



Association between functional gastrointestinal disorders and migraine in children and adolescents: a case-control study

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Summary

Background Functional gastrointestinal disorders and migraine are both common causes of medical attention. We have previously shown an association between migraine and infant colic. In this case-control study, we aimed to establish whether there is an association between migraine and other functional gastrointestinal disorders in children and adolescents.

Methods We included children and adolescents aged 6–17 years presenting to the emergency department of four tertiary hospitals in France and Italy. Patients diagnosed with either migraine or tension-type headache by the hospital's paediatric neurologist were enrolled as cases. Patients presenting to the emergency department with minor trauma and no history of recurrent headache were enrolled as controls. Investigators masked to a patient's group allocation diagnosed functional gastrointestinal disorders using the Rome III diagnostic criteria. Univariable and multivariable analyses were done to identify specific disorders and baseline factors associated with migraines and tension-type headache.

Findings Between Nov 1, 2014, and Jan 31, 2015, we enrolled 648 controls and 424 cases (257 patients with migraine and 167 with tension-type headache). 83 (32%) children and adolescents in the migraine group were diagnosed with functional gastrointestinal disorders compared with 118 (18%) in the control group ($p < 0.0001$). Multivariable logistic regression showed a significant association between migraine and three gastrointestinal disorders: functional dyspepsia (odds ratio 10.76, 95% CI 3.52–32.85; $p < 0.0001$), irritable bowel syndrome (3.47, 1.81–6.62; $p = 0.0002$), and abdominal migraine (5.87, 1.95–17.69; $p = 0.002$). By contrast, there was an inverse association between migraine and functional constipation (0.34, 0.14–0.84, $p = 0.02$). 41 (25%) participants with tension-type headache had functional gastrointestinal disorders, which did not significantly differ from the prevalence of these disorders in the control group ($p = 0.07$); no significant association was noted between any functional gastrointestinal disease and tension-type headaches.

Interpretation Three abdominal-pain-related functional gastrointestinal disorders were associated with migraine in children and adolescents. These findings are of value to the diagnosis and management of these common diseases. Future studies should investigate whether antimigraine drugs are of benefit in functional gastrointestinal disorders.

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Introduction

Functional gastrointestinal disorders are defined as chronic and recurrent gastrointestinal symptoms that cannot be explained by an underlying structural or tissue abnormality. Although the pathophysiological mechanisms of functional gastrointestinal disorders remain unclear, the results of several recent publications challenge the concept that these diseases are only functional in nature.¹ For example, patients with some functional gastrointestinal disorders can also have impaired epithelial barrier function, mucosal inflammation, immune activation, and aberrant neuronal sensitivity.²

The Rome III classification system for functional gastrointestinal disorders identifies 28 adult disorders and ten paediatric disorders using symptom-based diagnostic criteria. For children and adolescents, functional gastrointestinal disorders have been classified into three main categories of symptoms: vomiting and aerophagia, abdominal-pain-related functional

gastrointestinal disorders, and constipation and incontinence.³ In the general population, the most common functional gastrointestinal disorders are irritable bowel syndrome (IBS; prevalence 13–20%) and functional dyspepsia (prevalence 10–15%).⁴

Data for the epidemiology of these disorders in children and adolescents are less abundant. In North, Central, and South America, the prevalence of paediatric functional gastrointestinal disorders is estimated to be between 20% and 29% of children and adolescents, with IBS being the most common (3–7%).⁵ In a Japanese cross-sectional study,⁶ functional gastrointestinal disorders were reported in 14% of school children, with IBS in 6%. Prevalence rates in Europe vary considerably between countries and IBS prevalence remains constant throughout different age categories. Despite the important impact of paediatric functional gastrointestinal disorders on clinical practice, comorbidities, health-related quality of life,

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See [Comment](#) page 89

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Research in context

Evidence before this study

Interest has increased in the association between migraine and functional gastrointestinal diseases in adults. However, only a few studies have explored this association in children and adolescents. Recently we reported a link between migraine and infant colic, another common functional gastrointestinal disorders. Providing supporting data for a link between migraine and functional gastrointestinal disorders has substantial clinical and therapeutic implications.

Before undertaking this study (April 1–15, 2014), we searched for other studies in PubMed and Science Direct. We imposed no limitation to year of publication and included articles published in English, French, Italian, Spanish, and German. To avoid omitting relevant data about the epidemiology, association, or pathophysiological pathways between both diseases, we included both paediatric and adult publications. During the initial search, we used the search terms “functional gastrointestinal disorders”, “migraine”, and “headache”. The same search with the terms “migraine” and “headache” was done for each of the functional gastrointestinal disorders, separately, with no limit by age. In a secondary phase, we limited the search results to the field of paediatrics by adding the following terms: “paediatric OR pediatric”, “child*”, “adolescent*”. The reference lists of all examined full-text articles were screened for further relevant articles.

Aside from being scarce, the available evidence was mostly from studies of adults, which predominantly showed an association between irritable bowel syndrome (IBS) and migraine. Most of the identified studies were of mediocre quality because of small sample sizes, risk of biases, and confounding factors, as well as a lack of robust multivariable subanalyses. The few adult studies and the absence of quality-based paediatric studies proved to us the relevance and importance of conducting our case-control study.

Added value of this study

To our knowledge, this is the first study to show an association between three abdominal-pain-related functional gastrointestinal disorders and migraine in children and adolescents. It also lends support to recent findings showing an association between IBS and migraine in adults.

Implications of all the available evidence

Our findings provide additional supporting evidence for a possible common pathophysiological link between abdominal-pain-related functional gastrointestinal disorders and migraine, and thus could affect diagnosis and management of these frequent diseases. Additional clinical studies should be planned to investigate whether antimigraine drugs could be beneficial in treating pain-related functional gastrointestinal disorders, for which several treatment strategies have been suggested as being efficacious but the evidence is scarce.

and quality of school life,⁶ they receive little attention and their effects are still largely underestimated in children and adolescents.⁷

Migraine is the second most common cause of primary headaches in children and adolescents, with an estimated prevalence of more than 7%.⁸ The two major subtypes of migraines are those with aura and those without aura. The third edition of the International Classification of Headache Disorders (ICHD-3) provides the diagnostic criteria for paediatric migraine and four migraine equivalents: cyclic vomiting syndrome, abdominal migraine, benign paroxysmal vertigo, and benign paroxysmal torticollis.⁹ Tension-type headaches are the most common cause of primary headache in childhood and adolescence with an estimated prevalence of 10–25%.¹⁰ Children with tension-type headache show increased pain sensitivity compared with those without these headaches. Headache transformation between migraine and tension-type headache is known to occur. Cluster headaches, trigeminal autonomic cephalalgias, and other primary headaches are rare in the paediatric population.

Interest is increasing in the association between functional gastrointestinal disorders and migraine in adults.^{11–13} However, only a few studies have explored this association in children;^{14–16} one found a link between

recurrent abdominal pain and migraine.¹⁴ In 2013, we showed an association between migraine and infant colic, a common functional gastrointestinal disorder that ICHD-3 associates with migraine.¹⁷ Because of these findings, we aimed to establish the prevalence of functional gastrointestinal disorders in children and adolescents with primary headaches and investigate a possible relationship with migraine within this paediatric population.

Methods

Study design and participants

We did a case-control study of children and adolescents in four European tertiary care hospitals (Robert Debré, Paris, France; Sacco, Milan, Italy; Santa Maria della Misericordia, Udine, Italy; Santa Maria della Misericordia, Perugia, Italy). We included all patients aged 6–17 years who were diagnosed with primary headaches in the emergency department by a paediatric neurologist using the validated ICHD-3 criteria.¹⁸ We included only individuals older than 6 years so we could question the child, especially about headache type (eg, the pulsatile quality of pain, the presence of phonophobia), which can be very challenging in younger children. Only children and adolescents diagnosed with migraine or tension-type headache were included, irrespective of the concomitant presence of other

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