely did not (n = 6). Of the 2 patients with findings initially suggestive but not specific for SB CD, 1 of the subsequent CEs was again suggestive of CD while the other again only showed non-specific inflammation. They had a median FC of 35 (0–320) μg/g and LSs of 4464 and 1104 on initial CE. These scores would fall in the moderate to severe inflammation category, supporting the clinical impression reported [8]. Six patients had non-specific inflammation, less associated with CD on initial CE. 2/6 (33%) of the repeat