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Alosetron

A Viewpoint by Michael Camilleri

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Irritable bowel syndrome (IBS) is a heterogeneous disorder with a worldwide prevalence of 10 to 15%. Psychological disturbances, altered motility and heightened sensitivity of the gut contribute to symptom development: antecedent diarrhoeal illness may trigger long term IBS.

Current therapy for IBS focuses on the major symptoms experienced by the patient. Patients experience diarrhoea, constipation, alternation of bowel habit, or the frequently combined pain, gas and bloating. The mainstays of current pharmacotherapy are opioids for diarrhoea, fibre for constipation and antispasmodics or antidepressants for pain.

Alosetron, a 5-HT_3 receptor antagonist, is a promising agent that may provide significant improvement over current therapies in the management of diarrhoea-predominant IBS in female patients. Its effect has been consistently demonstrated in 12-week phase III trials; its dual action on adequate relief of pain and loose or frequent bowel movements is superior to placebo in US trials and to mebeverine in a European trial. Constipation may occur with daily administration of alosetron.

However, several important questions remain unanswered. These include the efficacy of alosetron in males and in patients with alternating bowel habits, the precise mechanism of action of the drug and the optimal mode of administration for long term therapy for a syndrome characterised by a fluctuating course. Physicians will also need to decide when to initiate treatment with this drug in individual patients with IBS. Certainly, in patients with prominent pain, urgency and diarrhoea, or in those with rebound constipation on exposure to opioids, alosetron appears to be a worthwhile addition to the short list of effective therapies for IBS.