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P. Oustamanolakis & J. Tack
Translational Research Center for Gastrointestinal Disorders, University Hospital Gasthuisberg, Leuven, Belgium.
E-mail: jan.tack@med.kuleuven.be

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Prucalopride for chronic intestinal pseudo-obstruction

We read with great interest the article by Emmanuel *et al.*[1] investigating the efficacy of prucalopride in patients with chronic intestinal pseudo-obstruction (CIP). In this study, the effect of prucalopride was tested on four cardinal symptoms of CIP (pain, nausea, vomiting and bloating). The data set included four patients who were followed up for a period of 48 weeks. Prucalopride decreased either the intensity or duration of at least one symptom in each of the four subjects of the study, and it was most effective in relieving the symptom of bloating.

Chronic intestinal pseudo-obstruction is a rare and heterogeneous condition with a paucity of evidence-based therapeutic approaches. Modest therapeutic effects have been reported in the past with cisapride, a prokinetic agent which has been withdrawn because of cardiovascular safety issues.[2, 3] We congratulate the authors for conducting the current study, which has two important strengths.

A first strength is the study design: the authors used an $n = 1$ cross-over study design, thereby allowing individual patients to act as their own controls. This design allows drug effects in every individual to be established and, unlike parallel-group study designs, does not under-estimate therapeutic efficacy, even when a positive effect is occurring only in a single patient.

A second strength is the duration of the study, which was 48 weeks (four 12-week periods of either drug or placebo). The long study duration helps to address the fluctuation of CIP symptoms over time, in terms of frequency, duration and severity. To our knowledge, this is the first long-term study to show a beneficial effect of a drug in CIP in a controlled manner.

Prucalopride significantly improved a number of the CIP symptoms, especially bloating, nausea and pain (the latter accompanied by a significant decrease in analgesic use). Surprisingly, given the actions of prucalopride in chronic constipation, stool consistency and frequency, and laxative use were not altered by prucalopride. Hence, the underlying mechanism remains unclear, and could at least partly be based on actions of prucalopride in the proximal gastrointestinal tract.[4]

Besides symptomatic benefit, restoring or maintaining the ability to be fed orally is an important therapeutic goal in CIP patients. The scope and size of the present study did not allow this issue to be examined. Furthermore, it is conceiv-

able that neuropathic CIP may respond better to prucalopride, which targets enteric nerves, than myopathic CIP. These issues will need to be addressed in future trials, probably multicentre, with higher number of 'patient-years'.

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