

Pediatric Pharmacotherapy 101: Gastrointestinal Symptom Management

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Disclosure

- We have no relevant financial relationships with manufacturers of any commercial products and/or providers of commercial services discussed in this presentation.
 - This discussion will include the use of medications for off-label indications.
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Objectives

- Determine potential pathophysiological mechanisms of nausea/vomiting in children
- Evaluate pharmacological and non-pharmacological treatment options based on pathophysiology of nausea/vomiting in children
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- Discuss pharmacological and non-pharmacological management of constipation in children

3

Patient Case: Canter

12 year-old male awaiting cardiac transplant

- 12 year-old male
 - Listed IB for transplant (failed Fontan) on ambulatory milrinone
 - Recently discharged from the hospital after prolonged course
- Weight: 24 kg Height: 127 cm
- Lives at home; Mom is primary caregiver
- PMH:
 - Complete AV canal and total anomalous pulmonary venous return connection status post Fontan
 - Failing physiology with ventricular dysfunction
 - History of thromboembolism
- CC:
 - Increasing side/back/abdominal pain and headaches
 - Slow decline of appetite and energy since initial transplant evaluation/listing
- Allergy: NKDA

4

Patient Case: Canter

12 year-old male awaiting cardiac transplant

Medications	Directions
acetaminophen (Tylenol®)	325 mg po q6hrs <i>13.5 mg/kg/dose</i>
amoxicillin	250 mg po BID
famotidine (Pepcid®)	20 mg po daily
furosemide (Lasix®)	40 mg po BID <i>1.7 mg/kg/dose</i>
milrinone	0.5 mcg/kg/min IV continuous infusion <i>via PICC line</i>
oxycodone (Roxicodone®)	2.5 mg po q4hrs prn pain
spironolactone/ hydrochlorothiazide (Aldactazine®)	25 mg po daily <i>~1 mg/kg/dose</i>
warfarin (Coumadin®)	3 mg po daily

5

Nausea & Vomiting

Nausea & Vomiting

- Prevalence
 - 40-63% of children receiving palliative care
- Nausea
 - Unpleasant feeling of needing to vomit
- Vomiting
 - Involuntary spasms resulting in the reflux of gastric contents through the mouth

Friedrichsdorf SJ, Drake R, Webster ML. Chapter 33, Gastrointestinal Symptoms. In: Wolfe J, Hinds PS, Sourkes BM, editors. Textbook of Interdisciplinary Pediatric Palliative Care. Philadelphia: Saunders; c2011. p.311-334.

7

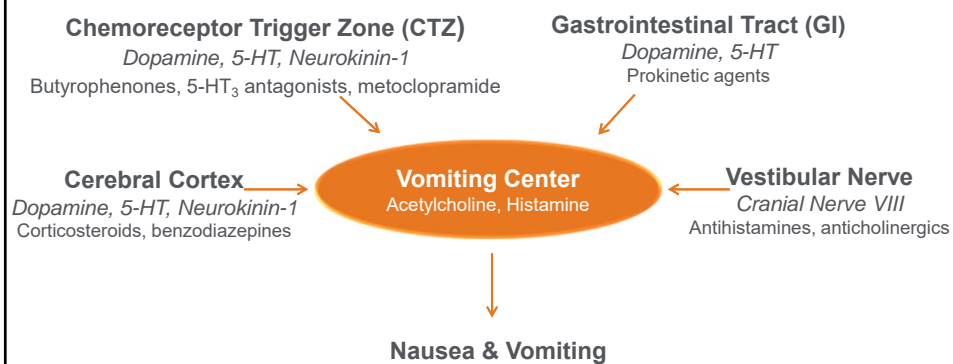
Mechanisms of Nausea & Vomiting

Mechanisms of Nausea & Vomiting

- 2 organ systems
 - Gastrointestinal tract (GI)
 - Brain
- Primary neurotransmitters
 - Dopamine (D₂)
 - Histamine (H₁)
 - Acetylcholine (ACh)
 - Serotonin (5-HT)

9

Mechanisms of Nausea & Vomiting



Neurotransmitter Key: D₂ = Dopamine; 5-HT = Serotonin; ACh = Acetylcholine; H₁ = Histamine

10

Mechanisms of Nausea & Vomiting

Chemoreceptor Trigger Zone (CTZ)

Causes	Neurotransmitters	Treatment Options
<ul style="list-style-type: none"> • Microbes • Medications • Metabolic products 	<ul style="list-style-type: none"> • Dopamine (D₂) • Serotonin (5-HT) • Neurokinin-1 	Butyrophenones <ul style="list-style-type: none"> • haloperidol (Haldol®) Phenothiazines <ul style="list-style-type: none"> • promethazine (Phenergan®) Prokinetic <ul style="list-style-type: none"> • metoclopramide (Reglan®) 5-HT ₃ receptor antagonists <ul style="list-style-type: none"> • ondansetron (Zofran®) Thienobenzodiazepine <ul style="list-style-type: none"> • OLANzapine (Zyprexa®) NK-1 receptor antagonists <ul style="list-style-type: none"> • aprepitant (Emend®) Cannabinoids <ul style="list-style-type: none"> • dronabinol (Marinol®)

11

Mechanisms of Nausea & Vomiting

Gastrointestinal (GI)

Causes	Neurotransmitters	Treatment Options
<ul style="list-style-type: none"> • Motility • Mechanical obstruction • Mucosal irritation • Medications 	<ul style="list-style-type: none"> • Dopamine (D₂) • Acetylcholine (Ach) • Serotonin (5-HT) 	Prokinetics <ul style="list-style-type: none"> • metoclopramide (Reglan®)

12

Mechanisms of Nausea & Vomiting

Cerebral Cortex

Causes	Neurotransmitters	Treatment Options
<ul style="list-style-type: none"> • Meningeal irritation • Mental anxiety 	<ul style="list-style-type: none"> • GABA 	<ul style="list-style-type: none"> • Mental anxiety Benzodiazepines – LORazepam (Ativan®) • Meningeal irritation Corticosteroids – dexamethasone (Decadron®)

13

Mechanisms of Nausea & Vomiting

Vestibular

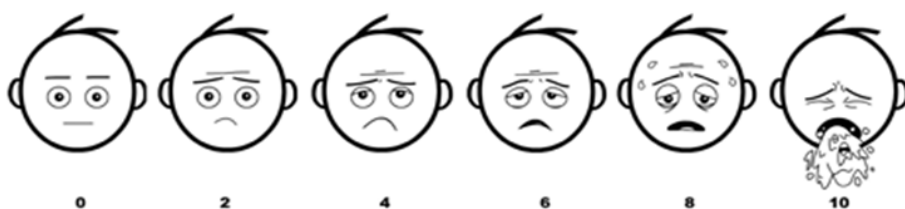
Causes	Neurotransmitters	Treatment Options
<ul style="list-style-type: none"> • Movement 	<ul style="list-style-type: none"> • Histamine (H₁) • Acetylcholine (Ach) 	<p>Antihistamines</p> <ul style="list-style-type: none"> • diphenhydrAMINE (Benadryl®) • hydroxyzine (Atarax®) <p>Anticholinergics</p> <ul style="list-style-type: none"> • glycopyrrolate (Robinul®, Cuvposa®) • scopolamine (Trans-Derm Scop®)

14

Nausea & Vomiting Assessment

Assessment

Baxter Retching Faces (BARF) Nausea Scale



Baxter AL, Watcha MF, Baxter WV, et al. Development and validation of a pictorial nausea rating scale for children. *Pediatrics* 2011;127:e1542-e1549.

Assessment

Onset

Presentation	Possible Causes of Nausea & Vomiting
Abrupt	Cholecystitis, food poisoning, gastroenteritis, pancreatitis, medications
Insidious	Reflux, gastroparesis, medications, metabolic disorders, pregnancy

17

Assessment

Pattern

Symptom Presentation	Possible Causes
Large, infrequent emesis that relieves nausea	Complete or partial bowel obstruction
Small-volume emesis	Gastric stasis
Projectile	Pyloric stenosis
Effortless, regurgitation	Reflux, rumination syndrome

18

Assessment

Timing

Symptom Presentation	Possible Causes
Before breakfast	↑ ICP, pregnancy, uremia
During or directly after eating	Pyloric stenosis, peptic ulcer disease, psychiatric causes
1-4 hr after meal	Dyspepsia, peptic ulcer disease, neoplasms, gastroparesis
Continuous	Conversion disorder, depression

19

Assessment

Appearance

Symptom Presentation	Possible Causes
Undigested food	Achalasia, esophageal disorders
Partially digested food	Gastric outlet obstruction, gastroparesis
Bile	Proximal small bowel obstruction
Feculent or odorous	Fistula, obstruction
Large Volume	Organic cause
Coffee-ground or bright red blood	GI bleed, ulcer, gastritis
Mucus	Upper respiratory infection, allergies, reflux

20

Assessment

Abdominal Pain

Symptom Presentation	Possible Causes
Right upper quadrant	Gallbladder disease, liver disease
Epigastric	Dyspepsia, pancreatic disease, peptic ulcer disease
Right lower quadrant	Appendicitis
Severe pain	Biliary disease, pancreatic disease, peritoneal irritation, small bowel obstruction
Severe pain proceeding vomiting	Small bowel obstruction

21

Assessment

Associated Symptoms

Symptom Presentation	Possible Causes
Headache, stiff neck, vertigo, focal neurologic deficits	↑ ICP, encephalitis/meningitis, head injury, mass, migraine
Morning symptoms; headache & neurological	↑ ICP
Altered mental status	Uremia, hyponatremia, or ↑ ICP
Weight loss	Malignancy, gastric outlet obstructions, peptic ulcer
Polyuria, polydipsia	Hyperglycemia or hypercalcemia
Syncope, early satiety	Autonomic insufficiency

22

Assessment

Associated Symptoms

Symptom Presentation	Possible Causes
Vertigo and movement symptoms	Vestibular dysfunction
Early satiety, postprandial bloating, abdominal discomfort	Gastroparesis
↓ bowel movement frequency, abdominal fullness, hard stools, straining	Constipation
Worry, emotional responses	Anxiety
Repetitive migraine headaches or irritable bowel syndrome symptoms	Cyclic vomiting syndrome
Diarrhea, myalgias, malaise, headache	Viral

23

Assessment

Physical Exam

Symptom Presentation	Possible Causes
Masses	Evaluate location and size
Bowel sounds, abdominal distention	Bowel obstruction, ileus, or constipation
Calluses on dorsal surfaces of hands	Bulimia
Jaundice	Kernicterus, liver failure, urinary tract infection (UTI)
Poor skin turgor, delayed capillary refill, tachycardia, hypotension	Signs of dehydration
Papilledema, neurological signs	↑ ICP
Fecal impaction, rectal exam	Constipation

24

Patient Case: Canter

12 year-old male awaiting cardiac transplant

What are some areas to focus on when assessing nausea/vomiting?

25

Patient Case: Canter

12 year-old male awaiting cardiac transplant

Assessment

Timing	Always, especially when family is eating
Abdominal Pain	Right upper quadrant
Symptoms	Headache Constipation
Physical Exam	Abdominal distention

26

Causes of Nausea & Vomiting

Causes of Nausea & Vomiting

11 M's of Emesis

- Microbes
- Medications
- Metabolic
- Myocardial
- Metastasis
- Movement
- Meningeal irritation
- Mental anxiety
- Mucosal irritation
- Mechanical obstruction
- Motility

Causes of Nausea & Vomiting

Chemoreceptor Trigger Zone (CTZ)

- Microbes (Infections)
 - Medications
 - Antibiotics
 - Chemotherapy/Radiation
 - Non-steroidal anti-inflammatory drugs (NSAIDS)
 - Opioids
 - Overdoses/Withdrawal
 - Ingestions
 - Metabolic
 - Metastasis
 - Myocardial
-

29

Causes of Nausea & Vomiting

Gastrointestinal (GI)

- Mucosal irritation
 - Mechanical obstruction
 - Motility
 - Medications
-

30

Causes of Nausea & Vomiting

Cerebral Cortex

- Meningeal irritation
- Mental anxiety

31

Causes of Nausea & Vomiting

Vestibular

- Motion sickness
- Medications
 - Opioids

32

Patient Case: Canter

12 year-old male awaiting cardiac transplant

What are possible causes of nausea/vomiting in Canter?

33

Patient Case: Canter

12 year-old male awaiting cardiac transplant

- Possible Causes of Nausea/Vomiting
 - Myocardial
 - Medications
 - Motility
 - Mental anxiety

34

Non-Pharmacological Options

General Non-Pharmacological Options

- Acupressure or acupuncture
- Aroma, massage, music, or pet therapy
- Familiar staff, family, objects, bedding, toys, & photographs available
- Play or distraction
 - Games, storytelling, art projects, television
- Relaxation techniques
 - Guided imagery or biofeedback for children >3 years of age
 - Swaddling or skin-skin contact for infants

Non-Pharmacological Options for Nausea

- Avoid strong odors, foods, or triggers
 - Small, frequent meals chosen by the child
 - Sip liquids slowly
 - Bland food
 - Peppermint
 - Ginger
 - Eliminate offending medications if possible
 - Promote good oral hygiene
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37

Patient Case: Canter

12 year-old male awaiting cardiac transplant

What non-pharmacological therapies would you consider?

38

Patient Case: Canter

12 year-old male awaiting cardiac transplant

- Non-Pharmacological Therapies
 - Acupressure (sea band!)
 - Familiar staff
 - Allow snacks
 - Make goals and use reward charts
 - Relaxation techniques
 - Play & distraction
 - Avoid strong odors
 - Eliminate offending medications if possible
 - Promote good oral hygiene
-

39

Management of Nausea & Vomiting

CTZ Treatment Options

- Butyrophenones
 - haloperidol (Haldol®)
 - Phenothiazines
 - chlorproMAZINE (Thorazine®)
 - prochlorperazine (Compazine®)
 - promethazine (Phenergan®)
 - 5-HT₃ receptor antagonists
 - ondansetron (Zofran®)
 - dolasetron (Anzemet®)
 - granisetron (Kytril®)
 - palonosetron (Aloxi®)
 - Prokinetics
 - metoclopramide (Reglan®)
 - Thienobenzodiazepines
 - OLANZapine (Zyprexa®)
 - Cannabinoids
 - dronabinol (Marinol®)
 - nabilone (Cesamet®)
 - NK-1 receptor antagonists
 - aprepitant (Emend®)
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41

CTZ Treatment Options

Butyrophenones

haloperidol (Haldol®)

- D₂ antagonist
 - Age Restrictions
 - PO: > 3 years
 - IV: > 18 years
 - Side Effects
 - Extrapyramidal symptoms
 - QT prolongation
 - Lowers seizure threshold
 - Dose
 - 0.01-0.1 mg/kg q8h
 - Routes
 - PO, SL, PR, IM, SQ
 - Solution, tablets, injection
-

42

Nausea & Vomiting Management



take note

- haloperidol (Haldol®) not recommended <3 years of age
 - Increased incidence of dystonic reactions in children

43

CTZ Treatment Options

Prokinetic

metoclopramide (Reglan®)

- Prokinetic, D₂ antagonist, & 5-HT₃ antagonist (weak)
- No Age Restriction
- Black Box Warning
 - Tardive dyskinesia
- Contraindication
 - Complete bowel obstruction
- Side Effects
 - Extrapyramidal symptoms, sedation, confusion
- Dose
 - 0.1-0.2 mg/kg q6h
- Routes
 - PO, PR, IV, IM, SQ
 - Solution, tablets, ODT, injection

44

CTZ Treatment Options

5-HT₃ Receptor Antagonist

ondansetron (Zofran®)

- Age Restriction
 - >1 month
- Side Effects
 - Headache, constipation
 - QT prolongation
- Dose
 - 0.1-0.15 mg/kg q6-8h
- Routes
 - PO, SL, PR, IV
 - Solution, tablets, ODT, soluble film, injection

palonosetron (Aloxi®)

- Age Restriction
 - >1 month
- Side Effects
 - Headache, constipation, anxiety
 - QT prolongation
- Dose
 - 20 mCg/kg 30 minutes prior to chemotherapy
- Routes
 - IV
 - Intravenous solution

45

CTZ Treatment Options

Thienobenzodiazepines

OLANzapine (Zyprexa®)

– 5-HT₃ antagonist, antihistamine, dopamine antagonist, antimuscarinic

- Age Restriction
 - >13 years
- Black Box Warning
- Special Alerts
 - Urinary retention, sleep apnea, combination with other CNS depressing drugs
- Side Effects
 - ↑ appetite, abdominal pain, constipation, diarrhea, muscle rigidity, fatigue, ↑ liver enzymes
- Dose
 - 1.25 – 2.5 mg daily
- Routes
 - PO, IM
 - Tablet, orally disintegrating tablet, intramuscular suspension

46

CTZ Treatment Options

Phenothiazines

chlorproMAZINE (Thorazine®)

- Age Restriction
 - >6 months
- Side Effects
 - Extrapyramidal symptoms, sedation, lowers seizure threshold
- Dose
 - 0.5-1 mg/kg q4-6h
- Routes
 - PO, SL, PR, IM, IV
 - Tablets, injection

prochlorperazine (Compazine®)

- Age Restriction
 - >2 years
- Side Effects
 - Extrapyramidal symptoms, sedation, lowers seizure threshold
- Dose
 - 0.1 mg/kg q8h
- Routes
 - PO, PR, IM, IV
 - Tablets, suppositories, injection

47

CTZ Treatment Options

Phenothiazines

promethazine (Phenergan®)

- D₂ antagonist, antihistamine
- Age Restriction
 - >2 years
- Black Box Warning
 - Severe respiratory depression
 - Risk of extravasation with IV administration
- Side Effects
 - Extrapyramidal symptoms, sedation, lowers seizure threshold
- Dose
 - 0.25-1 mg/kg q4-6h
- Routes
 - PO, PR, IM
 - Syrup, tablets, suppositories, injection

48

Nausea & Vomiting Management



take note

- promethazine (Phenergan®) Black Box Warning
 - Severe respiratory depression
 - Severe tissue injury with injection

49

CTZ Treatment Options

Cannabinoids

dronabinol (Marinol®)

- Age Restriction
 - Pediatric age not specified
- Side Effects
 - Euphoria, drowsiness, anxiety, confusion, palpitations, tachycardia, weakness
- Dose
 - 5 mg/m² 1 hour before chemotherapy
- Routes
 - PO
 - Capsule

nabilone (Cesamet®)

- Age Restriction
 - >18 years
- Side Effects
 - Euphoria, hallucinations, headache, anxiety, drowsiness, palpitations, dyspnea, abdominal pain, weakness
- Dose
 - 0.5 - 1 mg q8-12h
- Routes
 - PO
 - Capsule

50

GI Treatment Options

- Prokinetic
 - metoclopramide (Reglan®)
- Antibiotic
 - erythromycin (E-Mycin®)

51

GI Treatment Options

Prokinetics

- metoclopramide (Reglan®)**
- Prokinetic, dopamine antagonist, serotonin agonist
 - No Age Restrictions
 - Black Box Warning
 - Tardive dyskinesia
 - Contraindication
 - Complete bowel obstruction
 - Side Effects
 - Extrapyramidal symptoms
 - Sedation, confusion
 - Dose
 - 0.1-0.2 mg/kg q6h
 - Routes
 - PO, PR, IV, IM, SQ
 - Solution, tablets, ODT, injection

- erythromycin (E-Mycin®)**
- Macrolide antibiotic
 - No Age Restrictions
 - Side Effects
 - Diarrhea
 - Dose
 - 2.5 mg/kg q6h
 - Lower than used for infection
 - Routes
 - PO
 - Suspension, capsules, tablets
 - *Reserved for patients unable to take metoclopramide*

52

Cerebral Cortex Treatment Options

Mental Anxiety

- Benzodiazepines
 - LORazepam (Ativan®)
 - clonazepam (KlonoPIN®)
 - diazepam (Valium®)
 - midazolam (Versed®)

- Antihistamine
 - hydrOXYzine (Atarax®, Vistaril®)

Meningeal Irritation

- Corticosteroids
 - dexamethasone (Decadron®)
 - predniSONE
 - prednisoLONE (Orapred®)

53

Cerebral Cortex Treatment Options

Mental Anxiety

lorazepam (Ativan®)

- Benzodiazepine
- Age Restriction
 - None
- Side Effects
 - Paradoxical reactions
- Dose
 - 0.02-0.05 mg/kg q6h
- Routes
 - PO, SL, PR, IV, SQ
 - Solution, tablets, injection

hydrOXYzine (Atarax®, Vistaril®)

- Antihistamine
- Age Restriction
 - >2 years
- Side Effects
 - Paradoxical excitation, sedation
- Dose
 - 0.5-1 mg/kg q6h
- Routes
 - PO, IM
 - Solution, tablets, capsules, injection

54

Cerebral Cortex Treatment Options

Increased ICP

dexamethasone (Decadron®)

- No Age Restrictions
 - Side Effects
 - Adrenal suppression, Cushing's syndrome, hyperglycemia, immunosuppression, growth suppression, GI bleed, insomnia, fluid retention, mood alterations, myopathy
 - Dose
 - 0.3 mg/kg or 5 mg/m² q6h
 - Routes
 - PO, SL, PR, IM, IV
 - Solution, elixir, concentrate, tablets, injection
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55

Vestibular Treatment Options

- | | |
|--|--|
| <ul style="list-style-type: none"> • Antihistamines <ul style="list-style-type: none"> – dimenhyDRINATE (Dramamine®) – diphenhydrAMINE (Benadryl®) – hydrOXYzine (Atarax®, Vistaril®) – meclizine (Antivert®) – promethazine (Phenergan®) | <ul style="list-style-type: none"> • Anticholinergics <ul style="list-style-type: none"> – dicyclomine (Bentyl®) – glycopyrrolate (Robinul®, Cuvposa®) – hyoscyamine (Levsin®) – scopolamine (Transderm Scop®) |
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56

Nausea & Vomiting Management



take note

- Antihistamines not recommended <2 years of age
 - Serious adverse effects reported
 - Paradoxical excitation

57

Vestibular Treatment Options

Antihistamines

diphenhydrAMINE (Benadryl®)

- Age Restriction
 - >2 years
- Side Effects
 - Paradoxical excitation, constipation, sedation
- Dose
 - 0.5-1 mg/kg q4-6h
- Routes
 - PO, PR, IM, IV
 - Solution, tablets, capsules, orally dissolving strip, ODT, injection

58

Vestibular Treatment Options

Antihistamines

dimenhydrinate (Dramamine®)

- Age Restriction
 - >2 years
- Side Effects
 - Paradoxical excitation, constipation, sedation
- Dose
 - 1.25 mg/kg q6-8h
- Routes
 - PO, IM
 - Tablets, chewable, injection

meclizine (Antivert®)

- Age Restriction
 - >12 years
- Side Effects
 - Paradoxical excitation, constipation, sedation
- Dose
 - 12.5-25 mg q8h
- Routes
 - PO
 - Tablets, chewable

59

Vestibular Treatment Options

Anticholinergics

glycopyrrolate (Cuvposa®, Robinul®)

- No Age Restrictions
- Side Effects
 - Constipation, sedation, confusion, visual disturbances
- Dose
 - PO: 40-100 mcg/kg q6-8h
 - IV: 4-10 mcg/kg q3-4h
- Routes
 - PO, IM, IV, SQ
 - Solution, tablets, injection

hyoscyamine (Levsin®)

- Age Restrictions
 - PO: None
 - IV: > 18 years
- Side Effects
 - Constipation, sedation, confusion, visual disturbances
- Dose
 - <2 years: weight based
 - 2-12 years: 0.0625-0.125 mg
 - >12 years: 0.125-0.25 mg
- Routes
 - Elixir, solution, tablets, ODT, injection

60

Nausea & Vomiting Management



take note

- glycopyrrolate (Cuvposa®, Robinul®) does not cross the blood-brain barrier
 - Least likely to cause side effects
 - Confusion
 - Visual disturbances

61

Vestibular Treatment Options

Anticholinergics

dicyclomine (Bentyl®)

- Age Restriction
 - >6 months
 - Serious adverse reactions
- Side Effects
 - Constipation, sedation, confusion, visual disturbances
- Dose
 - 6 month- 2 years: 5 mg q6-8h
 - >2 years: 10 mg q6-8h
 - Adults: 20 mg q6-8h
- Routes
 - PO, IV
 - Syrup, capsules, tablets, injection

scopolamine (Transderm Scop®)

- Age Restriction
 - >12 years
- Side Effects
 - Constipation, sedation, confusion, visual disturbances
- Dose
 - 1 patch applied behind ear q72h
 - Do not cut patch
- Routes
 - TD
 - Patch

62

Nausea & Vomiting Management

Mechanism	Medication Options*	Drug Class	Receptor	Age Guide
CTZ	metoclopramide (Reglan®)	Prokinetic	D ₂	All ages
	ondansetron (Zofran®)	5-HT ₃ antagonist	5-HT ₃	>6 months
	haloperidol (Haldol®)	Butyrophenone	D ₂	>3 years
GI	metoclopramide (Reglan®)	Prokinetic	5-HT ₄	All ages
Vestibular	promethazine (Phenergan®)	Phenothiazine	H ₁ , D ₂	>2 years
	diphenhydrAMINE (Benadryl®)	Antihistamine	H ₁	>2 years
Cortex-Anxiety	lorazepam (Ativan®)	Benzodiazepine	GABA	All ages
Cortex- ↑ ICP	dexamethasone (Decadron®)	Corticosteroid		All ages

*First line agents

63

Patient Case: Canter

12 year-old male awaiting cardiac transplant

Possible causes of nausea & vomiting:

Causes	Mechanisms	Medications
Myocardial: heart failure	CTZ	Treat underlying disease
Medications: opioids	CTZ	metoclopramide (Reglan®)
		ondansetron (Zofran®)
		olanzapine (Zyprexa®)
Constipation	GI	metoclopramide (Reglan®)
Anxiety	Cortex	lorazepam (Ativan®)

64

Patient Case: Canter

12 year-old male awaiting cardiac transplant

- Management of possible nausea & vomiting in Canter:
 - Non pharmacologic therapy first!
 - Address underlying conditions, if able
 - Chemoreceptor trigger zone
 - Is ondansetron (Zofran®) an option?
 - Consider adding metoclopramide (Reglan®) 2 mg po q6h prn
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65

Refractory Treatment Options

- If initial approach is unsuccessful:
 - Ensure first line medication dose is optimized
 - Reassess to ensure appropriate mechanism is targeted
 - Evaluate appropriateness of
 - Rotating to a different agent based on mechanism
 - How are we providing nutrition?
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66

Summary

- Assess for potential causes of nausea & vomiting
 - Four pathophysiological mechanisms
 - Chemoreceptor Trigger Zone
 - Gastrointestinal Tract
 - Cerebral Cortex
 - Vestibular
 - Choose treatment based on likely mechanism
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67

References

- Hunt MO, Jenkins LS. Nausea and vomiting. In: Hunt MO, Protus BM, Winters JP, Parker DC. *Pediatric Palliative Care Consultant*. Dublin, OH: Hospiscript; 2014:181-192.
 - Baxter AL, Watcha MF, Baxter WV, et al. Development and validation of a pictorial nausea rating scale for children. *Pediatrics*. 2011;127:e1542-e1549.
 - Culy CR, Bhana N, Plosker GL. Ondansetron: a review of its use as an antiemetic in children. *Paediatr Drugs*. 2001; 3(6): 441-479.
 - Di Lorenzo C. Approach to the infant or child with nausea and vomiting. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA 2012.
 - Dupuis LL, Taddio A, Kerr EN, et al. Development and validation of the pediatric nausea assessment tool for use in children receiving antineoplastic agents. *Pharmacotherapy*. 2006;26:1221-1231.
 - Friedrichsdorf SJ, Drake R, Webster ML. Gastrointestinal symptoms. In: Wolfe J, Hinds PS, Sourkes BM, eds. *Textbook of Interdisciplinary Pediatric Palliative Care*. Philadelphia, PA: Saunders; 2011: 311-334.
 - Getto L, Zeserson E, Breyer M. Vomiting, Diarrhea, Constipation, and Gastroenteritis. *Emerg Med Clin N Am* 2011;29:211-237.
 - Hain RDW, Jassal SS. Nausea and vomiting. In: *Paediatric Palliative Medicine*. New York, NY: Oxford; 2010: 89-103.
 - Harris G. FDA panel urges ban on medicine for child colds. *New York Times* 2007 Oct 20.
 - Hernandez CG, Singleton JK, Aronzon DZ. Abdominal pain, vomiting, and diarrhea. In: *Primary Care Pediatrics*. Philadelphia, PA: Lippincott; 2001: 443-467.
-

68

References

- Lexi-Comp Online, Pediatric & Neonatal Lexi-Drugs Online, Hudson, Ohio: Lexi-Comp, Inc; July 23, 2012.
- Phillips RS, Gopaul S, Gibson F, et al. Antiemetic medication for prevention and treatment of chemotherapy induced nausea and vomiting in childhood. *Cochrane Database Syst Rev* 2010;9:CD007786.
- Santucci G, Mack JW. Common gastrointestinal symptoms in pediatric palliative care: nausea, vomiting, constipation, anorexia, cachexia. *Pediatr Clin N Am*. 2007; 54: 673-689.
- Siden HB. Haloperidol as a palliative anti-emetic in a toddler: an evidence based challenge. *J Pain Symptom Manage*. 2008; 35(3):235-238.
- Scorza K, Williams A, Phillips D, et al. Evaluation of Nausea and Vomiting. *Am Fam Physician* 2007;76(1):76-84.
- Sreedharan R, Liacouras CA. Major Symptoms and Signs of Digestive Tract Disorders. In: Kliegman RM, Stanton BF, Gemell JW, et al, editors. *Nelson Textbook of Pediatrics*, 19th ed. Philadelphia: Saunders, c2011. p. 1242-1243.
- Starke PR, Weaver J, Chowdhury BA, et al. Boxed Warning Added to Promethazine Labeling for Pediatric Use. *N Engl J Med* 2005;352:2653.
- Wood GJ, Shega JW, Lynch B, et al. Management of intractable nausea and vomiting in patients at the end of life. *JAMA*. 2007; 298(10): 1196-1207.
- Wrede-Seaman L. Nausea and vomiting. In: *Pediatric Pain and Symptom Management Algorithms for Palliative Care*. China: Intellicard, 2005. Nausea and Vomiting: 50-53.

69



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Constipation

Constipation

- Slow movement of fecal matter through the large intestine
 - Painful passage of dry, hard stools
- Possible presentation
 - Difficulty passing stools
 - Abdominal pain
 - Bloating
 - Flatulence
 - Anorexia
 - Nausea/vomiting
 - Fecal impaction

Stool Frequency Based on Age

Age	Range of Stools/Day	Average Stools/Day
0-3 months		
Breast-fed	1-6	2.9
Formula-fed	1-4	2
6-12 months	1-4	1.8
1-3 years	0-3	1.4
>3 years	0-2	1

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Evaluation and Treatment of Constipation in Children: Summary of Updated Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr.* 2006;43(3):405-7.
 Baker SS, Liptak GS, Colletti RB, et al. Constipation in Infants and Children: Evaluation and Treatment. A Medical Position Statement of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 1999;29(5):612-26.

73

Possible Causes of Constipation

Causes	Examples
Behavioral	Inactivity due to illness or treatment, fear of stool passage due to pain or "functional withholding"
Dehydration	Decreased fluid, food intake, or abnormal feeding patterns
Diseases	celiac disease, cystic fibrosis, Hirschsprung disease, inflammatory bowel disease, muscular dystrophy, systemic lupus erythematosus
Medications	5HT ₃ antagonists, anticholinergics, anticonvulsants, benzodiazepines, chemotherapy, H ₂ receptor antagonists, iron, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, phenothiazines, proton pump inhibitors (PPIs), tricyclic antidepressants (TCAs)
Metabolic	hypercalcemia, hypokalemia, hypothyroidism
Neurologic	damage to nerve pathways and musculature secondary to neurodegenerative disease
Tumors	Intra-abdominal tumors (direct compression on the gut or spinal cord)

Hunt MO, Jenkins LS. Constipation. In: Hunt MO, Protus BM, Winters JP, Parker DC. *Pediatric Palliative Care Consultant*. Dublin, OH: HospiScript; 2014:67-75.

74

Patient Case: Canter

12 year-old male awaiting cardiac transplant

What are possible causes of constipation in Canter?

75

Patient Case: Canter

12 year-old male awaiting cardiac transplant

- Possible Causes of Constipation
 - Behavioral
 - Dehydration
 - Medications








76

Constipation Assessment

Assessment of Constipation

- Bowel habits
 - Usual, current, last bowel movement
 - Change in consistency, color, size, odor
 - Description of quality type, texture, size, presence of blood, odor, painful
- Dietary habits and fluid intake
- Mobility
- Metabolic abnormalities
- Medication history
 - Contributing medications
 - Previously tried successful or unsuccessful therapies
- Physical exam

Bristol Stool Scale

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol* 1997;32(9):920-4.

79

Non-Pharmacological
Options

Non-Pharmacological Options

- Regular bowel routine
 - Increase activity
 - Increase fluid intake
 - Increase dietary fiber
 - Abdominal massage
 - Clockwise fashion
 - Rectal stimulation
 - Self-hypnosis
 - Biofeedback
 - Cognitive-behavioral therapy
-

81

Dietary Fiber Sources

- Whole-grain cereals
- Fruits
 - Apples, apricots, dates, figs, peaches, pears, plums, prunes, or raisins
- Vegetables
 - Beans, broccoli, cabbage, carrots, cauliflower, celery, or peas
- Fruit juice
 - Apple, pear, or prune juice
- Power pudding
- Fruit paste

Wrede-Seaman L. Pediatric Pain and Symptom Management Algorithms for Palliative Care. China: Intellicard, c2005. Constipation, p. 22-25.
Gibson C, Opalka P, Moore C, et al. Effectiveness of bran supplement on the bowel management of elderly rehabilitation patients. J Gerontological Nurs 1995;21(20):21-30.

82

Patient Case: Canter

12 year-old male awaiting cardiac transplant

What possible non-pharmacological options can we recommend for treatment of constipation?

83

Patient Case: Canter

12 year-old male awaiting cardiac transplant

- Non-Pharmacological Options:
 - Increase fluid intake, as clinically appropriate based on condition
 - Discuss with nutrition
 - Activity
 - Massage or PT/OT consult
 - Encourage routine

84

Management of Constipation

Pharmacotherapy Options

- Stool softeners
- Osmotic laxatives
- Stimulant laxatives
- Prokinetic agents

Constipation Management



take note

- Consider prophylactic treatment in patients on scheduled opioids
 - Stool softener
 - Stimulant laxative

87

Stool Softeners

- docusate (Colace®)
- glycerin

88

Stool Softener Options

glycerin

- No Age Restrictions
- Side Effects
 - Abdominal pain, rectal irritation
- Dose
 - 1 suppository bid prn
 - Tip or chip of suppository may be adequate
- Routes
 - PR
 - Suppository, solution
 - Pediatric & adult suppositories

docusate (Colace®)

- No Age Restrictions
- Side Effects
 - Abdominal cramping, nausea, diarrhea, intestinal obstruction
- Dose
 - 5 mg/kg/day divided q6h – q24h
- Routes
 - PO, PR
 - Liquid, capsules, enema
- *Use with adequate fluid to maximize benefit*

89

Constipation Management



take note

- Rectal stimulation alone is often adequate in infants
 - Glycerin suppositories are first line in infants
 - Avoid stimulants and enemas in infants
 - Avoid stimulants and enemas in neutropenic and/or thrombocytopenic oncology patients

90

Osmotic Laxatives

- lactulose (Generlac®)
 - magnesium citrate (Citroma®)
 - magnesium hydroxide (Milk of Magnesia®)
 - polyethylene glycol (MiraLAX®)
 - sodium phosphates (Fleet Enema®)
 - sorbitol
-

91

Osmotic Options

polyethylene glycol (MiraLAX®)

- Age Restrictions
 - >17 years
 - Warning
 - Reports of metabolic acidosis and neuropsychiatric adverse events
 - Side Effects
 - Abdominal bloating, cramping, nausea, diarrhea, flatulence
 - Dose
 - 0.5 – 1.5 g/kg/day
 - 17 g dose can be measured using bottle cap
 - Add to 4-8 ounces of beverage
 - Routes
 - PO
 - Powder for solution
-

92

Constipation Management



take note

- Polyethylene glycol (MiraLAX®) pediatric warning
 - Long-term effects unknown
 - Reports of metabolic acidosis
 - Reports of neuropsychiatric events
 - Seizures, tremors, tics, headache, anxiety, lethargy, sedation, aggression, rages, obsessive-compulsive behaviors, paranoia, mood swings

93

Osmotic Options

lactulose (Generlac®)

- No Age Restrictions
- Warning
 - Hyponatremia & dehydration in infants
- Contraindication
 - Galactose-restricted diet
- Side Effects
 - Abdominal pain, bloating, nausea, diarrhea
- Dose
 - 0.7 – 2 g/kg/day in divided doses
- Routes
 - PO, PR
 - Solution, crystals for solution

sorbitol

- Age Restrictions
 - >2 years
- Contraindication
 - Anuria
- Side Effects
 - Abdominal pain, bloating, nausea, diarrhea, xerostomia
- Dose
 - 2 mL/kg at infrequent intervals
- Routes
 - PO, PR
 - Solution
 - Dilute for rectal administration

94

Stimulant Laxatives

- bisacodyl (Dulcolax®)
 - senna (Senokot®)
-

95

Stimulant Options

senna (Senokot®)

- Age Restrictions
 - >2 years
 - Side Effects
 - Abdominal pain, bloating, nausea, diarrhea
 - May discolor urine (red/brown) or feces
 - Dose
 - 2 – 6 years: 4.4 – 6.6 mg q24h
 - 6 – 11 years: 8.8 – 13.2 mg q24h
 - >12 years: 17.6 – 26.4 mg q24h
 - Routes
 - PO, PR
 - Liquid, tablets, chewable, ODT
-

bisacodyl (Dulcolax®)

- Age Restrictions
 - >6 years
 - Side Effects
 - Abdominal pain, cramping, nausea
 - Dose
 - 5 - 15 mg q24h
 - Routes
 - PO, PR
 - Tablets (IR, EC, DR), suppository, enema
-

96

Constipation Management



take note

- Stimulant laxatives not recommended in children <2 years of age

97

Prokinetic Agents

- erythromycin (E-Mycin[®])
- metoclopramide (Reglan[®])
- amoxicillin/clavulanate (Augmentin[®])

98

Prokinetic Options

metoclopramide (Reglan®)

– Prokinetic, dopamine antagonist, serotonin agonist

- No Age Restrictions
- Black Box Warning
 - Tardive dyskinesia
- Contraindication
 - Complete bowel obstruction
- Side Effects
 - Extrapyrimalidal symptoms
 - Sedation, confusion
- Dose
 - 0.1-0.2 mg/kg q6h
- Routes
 - PO, PR, IV, IM, SQ
 - Solution, tablets, ODT, injection

erythromycin (E-Mycin®)

– Macrolide antibiotic

- No Age Restrictions
- Side Effects
 - Diarrhea
- Dose
 - 2.5 mg/kg q6h
 - Lower than used for infection
- Routes
 - PO
 - Suspension, capsules, tablets
- *Reserved for patients unable to take metoclopramide*

99

Constipation Management



take note

- Use suppositories and enemas with caution in neutropenic or thrombocytopenic patients

100

Patient Case: Canter

12 year-old male awaiting cardiac transplant

How would you manage constipation in Canter?

101

Patient Case: Canter

12 year-old male awaiting cardiac transplant

- Current therapy:
 - None
- Possible therapy:
 - polyethylene glycol (Miralax®) 8.5 grams po BID
 - *Will he take it?*
 - Consider senna 4.4 mg po qday

102

Summary

- Stool frequency varies greatly by patient
 - Monitor constipation based on change in frequency or consistency
 - Initiate dietary and non-pharmacological interventions prior to medications
 - Consider prophylactic therapy in patients receiving opioids
 - Stool softener
 - Stimulant
 - Osmotic laxatives are often considered first-line in pediatric patients
 - May be difficult to establish effective dose
 - May not be beneficial in patients with neuromuscular conditions or receiving opioids
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103

References

- Hain RDW, Jassal SS. Paediatric Palliative Medicine. New York: Oxford; c2010. Chapter 10, Constipation; p. 106-109.
 - Culbert TP, Banez GA. Integrative Approaches to Childhood Constipation and Encopresis. *Pediatr Clin N Am* 2007;54:927-47.
 - PL Detail-Document, Treatment of Constipation in Children. Pharmacist's Letter/Prescriber's Letter. February 2012.
 - North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Evaluation and Treatment of Constipation in Children: Summary of Updated Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr.* 2006;43(3):405-7.
 - Baker SS, Liptak GS, Colletti RB, et al. Constipation in Infants and Children: Evaluation and Treatment. A Medical Position Statement of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 1999;29(5):612-26.
 - Friedrichsdorf SJ, Drake R, Webster ML. Chapter 33, Gastrointestinal Symptoms. In: Wolfe J, Hinds PS, Sourkes BM, editors. Textbook of Interdisciplinary Pediatric Palliative Care. Philadelphia: Saunders; c2011. p. 311-34.
 - Santucci G, Mack JW. Common Gastrointestinal Symptoms in Pediatric Palliative Care: Nausea, Vomiting, Constipation, Anorexia, Cachexia. *Pediatr Clin N Am* 2007; 54: 673-689.
 - Sreedharan R, Liacouras CA. Major Symptoms and Signs of Digestive Tract Disorders. In: Kliegman RM, Stanton BF, Gemell JW, et al, editors. Nelson Textbook of Pediatrics, 19th ed. Philadelphia: Saunders, c2011. p.1242-3.
 - Feinberg AN, Feinberg LA, Atay OK. Gastrointestinal Care of Children and Adolescents with Developmental Disabilities. *Pediatr Clin N Am* 2008;55:1343-58.
 - Sandowski S, Jackson RM. Chapter 38, Abdominal Pain, Vomiting and Diarrhea. In: Hernandez CG, Singleton JK, Aronzon DZ. Primary Care Pediatrics. Philadelphia: Lippincott; c2001. p. 448-449.
-

104

References

- Getto L, Zeserson E, Breyer M. Vomiting, Diarrhea, Constipation, and Gastroenteritis. *Emerg Med Clin N Am* 2011;29:211-37.
- Wrede-Seaman L. Pediatric Pain and Symptom Management Algorithms for Palliative Care. China: Intellicard, c2005. Constipation, p. 22-25.
- Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol* 1997;32(9):920-4.
- Gibson C, Opalka P, Moore C, et al. Effectiveness of bran supplement on the bowel management of elderly rehabilitation patients. *J Gerontological Nurs* 1995;21(20):21-30.
- Bell EA, Wall GC. Pediatric Constipation Therapy Using Guidelines and Polyethylene Glycol 3350. *Ann Pharmacother* 2004;38(4):686-93.
- Gremse DA, Hixon J, Crutchfield A. Comparison of polyethylene glycol 3350 and lactulose for treatment of chronic constipation in children. *Clin Pediatr (Phila)* 2002; 41(4):225-229.
- Pashankar DS, Bishop WP, Loening-Baucke V. Long-term efficacy of polyethylene glycol 3350 for the treatment of chronic constipation in children with and without encopresis. *Clin Pediatr (Phila)* 2003; 42(9):815-819.
- Nurko S, Youssef NN, Sabri M, et al. PEG3350 in the Treatment of Childhood Constipation: A Multicenter, Double-Blinded, Placebo-Controlled Trial. *J Pediatr* 2008;153(2):254-61.
- Youssef NN, Peters JM, Henderson W, et al. Dose Response of PEG 3350 for the Treatment of Childhood Fecal Impaction. *J Pediatr*. 2002;141(3):410-4.
- Loening-Baucke V, Krishna R, Pashankar DS. Polyethylene Glycol 3350 Without Electrolytes for the Treatment of Functional Constipation in Infants and Toddlers. *J Pediatr Gastroenterol Nutr* 2004;39(5):536-9.

105

References

- Michail S, Gendy E, Preud'Homme D, et al. Polyethylene Glycol for Constipation in Children Younger Than Eighteen Months Old. *J Pediatr Gastroenterol Nutr* 2004;39(2):197-9.
- DS, Loening-Baucke V, Bishop WP. Safety of Polyethylene Glycol 3350 for the Treatment of Chronic Constipation in Children. *Arch Pediatr Adolesc Med* 2003;157(7):661-4.
- Voskuil W, de Lorijn F, Verwijs W, et al. PEG 3350 (Transipeg) Versus Lactulose in the Treatment of Childhood Functional Constipation: A Double Blind, Randomised, Controlled, Multicentre Trial. *Gut* 2004;53(11):1590-4.
- Lexi-Comp Online, Pediatric & Neonatal Lexi-Drugs Online, Hudson, Ohio: Lexi-Comp, Inc; September 17, 2012.
- Sondheimer JM, Gervaise EP. Lubricant versus laxative in the treatment of chronic functional constipation of children: a comparative study. *J Pediatr Gastroenterol Nutr* 1982; 1(2):223-226.
- Zanetti G, Marchiori E, Gasparetto TD, et al. Lipoid pneumonia in children following aspiration of mineral oil used in the treatment of constipation: high-resolution CT findings in 17 patients. *Pediatr Radiol* 2007;37:1135-39.
- Marchiori E, Zanetti G, Mano CM, et al. Lipoid pneumonia in 53 patients after aspiration of mineral oil: comparison of high-resolution computed tomography findings in adults and children. *J Comput Assist Tomogr* 2010;34(1):9-12.
- Charney EB, Bodurtha JN. Intractable Diarrhea Associated With the Use of Sorbitol. *J Pediatr* 1981;98(1):157-8.
- Hawley PH, Byeon JJ. A comparison of sennosides-based bowel protocols with and without docusate in hospitalized patients with cancer. *J Palliat Med* 2008; 11(4):575-581.
- Bellomo-Brandao MA, Collares EF, da-Costa-Pinto EA. Use of erythromycin for the treatment of severe chronic constipation in children. *Braz J Med Biol Res* 2003; 36(10):1391-1396.
- Loening-Baucke V. Prevalence, Symptoms and Outcome of Constipation in Infants and Toddlers. *J Pediatr* 2005;146(3):359-63.

106



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