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Lubiprostone

A Viewpoint by Michael Camilleri

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Simple constipation usually responds to dietary alteration, including the addition of fibre to the diet. When constipation persists, it may be due to medication-induced constipation, evacuation disorders (in which the dynamics of defecation are impaired) or a motor disorder of the colon that results in slow or erratic movement of increasingly solid stools.

When management directed toward the underlying cause does not result in symptom relief, treatment of constipation often involves one or a combination of bulk (e.g. fibre preparations), stool softeners (e.g. docusate), secretory agents (e.g. diphenylmethanes or ricinoleic acid) and motility-enhancing agents (e.g. bisacodyl or serotonin 5-HT_4 receptor agonists, such as tegaserod). There are experimental approaches to enhance many of these physiological process to achieve the goal of comfortable passage of a normal consistency bowel movement spontaneously and without excessive straining.

Lubiprostone is a first-in-class molecule that produces chloride and water secretion in the gut, and accelerates transit through the small bowel and colon (possibly secondary to the secretion induced). Mammalian colonic epithelial cells also express the same chloride channels; a direct effect of lubiprostone on colonic motility cannot be completely excluded, though its poor bioavailability suggests a greater likelihood of local action on intestinal epithelia.

Trials suggest potential clinical benefit of lubiprostone 24μg twice daily in patients with chronic constipation: rapid onset of action, durable efficacy with continued use and repeat efficacy after stopping it. Safety and efficacy were demonstrated in adults of both genders with no upper age limit. A single 24μg daily dose also may be efficacious; it is unclear whether reducing the total daily dose would reduce the incidence of nausea.

Lubiprostone is a welcome addition to the therapies available for the treatment of patients with constipation associated with hard stools, infrequent defecation or need of excessive straining in the absence of a physiological disorder of evacuation. ▲