Pharmacy and Wellness Review

Volume 1 | Issue 1 Article 4

May 2010

Role of the Pharmacist In Improving Treatment for Children with Concurrent Gastrointestinal and Autism Spectrum Disorders

Whitney R. Henry
Ohio Northern University

Kaitlin A. Sanders
Ohio Northern University

Jenna L. Schaffner
Ohio Northern University

Leslie M. Hart
Ohio Northern University

Whitney N. Detillion
Ohio Northern University

See next page for additional authors

Role of the Pharmacist In Improving Treatment for Children with Concurrent Gastrointestinal and Autism Spectrum Disorders

Authors

Whitney R. Henry, Kaitlin A. Sanders, Jenna L. Schaffner, Leslie M. Hart, Whitney N. Detillion, and Anne F. Gentry

Role of the Pharmacist in Improving Treatment for Children with Concurrent Gastrointestinal and Autism Spectrum Disorders

Whitney R. Henry, fourth-year pharmacy major from Yeadon, Pa.; Kaitlin A. Sanders, fourth-year pharmacy major from Kendallville, Ind.; Jenna L. Schaffner, fourth-year pharmacy major from North Canton, Ohio; Leslie M. Hart, fifth-year pharmacy major from Cooperstown, Pa; Whitney N. Detillion, fifth-year pharmacy major from Portsmouth, Ohio; Anne F. Gentry, PharmD

Abstract

Over the last several years, a noteworthy association between gastrointestinal (GI) disorders and autism spectrum disorders (ASD) has been documented, although no large population-based studies exist. GI disorders in ASD children may stem from the underlying behavioral, communication, sensory or neurological issues intrinsic to the autistic disorder itself; therefore, the incorporation of alternative therapies, including behavioral modification, may be compelling treatment additions to the GI care traditionally recommended in children. To improve GI symptoms and quality of life in ASD children, a multidisciplinary approach is optimal, with pharmacists playing an active role in determining appropriate pharmacotherapy. Although there is a need for additional clinical trials to determine if specialized treatments for GI disorders are necessary in this unique pediatric population, this article reviews the currently available published information.

Autism and GI disorders: is there a link?

Autism spectrum disorder (ASD) is a broad term used to characterize a variety of psychological disorders. Most often diagnosed in children less than 3 years of age, ASD is typically recognized as an impairment in communication and social interaction. Frequently, children diagnosed with these disorders will have noted restrictive and/or repetitive patterns of interests and behavior. Many ASD children never acquire functional speech and may meet the necessary diagnostic criteria to be considered developmentally disabled.[1] ASD can be further classified under a number of subset categories, including classic autism, childhood disintegrative disorder, Rett syndrome, Asperger's syndrome, and pervasive developmental disorder-not otherwise specified.[2]

The etiology of autism is unknown and has resulted in considerable controversy. While some researchers argue that there is a genetic link, other researchers disagree.[3,4] Overall, there is a clear lack of large population-based data to support or deny these claims. Over the last several years, a noteworthy association between gastrointestinal (GI) disorders and ASD children has been documented.

Diagnosis of GI disorders in ASD patients, regardless of etiology, proves challenging. Without adequate ability of many of these children to verbally express themselves, these symptoms can often go unnoticed and untreated. A further confounder may exist in determining if the child is displaying typical autistic behaviors or complaining of symptoms related to a distinct GI disorder.

There are currently no established treatment guidelines for ASD patients with GI disorders and only a limited number of studies evaluating appropriate therapies specifically in this population or comparing treatment to non-ASD children. Despite this fact, children with ASD deserve equal medical attention and appropriate treatment as their non-ASD counterparts. Health care professionals should expand their knowledge about this topic and be vigilant in determining how to address this important concern. A multidisciplinary approach is fundamental to ensure proper care of ASD children, and pharmacists can play a crucial role in the management of this emerging issue.

What is currently known about the treatment of GI disorders in children with ASD?

GI disorder prevalence in children with ASD is much debated. Conflicting study data estimates rates anywhere from 9-70 percent.[2] There are a number of GI-related disorders that have been commonly known to afflict children with ASD. These can include, but are not limited to, gastroesophageal reflux disease (GERD), diarrhea, constipation and chronic abdominal pain.[2,6,7] Often, these children present with atypical symptoms when compared to children without ASD (Table 1).

Table 1: Possible Presentation of GI Disorders in ASD Children

Symptom	Possible GI Disorder
Bloating, flatulence or a combination	Lactose intolerance, constipation, GI infection
Chronic diarrhea	Maldigestion, malabsorption
Signs of abdominal discomfort such as holding or pushing on stomach, crying	GERD, intestinal inflammation, constipation, maldigestion, malabsorption
Sleep disruption	GERD
Straining to pass stool, hard or infrequent stool	Constipation
Aggression, irritability or hurting oneself	Gastritis, constipation, intestinal inflammation, GERD
Any or all of the above	Familial adenomatous polyposis (FAP), Irritable Bowel Syndrome (IBS)

Adapted from: Evaluation, Diagnosis, and Treatment of Gastrointestinal Disorders in Individuals With ASDs: A Consensus Report2

GERD

GERD occurs when the frequent regurgitation of gastric contents leads to the development of secondary disease states or interferes with growth. Diagnosis in children is based primarily on patient history, supplemented by data from pH monitoring tests and endoscopy.[8,9] Prevalence of GERD in all children, including those with ASD, is approximately 2.5 percent of children aged 3-9 years and 8.5 percent of those aged 10-17 years.[10] Discharge diagnosis of GERD represented almost 4 percent of pediatric hospitalizations in 2002, much higher than in previous years.[9] In children with ASD, GERD can occur as a result of an obstruction caused by malrotation or antral web.[6] This can cause the child to regurgitate many times throughout the day. Treatment goals for both ASD and non-ASD children are to alleviate symptoms, promote normal growth and prevent complications.[8]

Treatment of GERD with a proton pump inhibitor (PPI) typically taken once daily, 30 minutes before the morning meal, is one treatment option that has been studied specifically in children with ASD[6] (Table 2). While GERD treatment with PPIs may be common in pediatrics as a whole, the

assessment of the efficacy of PPI treatment in ASD children may specifically require notation of behavioral changes by teachers or parents.

Table 2: Normal Daily Dosing of PPI Therapy for GERD

Medication	Dosage
Pantoprazole	Adult: 40 mg/day for 8 weeks
Rabeprazole	Ages 12-adult: 20 mg/day for 4-8 weeks
Omeprazole	Adult: 20 mg/day for 4-8 weeks 1-16 years of age: 5-10 kg= 5 mg/day; 10-20 kg= 10 mg/day
Esomeprazole	Adult: 20-40 mg/day for 4-8 weeks 12-17 years of age: 20-40 mg/day for <8 weeks 1-11 years of age: 10-20 mg/day for <8 weeks
Lansoprazole	Adult: 15-30 mg/day for 8 weeks 12-17 years of age: 15-30 mg/day for 8 weeks 1-11 years of age: <30 kg= 15 mg/day; >30 kg= 30 mg/day

Adapted from: Recommendations for Evaluation and Treatment of Commons Gastrointestinal Problems in Children with ASDs[4]

In 2009, a systematic review of 508 recent publications was conducted indicating that ranitidine, omeprazole and probably lansoprazole are safe and effective treatments in infants. Symptoms were reversed and histological healing of esophagitis was observed as a result of these therapies. Gaviscon Infant® (simethicone) was also considered safe and able to aid in symptom reduction. In older children, evidence supports using H_2 receptor antagonists and PPIs as initial treatment.[8] Lifestyle modifications for infants, including eliminating cow's milk, thickening formula with rice and/or introducing a trial of hypoallergenic formula, are also considered possible treatment strategies.[9] Lifestyle modifications for older children and adolescents may include avoidance of caffeine, chocolate, spicy foods and alcohol; weight reduction (if applicable); and elimination of exposure to or cessation of smoking.[9]

Diarrhea

In the US, diarrheal-related illnesses cause an estimated 220,000 hospitalizations among young children (10.6 percent of all hospitalizations for this population). Concerns include nutrient malabsorption, malnutrition, loss of appetite and missed school days.[11] Chronic diarrhea is a condition of loose, watery stools that lasts longer than two weeks with or without an increase in stool frequency.[12] Chronic diarrhea can be caused by a number of conditions, including infections, celiac disease, irritable bowel disease (IBD), irritable bowel syndrome (IBS), lactose intolerance, antibiotic associated colitis and food allergies. Loose stool in children with ASDs may be misdiagnosed as diarrhea. Constipation is a common cause of loose stool and may be difficult to confirm by history or physical examination.[6]

Diagnosis should begin by obtaining a complete patient history and a physical examination.[12] Testing for chronic diarrhea commonly includes a CBC, electrolyte panel, kidney function evaluation, albumin level and a possible stool examination. For a more specific diagnosis, an endoscopic examination may also be used. Treatment usually consists of oral rehydration solutions, IV fluids and a restricted diet. Health care professionals should exercise clinical judgment when considering the appropriate treatment option for children with ASDs.[6]

Constipation

Constipation has been defined by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPHGHAN) as a delay or difficulty in defecation, continuing for two or more weeks and causing patient distress.[13] Studies have estimated that the prevalence of childhood constipation is between 2-38 percent. Normally, a diagnosis is made based on the patient's description of symptoms and a physical examination. Most children do not need additional tests for a diagnosis to be determined. However, additional tests, which include an abdominal X-ray, motility test, barium enema, rectal biopsy, transit study or colonoscopy, may be needed.[14]

Often in children with ASD, constipation is a result of sensory abnormalities and stool withholding behaviors.[6] Physicians recommend behavioral management, such as altering food choices and/or exercise, and pharmacotherapy to treat constipation in children with ASD.[6] Many of the pharmacotherapy choices used for children with ASD are similar to the treatments in non-ASD children, including mineral oil, magnesium hydroxide, lactulose, sorbitol, polyethylene glycol (PEG), or a combination of a lubricant and a laxative for daily management of constipation.

Abdominal pain

Chronic abdominal pain is defined as intermittent or constant abdominal pain that exceeds one or two months in duration, but for children with ASD, this remains a challenging assessment.[6] Some children with ASD may relay their pain by language, but those with communication disorders may show pain through atypical behaviors. These behaviors include pushing on the abdomen, tapping the area of distress, altered sleep patterns or displaying aggressive behaviors. Education of both health care professionals and parents is a vital role in treatment. Studies have not been conducted to help treat those with autism for abdominal pain.[6]

Dietary concerns

A number of other GI symptoms have been noted in children with ASD beyond that of the general pediatric population. Research shows that children with ASD may be allergic or sensitive to certain foods; the removal of these foods is essential to improve behaviors occurring from GI disorders. Implementing a gluten-free and casein-free diet may help these children, although no substantial evidence is available to support this claim.[2,15] Use of immunoglobulin administered orally to decrease GI dysfunction was also attempted. After eight weeks of treatment, 50 percent of the subjects showed significant behavioral improvement.[16] Potential use of vancomycin to reduce harmful gut flora is another studied treatment. This treatment is not recommended by all physicians because of the small, non-blinded study design, although it did show some promising results.[15]

Secretin

Many researchers think that the use of secretin may decrease GI dysfunction, but again, studies of this treatment show controversial results.[15] Secretin was suggested by three case reports where significant improvements in language and behavior occurred following the administration of secretin during upper endoscopy.[15] Three single-dose, double-blind, placebo-controlled studies were conducted, and only one of the three showed no difference of GI complaints between drug and placebo in children with ASDs. None of the single-administration studies indicate that secretin is more beneficial than placebo for improving the symptoms of children with autism.

Impact of GI disorders and ASD in practice

GI disorders in ASD children may stem from the underlying behavioral, communication, sensory or neurological issues intrinsic to the autistic disorder itself, thereby indicating that incorporation of alternative therapy, especially behavioral modification, may be a compelling treatment option. In order to appropriately apply treatment, more research needs to be conducted to determine the general etiologies of the GI disorders found among these children. Several treatment options previously mentioned have been suggested based on trial research; however, many treatment suggestions are derived from case reports, small sample size studies, or studies that examined combinations of treatments and are unable to reveal the true value of any single agent.

Although a true link between ASD and GI disorders continues to be a controversial issue, the commonality of GI-related disorders in ASD patients cannot be overlooked. While these GI disorders may be challenging to discover, diagnose and treat, awareness needs to be raised about this issue to promote further research, trials and attention in the future. The atypical presentation and symptoms experienced in many of these children suggest specialized treatment may be required, but regrettably, much of this treatment is still undefined or understudied.

A multidisciplinary approach, with pharmacists playing a crucial role, is fundamental to ensure proper care of ASD children. The general accessibility of the pharmacist in the community setting provides a great opportunity for patient education and intervention. Pharmacists should play an active role in determining what pharmacotherapy is appropriate for these children. Equipped with the information that ASD children may be more likely to experience GI symptoms and also that they may have altered social behaviors as a result of ASD, pharmacists will be more prepared to recommend a proper OTC therapy and/or refer patients with concerning symptoms to a physician. Unfortunately, more research needs to be done on this topic to determine if pediatric treatments in non-ASD patients are indeed appropriate for use in the same GI disorders in ASD patients. Pharmacists can also educate families on the often atypical symptoms observed in ASD children associated with GI ailments as well as the prevalence and current research on this topic. In addition to these services, pharmacists can monitor for drug interactions between the child's prescription medications and any OTC therapies that may be used for symptom management.

This is a topic of growing interest where many more trials need to be completed to determine if specialized treatments for GI disorders are necessary in this unique pediatric population. Further research should involve a multidisciplinary health care team, including the pharmacist, to determine the best therapies to improve the quality of life in ASD children. While large steps have been made recently, continuing to raise awareness of this issue among health care professionals will likely enhance the interest to strive for more definitive conclusions and future treatment guidelines specific to GI disorders in ASD patients.

References:

1. Molloy C, Manning-Courtney P. Prevalence of chronic gastrointestinal symptoms in children with autism and autistic spectrum disorders. Autism 2003; 7(2):165-171.
2. Buie T, Campbell D, Fuchs G, Furuta G, Levy J, VandeWater J, et al. Evaluation, diagnosis and treatment of gastrointestinal disorders in individuals with ASDs: a consensus report. Pediatrics 2010; 125: S1-S18.
3. Campbell D, Buie T, Winter H, Bauman M, Sutcliffe J, Perrin J, et al. Distinct genetic risk based on association of MET in families with co-occurring autism and gastrointestinal conditions. Pediatrics 2009; 123 (3):1018-1024.
4. Ibrahim S, Voigt R, Katusic S, Weaver A, Barberesi W. Incidence of gastrointestinal symptoms in children with autism: a population-based study. Pediatrics 2009;124: 680-686.
5. Erickson CA, Stigler KA, Corkins MR, Posey DJ, Fitzgerald JF, McDougle CJ. Gastrointestinal factors in autistic disorder: a critical review. J Autism Dev Disord 2005;35(6):713-727.
6. Buie T, Fuchs G, Furuta G, Kooros K, Levy J, Lezis J, et al. Recommendations for evaluation and treatment of commons gastrointestinal problems in children with ASDs. Pediatrics 2010; 125: S19-S29.
7. Adams J, Holloway C. Pilot study of a moderate dose multivitamin/mineral supplement for children with autistic spectrum disorder. J Altern Complement Med 2004; 10 (6): 1033-1039.
8. Tighe MP, Afzal NA, Bevan A, Beattie RM. Current pharmacological management of gastro- esophageal reflux in children: an evidence-based systematic review. Pediatr Drugs 2009;11(3):185-202.
9. Gold BD, Freston JW. Gastroesophageal reflux in children: pathogenesis, prevalence, diagnosis, and role of proton pump inhibitors in treatment. Pediatr Drugs 2002;4(10):673-685.
10. Jones NL, Wine E. Pediatric gastrointestinal diseases: are drugs the answer? Curr Op in Phrmclgy 2005;5(6):604-609.
11. Davila EP, Trepka MJ, Newman FL, Huffman FG, Dixon Z. Diarrheal illness among women, infants, and children (WIC) program participants in Miami, Florida: implications for nutrition education. J Nutr Educ Behav 2009;41(6):420-424.
12. Surawicz CM, Ochoa B. Diarrheal Diseases. 2007.
13. Inan M, Aydiner CY, Burcu T, Aksu B, Ayvaz S, Ayhan S, et al. Factors associated with childhood constipation. Journal of Pediatrics & Child Health 2007;43(10):700-706.
14. Kay M, Tolia V. Common gastrointestinal problems in pediatric patients. Available at www.acg.gi.org/patients/gihealth/pdf/pediatric.pdf. Accessed Jan. 24, 2010.
15. Erickson C, Stigler K, Corkins M, Posey D, Fitzgerald J, McDougle C. Gastrointestinal factors in autistic disorder: a critical review. J Autism Dev Disord 2005; 35 (6): 713-727.
16. Schneider C, Melmed R, Enriquez F, Barstow L, Ranger-Moore J, Ostrem J. Oral human immunoglobulin for children with autism and gastrointestinal dysfunction: a prospective, open-label study. J Autism Dev Disord 2006; 36: 1053-1064.