Antidepressants for functional gastrointestinal disorders in children

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Abstract

Question Functional gastrointestinal disorders (FGIDs) are complex conditions I see in some of my pediatric patients. The indications for antidepressants such as selective serotonin reuptake inhibitors (SSRIs) do not include treatment of FGIDs; however, some children are prescribed SSRIs for this condition. Are antidepressants effective and safe to use for treating FGIDs in children and adolescents?

Answer The pathogenesis of FGIDs is largely idiopathic, and although theories exist to explain why SSRIs might be used to treat FGIDs, there is no conclusive evidence of their effectiveness. No large, well controlled studies have investigated the use of SSRIs to treat FGIDs in the pediatric population. There is also evidence that suggests an increased risk of suicidal thoughts when adolescents use SSRIs. Currently, there is no recommendation to use SSRIs to treat FGIDs in children.

Des antidépresseurs pour les troubles fonctionnels gastro-intestinaux chez l'enfant

Résumé

Question Les troubles fonctionnels gastro-intestinaux (TFGI) sont des problèmes complexes que je rencontre chez certains de mes patients pédiatriques. Les TFGI ne figurent pas parmi les problèmes où il est indiqué de prescrire des antidépresseurs comme les inhibiteurs sélectifs du recaptage de la sérotonine (ISRS); par ailleurs, certains enfants reçoivent des prescriptions d'ISRS pour ce problème. Les antidépresseurs sont-ils efficaces et sûrs pour traiter les TFGI chez les enfants et les adolescents?

Réponse La pathogénèse des TFGI est largement idiopathique et, même si certaines théories expliquent pourquoi on pourrait utiliser des ISRS pour traiter les TFGI, il n'existe pas de données concluantes corroborant leur efficacité. Aucune étude d'envergure bien contrôlée ne s'est penchée sur l'utilisation des ISRS pour traiter les TFGI dans la population pédiatrique. Il existe aussi des données probantes qui indiquent qu'il y a des risques accrus de pensées suicidaires lorsque des adolescents prennent des ISRS. À l'heure actuelle, il n'est pas recommandé d'utiliser des ISRS pour traiter les TFGI chez les enfants.

Functional gastrointestinal disorders (FGIDs) are chronic or recurrent gastrointestinal symptoms not explained by structural or biochemical abnormalities. Functional abdominal pain (FAP) and irritable bowel syndrome (IBS) in particular are common in the pediatric population. One study reported that FAP and IBS were seen in 6% of middle school students and 14% of high school students (mean age 12.6 years and 15.6 years, respectively; N=507 adolescents).[1] Another study found that symptoms persisted in a quarter of children for longer than 8 weeks (N=237, aged 8 to 15 years from 2 Chicago private schools).[2] The Rome III criteria are standardized diagnostic criteria with specific classification for FGIDs in childhood (such as functional dyspepsia, IBS, and functional constipation).[3] The pathogenesis of FGIDs is believed to be linked to genetic, physiologic, and psychological factors. As such, pharmacologic interventions such as prokinetic agents, tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and antinociceptive agents have been used in recent years to treat FGIDs.

Antidepressants for FGIDs

Two main classes of antidepressants have been suggested to treat FGIDs: SSRIs and TCAs. The anticholinergic effects of these drugs are thought to reduce pain perception, improve mood and sleep patterns, and modulate the gastrointestinal tract.[4] Tricyclic antidepressants act on noradrenergic and serotonergic pathways, but their use for FGIDs is largely attributed to their antimuscarinic, antihistaminic, and anticholinergic properties. The theoretical basis for SSRI treatment is that serotonin is an important neurotransmitter in the gastrointestinal tract, with 80% of the body's stores located in enterochromaffin cells of the gut.

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A 2009 systematic review and meta-analysis of 32 studies including adult patients (age older than 16 years) with IBS reported that TCAs and SSRIs were beneficial for treatment of FGIDs, with symptomatic improvement of global IBS symptoms or abdominal pain in the group taking antidepressants (relative risk 0.66, 95% CI 0.57 to 0.78).[5] However, studies in this meta-analysis had demonstrated substantial heterogeneity, limiting their comparability.[5]

The efficacy of amitriptyline was addressed in a multicentre, randomized, placebo-controlled trial in children (N=83) aged 8 to 17 years diagnosed with FAP or IBS (based on Rome II criteria[6]). The study found no significant difference between the groups, with 63% of children in the amitriptyline group and 57% of children in the placebo group reporting improvement after 4 weeks (P=.63).[6] A recent Cochrane systematic review consisting of 2 studies examining the use of amitriptyline for treatment of FGIDs in adolescents (age 8 to 17 years, N=90; and age 12 to 18 years, N=33) concluded there was insufficient evidence to support the use of amitriptyline for the treatment of abdominal pain–related FGIDs in children and adolescents owing to a lack of statistically significant differences between amitriptyline and placebo for most efficacy outcomes.[7]

The reported benefit of antidepressants for adults with FGIDs and the lack of efficacy in pediatric studies might not reflect true difference in treatment effects in these populations but rather methodologic differences between studies (eg, differing diagnostic criteria were used to select study participants in different studies).

There is a paucity of evidence for the use of SSRIs for FGIDs in children. A small study of citalopram for recurrent FAP in children (N=25) demonstrated a significant improvement in abdominal pain over a 12-week period (Clinical Global Impression Scale of Improvement: P<.001).[8] The study had no placebo group, had a small sample size, and used an open-label, flexible-dosing design, limiting the practical generalizability of the study. In contrast, a randomized controlled trial of the effectiveness of citalopram in adults with IBS (N=54) found no significant benefit of self-reported "adequate relief" of IBS symptoms after 8 weeks of treatment (P=.54).[9]

Safety profile of SSRIs in children

The safety profile of SSRIs is the subject of 1 meta-analysis and 1 review.[10,11] A Cochrane review of 12 studies in children 6 to 18 years old reported that there was evidence supporting an increase in suicidal thoughts and suicide attempts (relative risk 1.80, 95% CI 1.19 to 2.72).[11] The US Food and Drug Administration recommended an existing black box warning[12] be updated to ensure monitoring for adverse events including changes in mood and thought. Hetrick et al[11] recommended caution in the interpretation of these results, as the importance of the association between SSRIs and suicide is unclear, particularly as untreated depression is associated with risk of suicide. Clinicians should counsel patients and their parents on the risks of taking SSRIs and the risk of untreated depressive disorders. Patients should be monitored closely for mood and thought changes.

Conclusion

The role of antidepressants in FGIDs in children is still unclear. While there is some evidence for the use of TCAs in adults, there is no evidence to support their use in children. The use of SSRIs might be associated with increased suicidal thoughts in adolescents, and without properly conducted studies of their use for FGIDs in this population, the use of SSRIs to treat FGIDs cannot be recommended.

Competing interests
None declared

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