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NIHR ALERTS

Irritable bowel syndrome: low dose antidepressant improves symptoms

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THE STUDY

Ford AC, Wright-Hughes A, Alderson SL, et al. Amitriptyline at low-dose and titrated for irritable bowel syndrome as second-line treatment in primary care (ATLANTIS): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2023;402:1773-85.
To read the full NIHR Alert, go to: https://evidence.nihr.ac.uk/alert/irritable-bowel-syndrome-low-dose-antidepressant-improves-symptoms/

Why was the study needed

People with irritable bowel syndrome (IBS) are usually managed in primary care. First-line treatments include dietary changes and medicines (for constipation, diarrhoea, and abdominal spasms) but they are not always effective. In guidelines from the National Institute for Health and Care Excellence (NICE), a next potential step is to consider a low dose of an antidepressant medicine, such as amitriptyline. Before this study, limited research evidence had been available on amitriptyline for IBS, and GPs did not prescribe it often.

The ATLANTIS research trial compared low dose amitriptyline with placebo in people with IBS whose symptoms had not improved with first line treatments.

What did the study do?

Conducted between 2019 and 2022, the ATLANTIS study recruited people with IBS from 55 general practices in England. Most had moderate to severe symptoms of IBS. Participants were aged 49 on average; most (68%) were female.

In this randomised controlled trial, half the participants (232) took low dose amitriptyline (10 mg per tablet) and the other participants (231) took an identical placebo tablet for six months. They all received an information leaflet to help them manage their dose (starting at one tablet each evening and increasing to two or three tablets depending on their symptoms and side effects). Participants continued to receive usual care for IBS from their GP (such as dietary advice). Some 338 participants completed six months of treatment: 173 (75%) in the amitriptyline group and 165 (71%) in the placebo group.

To compare the groups, the researchers used the IBS severity scoring system (IBS-SSS). A score of 75-174 indicates mild symptoms; 175-299 moderate symptoms; and 300+ severe symptoms.

What did it find?

The primary outcome of the study at six months showed:

- People in the amitriptyline group reported greater improvements in IBS symptoms (their average IBS-SSS score improved by 99 points compared with 69 points for people in the placebo group).

Secondary outcomes showed that people in the amitriptyline group:

- Were more likely to report relief of their IBS symptoms (61% participants) compared with those taking placebo (45%)
- Were more likely to find their treatment acceptable (58% participants) compared with those taking placebo (47%)
- Had similar anxiety, depression, and work and social adjustment scores (ability to work and take part in other activities) to people in the placebo group
- Were less likely to discontinue treatment during the trial (20% participants) compared with the placebo group (26%).

People in the amitriptyline group experienced more dry mouth and drowsiness side effects but less insomnia than the placebo group. Few serious adverse events occurred in either group (two in the amitriptyline group; three in the placebo group).

At three months, similar numbers in each group said they were still taking the pills as prescribed. By six months, more were still taking amitriptyline (74%) than placebo (68%).

Why is this important?

The researchers say this is the largest trial of a tricyclic antidepressant in IBS to date. The findings suggest that low dose amitriptyline reduces the severity of IBS symptoms and is safe and well tolerated.

The results will inform shared decision making and provide information to GPs and people with IBS on trying low dose amitriptyline if first line options have not been effective.

The researchers have developed guidance to help people with IBS manage their amitriptyline dose.

What's next?

The researchers hope their findings will inform the next update on NICE guidelines for treatment of IBS.

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