

# Integrative Approach to Pediatric Nausea

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## ABSTRACT

Nausea is a bothersome symptom that is commonly seen in the pediatric population. The pathophysiology of nausea is complex and involves the central nervous system, the enteric nervous system, gastrointestinal tract motility, and psychologic influences. Pharmacologic and nonpharmacologic therapies are available for treating nausea. Mind-body interventions (hypnosis, biofeedback), botanicals and supplements (ginger, enteric-coated peppermint oil), aromatherapy, and acupuncture have emerging evidence for effectively treating pediatric nausea. [*Pediatr Ann.* 2019;48(6):e236-e242.]

Pediatricians often encounter patients with nausea, which is an unpleasant sensation in the stomach accompanied by an urge to vomit. Nausea is commonly seen with vomiting as part of a short-lived bout of acute viral gastroenteritis or motion sickness. Patients undergoing surgery may experience postoperative nausea and vomiting (PONV), and oncology patients may experience chemotherapy-induced nausea and vomiting (CINV). Functional nausea, or nausea in the absence of known organic etiology, is a chronic debilitating symptom that is part of the symptom profile for functional abdominal pain (FAP); it has been reported as a concomitant symptom in 50% of patients with functional gastrointestinal

disorders (FGID).<sup>1</sup> According to the Rome IV criteria, an isolated diagnosis of functional nausea requires nausea as the predominant symptom at least twice a week for at least 2 months, nausea generally not related to meals, nausea not consistently associated with vomiting, and nausea that cannot be explained by another medical condition.<sup>2</sup> Patients with functional nausea may be particularly challenging to treat, and childhood nausea may predict gastrointestinal (GI) distress, and anxiety and depression in adulthood.<sup>3</sup>

This review discusses the pathophysiology and treatment of nausea. At presentation, patients who endorse nausea as a primary symptom require a complete history of illness, review of systems,

physical examination, and a thorough investigation to distinguish between FGID and an organic etiology. Any “red flag” symptoms (**Table 1**) should prompt the provider to pursue testing to rule out infectious, malignant, anatomic, or inflammatory etiologies. This testing (the finer details of which are beyond the scope of this article) may include laboratory and stool studies, imaging, breath testing, or referral to pediatric gastroenterology depending on patient presentation. In the absence of red flag symptoms, it may be appropriate to not pursue invasive testing when functional nausea is suspected. Functional nausea remains a diagnosis of exclusion.

## PATHOPHYSIOLOGY OF NAUSEA

The proposed pathophysiology of nausea involves a complex interplay between GI motility, sensory pathways, central nervous system regulation, autonomic regulation, and psychological health. Often, and particularly in the case of functional nausea, it can be difficult to determine the exact nausea trigger. Altered GI motility may cause nausea if there are abnormalities in gastric emptying or gastric accommodation (the ability of the stomach to relax and store ingested food).<sup>4</sup> An abnormal gastric accommodation may cause symptoms of functional dyspepsia, including early satiety, fullness, bloating, and nausea. Recent work has also started to link autonomic dysfunction with chronic nausea, although whether autonomic

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dysfunction is causal or correlational to nausea remains to be seen. In a report by Chilemsky et al.,<sup>5</sup> 93% of patients with chronic GI pain and dizziness reported chronic nausea as a concurrent symptom, and patients with postural orthostatic tachycardia syndrome diagnosed by tilt-table test also frequently complain of nausea.

Psychologic factors such as anxiety may also play a significant role in nausea. The vasovagal reflex pathway mediates GI motility as well as accommodation, and psychological factors can significantly influence this reflex.<sup>6</sup> An example of this can be seen in CINV, where patients may experience anticipatory nausea prior to the actual chemotherapy infusion. In a retrospective review of patients with a primary symptom of chronic nausea, investigators found a high prevalence of comorbid conditions, including anxiety (70%), dizziness (79%), fatigue (53%), and sleep problems (61%).<sup>1</sup> In the classic “chicken or the egg question,” comorbid psychiatric disturbances (such as anxiety) may be the cause, effect, or an exacerbating factor of chronic nausea.

## PHARMACOLOGIC TREATMENTS

Current pharmacologic treatments for nausea are empiric. Medications used for acute types of nausea include antiemetics such as 5HTP-3 antagonists (ondansetron), antihistamines (promethazine, diphenhydramine, cyproheptadine), and antimuscarinics (hyoscine). Medications for acute nausea have been trialed for chronic nausea with variable success, as physiologic treatment targets for chronic nausea may be different than acute nausea.<sup>1</sup> Given the likely multifactorial triggers for nausea, treating concurrent symptoms may also improve nausea. For instance, patients with concurrent acid reflux symptoms may benefit from antireflux medications such as a

TABLE 1.

**“Red-Flag” Symptoms Associated with Nausea That Should Prompt Thorough Evaluation into Organic Etiology**

History	Physical	Diagnostic Testing
Abdominal pain	Failure to thrive	Iron-deficiency anemia
Sudden change in stool pattern	Abnormal neurologic examination	Elevated liver function
Bilious vomiting	Rebound tenderness or guarding	Elevated inflammatory markers
Early morning vomiting	Lymphadenopathy	Elevated fecal calprotectin
Persistent or forceful vomiting	Abdominal mass	
Blood in stool	Orthostasis	
Weight loss		
Headache		
Neurologic symptoms		
Family history of inflammatory gastrointestinal disorders		

histamine-H2 receptor blocker or proton pump inhibitor. Patients with delayed gastric emptying and nausea may benefit from prokinetics such as erythromycin and metoclopramide.<sup>7</sup> Further, patients with signs of autonomic dysfunction (dizziness, orthostatic hypotension) may benefit from increasing fluid and salt intake or a trial of a low-dose mineralocorticoid such as fludrocortisone.<sup>7</sup> A low dose of amitriptyline, a tricyclic antidepressant, improved symptoms by at least 50% in 44% of children with chronic nausea, with a mean dose of 50 mg nightly.<sup>1</sup> However, side effects such as dizziness, fatigue, dry mouth, and weight gain may limit amitriptyline use.

## NONPHARMACOLOGIC TREATMENTS

Nonpharmacologic treatments for nausea include mind-body interventions, botanicals and supplements, aromatherapy, and acupuncture. There is modest evidence for some of these treatments for acute PONV and CINV; however, there is a paucity of research

dedicated to pediatric functional nausea as a discrete entity because it is a newly established clinical diagnosis. As a whole, these nonpharmacologic treatments are safe with minimal side effects and thus may be empirically trialed individually or in combination to provide nausea relief, except as noted. As with all patient recommendations, side effects and drug-supplement interactions (not included here) should be reviewed before recommendation or prescription. **Table 2** summarizes select therapeutics with example dosages and commentary based on existing literature.

## Mind-Body Modalities

**Hypnotherapy.** Clinical hypnosis uses a patient’s focused attention to help develop skills in self-regulation, control of behavior and emotion, and confidence in their ability to self-heal. Hypnosis is used to treat nausea and vomiting associated with cancer therapy. The National Comprehensive Cancer Network guidelines<sup>8</sup> advocate for the use of hypnosis for anticipatory nausea and vom-

TABLE 2.  
Nonpharmacologic Treatments for Nausea: Summary of Evidence

Intervention	Dose/Administration	Evidence	Study Population	Side Effects/Contraindications	Recommendation
Hypnotherapy	One to six 15- to 40-minute sessions <sup>9</sup> Six 50-minute sessions over 3 months <sup>10</sup>	Meta-analysis  RCT	Pediatric pain and anxiety related to chemotherapy Pediatric FGID	Contraindicated in patients with history of psychosis	Possible benefit, low risk
Biofeedback	Six training sessions <sup>11</sup>	Open-label controlled trial	Pediatric FAP	No known side effects	Possible benefit, low risk
Cognitive-behavioral therapy	10 weekly sessions <sup>13</sup>	Pilot	Pediatric FGID	No known side effects	Possible benefit, low risk Consider for children with comorbid anxiety, depression, mood disorder
Ginger ( <i>Zingiber officinale</i> )	10 mg PO daily <sup>14</sup> 1 to 1.5 g PO 1 h prior to surgery <sup>15</sup>	RCT Systematic review	Pediatric AGE Adult PONV	Side effects: heartburn, potentiation of anticoagulant; prolonged bleeding time	Possible benefit, well tolerated
Peppermint ( <i>Mentha piperita</i> )	0.2 mL (187-374 mg) PO enteric coated, with meals three times daily <sup>16</sup> 180-200 mg PO 3 times daily <sup>17</sup>	RCT  Review	Pediatric IBS  Adult IBS	Side effects: abdominal pain, heartburn, hypersensitivity, anal burning	Possible benefit, enteric-coated capsule is well tolerated
Vitamin B6	Dose not specified <sup>19</sup>	RCT	Pediatric AGE	Side effects: nausea, vomiting, stomach pain, headache	No evidence of benefit, well tolerated
Marijuana	Inhalation Edibles Oil extract	None	Not applicable	Side effects: cannabinoid hyperemesis syndrome, impact on brain development, abuse potential, fatigue, anorexia	Insufficient evidence to recommend with potential for harm
Aromatherapy	Topical (dilution) and inhalation <sup>24</sup> Peppermint aromastick <sup>25</sup> Inhalation of ginger essential oil <sup>26</sup> Inhalation <sup>26</sup>	Systematic review  Retrospective review Randomized trial  RCT	Adult and pediatric PONV  Adult CINV Adult PONV  Pediatric CINV	Side effects: not reported	Unclear benefit, well tolerated

TABLE 2. (continued)  
Nonpharmacologic Treatments for Nausea: Summary of Evidence

Intervention	Dose/Administration	Evidence	Study Population	Side Effects/Contraindications	Recommendation
Acupuncture Acupressure	Electroacupuncture <sup>29</sup> Varied <sup>30</sup>	Systematic review Meta-analysis	Adult CINV Pediatric CINV	Few studies report adverse events; no fatal, most commonly with pain at needle insertion, erythema at needle insertion  Relative contraindication in neutrope- nia, thrombocytopenia for acupuncture	Possible benefit, well-tolerated

Abbreviations: AGE, acute gastroenteritis; CINV, chemotherapy-induced nausea and vomiting; FAP, functional abdominal pain; FGID, functional gastrointestinal disorders; IBS, irritable bowel syndrome; PO, by mouth; PONV, postoperative nausea and vomiting; RCT, randomized controlled trials.

iting associated with chemotherapy. A 2018 meta-analysis of 15 studies found large, statistically significant reductions in both anxiety and pain after hypnosis for children undergoing chemotherapy compared with treatment as usual.<sup>9</sup> As anxiety is highly correlated with nausea in childhood, it follows that treating anxiety with mind-body modalities may be effective in ameliorating nausea, although this has not been sufficiently studied. For nausea related to FGID, a randomized controlled trial (RCT) in children with FGID also found that bi-weekly hypnosis sessions for 3 months significantly decreased FGID symptoms (including nausea) more than standard medical therapy.<sup>10</sup> It should be noted that hypnotherapy is contraindicated in any child with a history of psychosis. Overall, there is not enough evidence to formally support clinical hypnosis for the treatment of nausea in children, but it is a promising modality with little risk of harm.

**Biofeedback.** Biofeedback is a technique that uses wearable sensors to give the patient information about their body (such as heart rate, respiratory rate and pattern, blood pressure, sweating, body heat, and muscle tension). Biofeedback allows the patient to gain control of normally involuntary processes to benefit their health and has been used with some success in patients with FAP.<sup>11</sup> Additionally, game-based biofeedback has been studied as an effective adjuvant therapy in treating anxiety.<sup>12</sup> As with hypnotherapy, biofeedback for nausea is a potential low-risk therapy that deserves further research in the pediatric population before formal recommendation can be made.

**Cognitive-behavioral therapy.** There is a high incidence of psychologic comorbidities (particularly anxiety and depression) in children with FGID and functional nausea.<sup>1,3</sup> For this reason,

children with functional nausea should be screened and referred to mental health services as needed for psychotherapy. Exposure-based cognitive-behavioral therapy (CBT) is effective for adults with irritable bowel syndrome (IBS). More recently, CBT has been shown to sustainably improve pain associated with FGID, GI symptoms, pain frequency, quality of life, depression, anxiety, absenteeism, and somatic symptoms.<sup>13</sup> Although not yet supported by evidence for chronic nausea specifically, referral for CBT could be considered for children with comorbid anxiety, depression, or mood disorder.

## Botanicals and Supplements

**Ginger.** Clinical studies show ginger, touted as a promotility and antispasmodic agent, is possibly effective for gastroenteritis-related, postoperative, pregnancy-induced, and antiretroviral-induced nausea and vomiting. In a RCT of 141 children with suspected acute gastroenteritis (AGE), a 10-mg oral dose of ginger significantly decreased vomiting and resulted in fewer missed days of school compared with placebo.<sup>14</sup> A systematic review and meta-analysis showed that taking 1 to 1.5 mg of ginger 1 hour prior to surgery significantly reduced the incidence of PONV.<sup>15</sup> Ginger can prolong bleeding time, and its use requires especially close monitoring in any patient taking anticoagulants. Although there have not been any dedicated studies of ginger for children with functional nausea, it is a potentially beneficial therapy that carries low risk to the patient.

**Peppermint.** Peppermint oil, given its antispasmodic properties, has been used for the treatment of IBS in children as young as age 8 years.<sup>16</sup> IBS symptoms are known to be triggered by a person's level of stress and anxiety, both of which can also be associated with nausea. Sev-

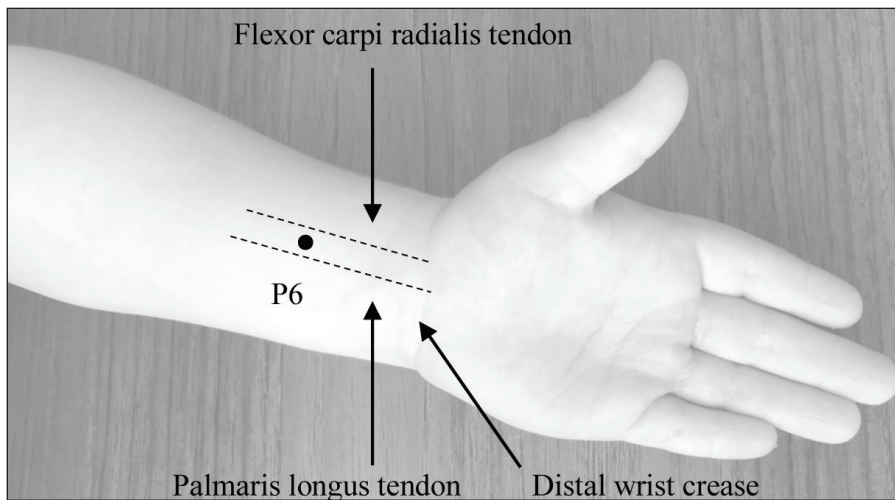


Figure 1. Pericardium 6 acupuncture and acupressure point for nausea relief. The point is found approximately three finger-widths (patient's fingers) proximal to the distal wrist crease between the palmaris longus and flexor carpi radialis tendons.

eral clinical trials show reduction in IBS symptoms, including nausea, at a dose of 0.2 mL (187 mg) 3 times daily before meals with no significant side effects.<sup>16</sup> Treatment effect for IBS symptoms, as determined by a 2005 review of 16 clinical trials (including pediatric patients), ranges from 39% to 79% improvement in symptoms.<sup>17</sup> The most common side effects for oral peppermint oil are gastroesophageal reflux and anal burning, but these were generally mild if present.<sup>17</sup> To minimize these side effects, and to decrease reflux, peppermint oil is taken orally in enteric-coated, pH-dependent capsules. Again, although no dedicated research for the effectiveness of peppermint in children with nausea alone has been conducted, the minimal risk of serious side effects means peppermint may be considered as a treatment option.

**Vitamin B6.** Vitamin B6 is regularly used in women who are pregnant and is considered a first-line treatment for pregnancy-induced nausea and vomiting.<sup>18</sup> Beyond this application, the literature affirming vitamin B6's anti-nausea effect is sparse. A double-blind controlled trial in 2013 with 96 children with AGE did not show a statistically

significant improvement in dehydration or vomiting in response to vitamin B6 versus placebo.<sup>19</sup> Given the paucity of data supporting its benefit but its limited potential for harm, further investigation is required for this supplement.

**Marijuana and derivatives.** Although cannabis use is reported in patients with intractable seizures and pediatric oncology, its use remains controversial and, in certain states, illegal.<sup>20</sup> There is quality evidence that some tetrahydrocannabinol (THC) cannabinoids are effective anti-emetics for children receiving chemotherapy.<sup>21</sup> However, the long-term safety of its use in children with nausea is not fully realized, and side effects, including dizziness and drowsiness, are common. In contrast, cannabidiol is a nonpsychotropic component of cannabis that warrants further exploration, apart from THC, for its use in pediatric nausea. Cannabis and its derivatives can also be used as appetite stimulants, although chronic and heavy use can cause cannabinoid hyperemesis. Cannabinoid hyperemesis should be considered in patients who present with persistent nausea and vomiting, especially if improved with a hot

bath or shower. Other concerns around THC cannabinoid use include potential for abuse and addiction, impaired lung health with the inhaled forms, and adverse effects on cognition in the adolescent brain (particularly impaired working memory and inhibitory control).<sup>20,22,23</sup> Given all of the above risks, marijuana and its derivatives are not recommended for the treatment of pediatric nausea at this time.

### Aromatherapy

Aromatherapy is the therapeutic use of essential oils (aromatic constituents of particular plant flowers, fruits, and seeds) administered topically or by inhalation to improve well-being. In adults, several studies have investigated aromatherapy, in particular using lemon, ginger, and peppermint essential oils, for various forms of nausea. A 2018 Cochrane review of aromatherapy (peppermint oil, ginger, isopropyl alcohol, or mixtures) for PONV found more participants who received aromatherapy were free of nausea compared to controls and required fewer antiemetic medications, but effects were similar to those seen with placebo.<sup>24</sup> Unfortunately, study quality limited the clinical significance of the findings. Other RCTs have found improved anxiety and nausea with peppermint aromasticks in oncology patients, and PONV relief using ginger essential oil compared to a blend of ginger, spearmint, peppermint, and cardamom.<sup>25,26</sup>

A randomized, controlled, double-blind placebo study of 49 children with chemotherapy-induced nausea failed to detect a difference in nausea in response to inhalation of ginger essential oil, baby shampoo, or placebo.<sup>27</sup> Despite this, given the low risk of toxicity and noninvasive nature of aromatherapy with potential benefit identified in the adult population, this modality de-



serves more robust research on safety and efficacy for its application to pediatric nausea.

### Acupuncture and Acupressure

Acupuncture and acupressure are forms of traditional Chinese medicine that involve insertion of thin needles (acupuncture) or applying firm pressure and massage (acupressure) at specific points in the body. No studies to date have investigated the efficacy of acupuncture and acupressure for functional nausea in children. However, the National Institutes of Health consensus statement cites promising evidence for acupuncture for CINV and PONV in adults.<sup>28</sup> A Cochrane review in 2006 showed electroacupuncture (acupuncture accentuated by electric stimulation) has a protective effect on CINV, but the effect in combination with newer antiemetics was unclear.<sup>29</sup> The most studied acupuncture point is pericardium 6, which lies approximately 4 cm proximal to the distal wrist crease between the palmaris longus and flexor carpi radialis tendons (**Figure 1**). Over-the-counter products marketed generically as “sea bands” can also be worn over this site, making it an accessible modality.

More research is required for the pediatric population. A metanalysis of 12 studies that used acustimulation (acupuncture, acupressure, and electric stimulation) for PONV in children concluded that acupuncture and acupressure are as effective as medications to reduce PONV in children.<sup>30</sup> Although promising, the overall published evidence for acustimulation for pediatric PONV and CINV is mixed, with most studies having low rigor, high attrition, and significant heterogeneity in study design.<sup>31</sup> However, given the encouraging evidence on nausea in the adult population, the easy accessibility of point PC6, low

risk of side effects, and strong safety profile,<sup>31</sup> acupuncture and acupressure remain a possible emerging therapy for nausea in children.

### CONCLUSION

Nausea is commonly seen in pediatric patients, and the pathophysiology involves complex interactions between the GI tract, autonomic nervous system, central nervous system, and psychology. Anti-emetic medications may not sufficiently treat functional nausea and other forms of pediatric nausea. Integrative medicine modalities may be trialed to treat nausea that is refractory to medications. Mind-body interventions such as hypnotherapy and biofeedback have a modest body of evidence to treat pediatric conditions associated with nausea (FAP, IBS). Other treatment modalities such as aromatherapy, acupuncture, acupressure, ginger, enteric-coated peppermint oil, and vitamin B6 have a good safety profile. These emerging therapies are promising and require further investigation before they can be recommended for pediatric nausea.

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