

## The use of prucalopride in real life for the treatment of constipation subtypes: ups and downs

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Chronic constipation is a symptom the physician faces almost daily. Treatment consists of several pharmacological and non-pharmacological options; the fact that to date, no treatment is completely effective justifies the numerous drugs available for this condition [1]. Moreover, there is a subset of constipated patients who have an unsatisfactory response to medical treatment or do not respond at all [1]. Until recently, these patients were often referred for surgical or other invasive approaches, with results that were far from optimal [2].

However, in recent years, new compounds have been developed for the treatment of chronic constipation, compounds that seem to have good efficacy with relatively few side effects [3]; one of these, prucalopride, has recently been released on the European market as an alternative treatment for female patients (representing more than 85 % of the overall population of constipated subjects) that show an insufficient response to laxatives [4].

To date, prucalopride has been mainly tested on patients recruited for clinical trials, and some authors claim that further subgroup analysis of the actual patient group of interest may be helpful in guiding clinical decision-making

[5]. Thus, data on “real-life” patients or those with subtypes of constipation are still not available.

In this issue, Jadav and colleagues [6] try to give us some answers concerning the above points, by reporting in a retrospective study the treatment data of patients with constipation (defined according to the Rome III criteria) due to obstructed defecation (OD), to delayed transit (slow-transit constipation, STC), to a mixed-type (ODSTC), or to irritable bowel syndrome (IBS-C). These patients were given treatment according to the National Institute for Health and Clinical Excellence guidelines and had no relief from constipation despite trying at least two different types of laxatives and lifestyle modification for at least 6 months [7]. The authors compared the efficacy of prucalopride with the constipation subtypes according to simple criteria, most likely similar to those adopted in daily clinical practice: After 4 weeks, patients were asked whether they were satisfied with the treatment, and whether they wanted to continue with the treatment.

Overall, 42 % of the entire group benefitted from the treatment after 4 weeks, and after an average follow-up period of 5 months, the benefit persisted in 36 % of patients. These results (including dropouts) are comparable with results of larger published trials [8].

The interest of the study lies in the fact that the response to prucalopride was also observed in well-defined subgroups of constipated patients. There was a similar response between subgroups (59 % OD, 31 % STC, 43 % OD-STC, 44 % IBS-C), with surprisingly better results in OD patients. The surprise is due to the fact that previous studies suggested that the effect of the drug is lower on straining at stool [9], a symptom often considered as the hallmark of OD and mainly responding to biofeedback treatment [10]. However, OD itself is an umbrella term under which several pathophysiologic abnormalities may

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be found [11, 12], and it is likely that some patients with specific alterations may be more responsive to a pharmacological treatment. On the other hand, the patients with STC, in whom one would expect the best response, actually had the worst outcome. This fact, however, is not completely unexpected, since these are the patients who most frequently have features of intractable constipation, including a true colonic inertia [13], often due to important abnormalities of the enteric nervous system [14, 15]. These abnormalities led to the reclassification of many form of constipation (especially the more severe ones) as true enteric neuro-gliopathies [16, 17]. Interestingly, prucalopride worked well in IBS-C patients too, without an increased number of side effects such as abdominal pain (normally present in the symptoms cohort of these patients, and one of the most frequent side effects related to prucalopride). Thus, it is likely that the drug could also be effectively used in the subgroup of constipated patients, not fulfilling criteria for IBS, in whom pain is an important feature associated with constipation (painful constipation patients) [18].

In conclusion, the recent introduction of prucalopride for the treatment of constipated women (and, hopefully, also men in the near future), even though it cannot be considered as the “magic bullet,” since it does not work in all patients, has improved our chances to offer an effective treatment for this symptom, especially in those with scarce or no response to previous measures. Moreover, we must not forget that constipation is a complex, difficult symptom to treat, thereby often requiring complex therapeutic approaches [19]. Extensive knowledge of the available drugs and use of a multi-drug approach could eventually lead to better therapeutic success.

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