PEDIATRICS

Amitriptyline and placebo in children with functional gastrointestinal disorders

Amitriptyline and placebo are equally effective in the management of pain-predominant functional gastrointestinal disorders (FGIDs) in children, according to the results of a new multicenter study reported in *Gastroenterology*.

FGIDs (including IBS, functional dyspepsia and functional abdominal pain) are some of the most common medical conditions in children. The pain associated with these conditions can reduce a child's quality of life, and reduce their ability to carry out daily activities.

Amitriptyline is a tricyclic antidepressant that has been shown in adult studies and one small, single-center pediatric study to have a positive effect on the treatment of IBS. "Amitriptyline has been used for a long time in the treatment of FGIDs in children and adults," says Miguel Saps, lead author of the study. However, according to Saps, "There is very little evidence for any treatment for FGIDs in children." In fact, only a few, small clinical trials have investigated the efficacy of drugs for the treatment of children with these disorders.

Saps and colleagues therefore carried out a prospective, double-blind, multicenter, placebo-controlled, randomized study to investigate the efficacy of amitriptyline in children with pain-predominant FGIDs. According to the authors, "This [study is] the largest nonindustry-sponsored pharmacological clinical trial in pediatric [gastroenterology]."

A total of 90 children and adolescents aged between 8 and 17 years with a diagnosis of functional abdominal pain, functional dyspepsia or IBS were recruited from six centers. Children were randomly allocated to receive either amitriptyline (10 mg or 20 mg daily, according to weight) or placebo for 4 weeks.

Each child completed a questionnaire at baseline and throughout the treatment

period about their ability to perform daily activities (such as sleep, play and attend school), and about gastrointestinal symptoms and pain. Further assessment of gastrointestinal symptoms and pain was carried out at the end of the study. Patients also answered psychological questionnaires at the beginning and end of the study to assess coping mechanisms, depression, anxiety, disability and somatization.

The primary outcome was overall response to treatment; this outcome was assessed using a further standardized questionnaire at the end of the study. Children were asked to report if their problem was better, worse or the same, and how well the medication had relieved pain. Secondary outcomes included treatment effects on psychosocial traits and ability to perform daily activities.

83 children completed the study—40 received placebo and 43 received amitriptyline. In the per-protocol analysis, 63% of children in the amitriptyline group reported feeling better, compared with 57.5% in the placebo group. 53% of patients in the amitriptyline group and 50% in the placebo group felt that their medication was good or excellent at relieving pain. These differences between the groups were not significant.

There was an improvement in both groups in all psychological variables. The two groups were only different in terms of anxiety—which improved more in the amitriptyline group than the placebo group.

"Our study showed that patients benefit from the use of the drug but also greatly benefit from placebo..." says Saps. The authors hypothesize that the high placebo effect in this study might be due to good relationships between the physicians, patients and families. "We should further investigate the placebo effect in children," he says.

The study demonstrates that amitriptyline is a safe and effective treatment option for children who have FGIDs. "We plan to continue conducting large randomized clinical trials to assess the benefits of various treatment approaches in children with FGIDs," concludes Saps.

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