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Constipation and GI diagnoses in children with solid tumours: prevalence and management

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ABSTRACT

Objectives Despite continued development of targeted therapies for children with cancer, patients continue to experience an array of unwanted side effects. Children with solid tumours may experience constipation as a result of vinca alkaloid therapy, psychological stressors, periods of inactivity and opioid use. Our objective was to investigate the prevalence and treatment of constipation in hospitalised children with solid tumours treated with chemotherapy.

Methods We retrospectively analysed data from 48 children's hospitals in the Pediatric Health Information System, extracting patients 0–21 years of age with a solid tumour diagnosis hospitalised from October 2015 through December 2019.

Results We identified 13 375 unique patients with a solid tumour diagnosis receiving chemotherapy. Constipation was the most common gastrointestinal complaint with 8658 (64.7%; 95% CI: 63.9% to 65.5%) having a constipation diagnosis or having received at least two laxatives during admission. Bone cancers had the highest percentage (69.9%) of patients with constipation, while Hodgkin's lymphoma had the lowest, although 52.1% of patients were affected. A total of 44% (n=35 301) of encounters received an opioid at some point during admission. Of patients receiving constipation medications, the most commonly prescribed was polyethyl glycol (n=25 175, 31.7%), followed by docusate (n=11 297, 14.2%), senna (n=10 325, 13.0%) and lactulose (n=5501, 6.9%).

Conclusions Constipation is the most common gastrointestinal issue that children with solid tumours experience while receiving chemotherapy in the inpatient setting. Increased attention should be given to constipation prophylaxis and treatment in children with solid tumours undergoing chemotherapy, particularly those identified as high risk.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Constipation in the paediatric population is common.
⇒ Constipation in oncology is multifactorial.

WHAT THIS STUDY ADDS

⇒ Children with solid tumours receiving chemotherapy suffer from constipation.
⇒ There is no standard-of-care constipation treatment in paediatric oncology.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Attention to populations most at risk would result in proactive constipation management leading to increased survival.
⇒ Clinical practice guidelines for constipation supportive care are missing in paediatric oncology.

INTRODUCTION

Childhood cancer remains the second leading cause of death in children aged 5 to 14 years.[1] The most common diagnoses in the USA include leukaemias, central nervous system (CNS) tumours and lymphomas along with a variety of other solid tumors.[2] Children with cancer undergoing treatment suffer a litany of unwanted side effects during and after their therapy. While survival rates continue to improve with the incorporation of immunotherapy and targeted therapy, many CNS and non-CNS solid tumour treatments continue to rely on traditional cytotoxic and radiotherapy-based treatment agents. Chemotherapy-induced constipation (CIC) has been well studied in the adult oncology literature and is the third most common unwanted side effect in patients receiving cytotoxic chemotherapy, with 50%–87% of patients experiencing CIC.[3] Vinca alkaloids are a common cause of constipation, with 80%–90% of adult oncology patients receiving them reporting CIC.[4] While

data exist for constipation in the general paediatric population, no studies have explored constipation burden or sequela in children with solid tumours. In addition, literature has not investigated the use of preemptive constipation management during treatment for children receiving chemotherapy.

Constipation accounts for 3% of general paediatric outpatient visits and 25% of paediatric gastrointestinal (GI) specialist visits in the USA.[5] Children with constipation suffer from an array of physical symptoms including abdominal pain, cramping, faecal incontinence, rectal fissures, enuresis and urinary tract infections.[6] In children without cancer, functional constipation has an increased healthcare burden compared with children without constipation. Treatment can be challenging in otherwise healthy children but creates unique challenges for the child undergoing cancer treatment. Constipation management uses both pharmacological and non-pharmacological interventions to improve symptoms.[4] Non-pharmacological interventions, such as increased activity and hydration, may be difficult for children with cancer to adhere to due to nausea, mucositis, anorexia, fatigue or other treatment effects. In addition, some supportive care interventions, including total parenteral nutrition (TPN), have demonstrated an increased risk of developing constipation.[7] Despite ongoing advancements in the paediatric oncology field, there remains a lack of guidance for oncology teams with regard to constipation management.

Literature is bereft of studies investigating the incidence and management of constipation in paediatric oncology patients. A prospective questionnaire from 2011 estimated that 57%–77% of children requiring chemotherapy treatment for an oncology diagnosis experienced constipation, as defined by the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition Criteria.[8] Constipation is the most common GI diagnosis during acute lymphoblastic leukaemia (ALL) induction therapy affecting 34% of children, and demonstrating a higher prevalence in females, those with extended hospital stays and patients receiving opioids. In addition, a wide variety of constipation medications were identified, with 81% of patients receiving at least one laxative during induction.[9] Most children receiving chemotherapy for a solid tumour diagnosis undergo multiple extended hospital admissions, may require surgical resections impairing mobility and often receive adjunct radiation therapy. In addition, side effects including mucositis resulting in dehydration and pain control can predispose patients to constipation.

Despite ongoing advancements in the paediatric oncology field, there remains a lack of guidance with regard to constipation management. The objective of our study was to use a national administrative database to describe the prevalence of constipation, GI diagnoses and variability of inpatient management, and investigate potential risk factors associated with constipation during hospitalisations for paediatric patients with solid tumours in the USA.

METHODS

Data source

Data for this retrospective multicentre cohort study were obtained from the Pediatric Hospital Information System (PHIS) database. Managed by the Children's Hospital Association (CHA) (Overland Park, Kansas), the PHIS database provides detailed information about hospital-based discharges from 48 of the largest free-standing children's hospitals across the USA. The participating institutions represent all US census geographical regions and the majority of US tertiary care paediatric hospitals. Reliability and validity are continuously assured by data quality assessments from both CHA and participating institutions. Patient data are deidentified and given a unique patient identification number, thus allowing patients to be tracked over time and across multiple admissions.

Study population

Our study population included patients aged 0 to 21 years with a solid tumour diagnosis admitted to the hospital between October 2015 and December 2019. To ensure patients were receiving chemotherapy for an active solid tumour malignancy, patients were required to have an ICD-10-CM diagnosis code for a solid tumour and a billing code for a central line supply code, chemotherapy administration procedural code or a chemotherapy medication code at any point during the study time period. Solid cancers of interest were grouped by organ system and included CNS, bone, liver/biliary, kidney, retinal, non-specific abdominal/pelvic and non-specific adrenal tumours, and the remaining diagnoses, including soft-tissue sarcomas, were classified as other solid tumours. Hodgkin's and non-Hodgkin's lymphomas (NHLs) were also identified (online supplemental file 1). Patients with cancer diagnoses in multiple cancer groups were excluded.

Study definitions

Previously published methods were used for consistency.[9] ICD-10-CM codes were used to identify diagnoses of constipation (K59.XX) and other GI diagnoses, such as appendicitis, gastritis and ulcers; and GI symptoms, such as nausea and abdominal pain (online supplemental file 1). Billing codes were used to identify the receipt of chemotherapy agents, opioids and constipation medications, as well as operating room (OR) and total parenteral nutrition (TPN) charges. Patients who lacked a diagnosis code of constipation but received at least two unique constipation medications were also defined as a case of constipation. Dates of medication administration were extracted to calculate the start and duration of medication use. To evaluate the possible effect of opioid use on the risk

of constipation during the admission, we categorised patients into four groups to best distinguish opioid use between anaesthesia and pain: (1) no occurrences of opioid use, (2) patient received fentanyl only, (3) patient received other, non-fentanyl opioids for 1 or 2 days, and (4) patient received ≥2 days of other, non-fentanyl opioids.

Demographic information, such as patient sex, race and geographical region, and hospitalisation information, including length of stay, intensive care utilisation and mortality, was also obtained from the PHIS database. Patient age was calculated as the age at their last encounter during the study period.

Statistical analysis

All data were summarised using descriptive statistics. Median and range were used to describe quantitative variables and frequency and percentage were used for qualitative variables. The prevalence of constipation among all solid cancers (as well as in specific cancer groups) was calculated as a percentage. The management of constipation was summarised descriptively. Univariate comparisons between those with and without constipation were performed using χ^2 tests for qualitative variables and Wilcoxon rank-sum tests for quantitative variables. Statistical significance was determined by p value <0.05. Statistical analyses were performed using Statistical Analysis System software V.9.4 (SAS Institute, Cary, NC).

RESULTS

Demographics

We identified 13 375 unique patients (79 530 unique admissions) who were admitted with a solid tumour diagnosis from 48 PHIS hospitals during the 4-year period evaluated (table 1).

The majority of patients were male (n=7465, 55.8%) with a median age of 9.3 years (range: 0.0–21.9 years). CNS cancers were the most commonly identified solid tumour group (24.4%), followed by NHL (14.4%), bone (12.9%), Hodgkin's lymphoma (10.2%), kidney (8.3%), abdomen/pelvis (6.8%), adrenal (6.7%), liver/biliary (5.1%) and retinal (2.8%). Solid tumours of other organ systems and soft-tissue sarcomas that are not specified here accounted for 8.3% of the cohort (online supplemental file 1).

Table 1 Demographics and clinical characteristics of paediatric patients with solid tumours (Pediatric Hospital Information System, 2015–2019)

Characteristic	N (%)
Unique patients	13 375
Male sex	7465 (55.8)
Race	
White	8550 (63.9)
Black	1757 (13.1)
Asian	605 (4.5)
Other/unknown	2463 (18.4)
Age at first encounter (years)	
<1	1007 (7.5)
1–4	3374 (25.2)
5–12	4307 (32.2)
13–17	3732 (27.9)
≥18	955 (7.1)
Solid cancer diagnosis	
CNS	3264 (24.4)
Bone	1730 (12.9)
Lymphoma	
Hodgkin's	1365 (10.2)
Non-Hodgkin's	1925 (14.4)
Liver/biliary	686 (5.1)
Kidney	1111 (8.3)
Retinal	378 (2.8)
Abdominal/pelvic NOS	910 (6.8)
Adrenal tumours NOS	896 (6.7)
Other solid tumours*	1110 (8.3)

*Includes other solid tumours/masses of other organ systems not listed.
CNS, central nervous system; NOS, not otherwise specified.

Prevalence of constipation and GI diagnoses

Constipation was the most common GI complaint identified in patients with unique solid tumour, with 8658 (64.7%) being diagnosed with constipation or receiving at least two constipation medications during any single admission (table 2).

Bone cancers had the highest prevalence (79.7%) of patients with constipation, while retinal tumours had the lowest at 23.3% (figure 1). Nausea/vomiting (n=5439, 48.6%) and abdominal pain (n=1044, 9.3%) were the next most commonly observed GI diagnoses. Other GI symptoms commonly reported in patients with solid cancer included mucositis (n=3017, 26.9%) and gastro-oesophageal reflux disease (n=1419, 12.7%). Mucositis was most common in patients with NHL (42.7%), bone cancers (41.7) and adrenal tumours (38.5%), and least commonly seen in kidney (10.4%) and abdominal/pelvic (10.2%) tumours. GI infections were present in all diagnoses, with adrenal tumours (n=195, 21.8%) having the most, and patients with Hodgkin's lymphoma (n=101, 7.4%) with the fewest reported GI infections.

Characteristics of admissions with a diagnosis of constipation

Inpatient admissions with constipation were more likely to be female (n=23 420, 57.3%) and/or use a narcotic (n=14 044, 56.8%) (table 3).

In addition, admissions with a diagnosis of constipation were more likely to have OR charges (56.8% vs 39.9%; p<0.0001), TPN use (10.5% vs 6.7%; p<0.0001) and abdominal/pelvic imaging compared with admissions without constipation.

Table 2 Patient prevalence of most commonly identified solid tumour diagnoses with various GI diagnoses (Pediatric Hospital Information System, 2015–2019)

Diagnosis	All solid tumours N (%)	CNS cancers N (%)	Bone cancers N (%)	Kidney N (%)	Abd/pelvic N (%)	Adrenal tumours N (%)	HL N (%)	NHL N (%)
Total patients		3264	1730	1111	910	896	1365	1925
Defined constipation*	8658 (64.7)	2281 (69.9)	1379 (79.7)	734 (66.1)	547 (60.1)	508 (56.7)	711 (52.1)	1307 (67.9)
Constipation (Dx only)	6477 (48.4)	1583 (48.5)	1143 (66.1)	515 (46.4)	419 (46.0)	422 (47.1)	536 (39.3)	984 (51.1)
GI symptoms								
Abdominal pain	1185 (8.9)	255 (7.8)	182 (10.5)	86 (7.7)	86 (9.5)	101 (11.3)	104 (7.6)	230 (12.0)
Nausea/vomiting	6423 (48.0)	1440 (44.1)	1204 (69.6)	367 (33.0)	412 (45.3)	445 (49.7)	646 (47.3)	925 (48.1)
Other GI diagnoses								
GORD	1587 (11.9)	415 (12.7)	271 (15.7)	66 (5.9)	90 (9.9)	103 (11.5)	121 (8.9)	254 (13.2)
Ulcer	96 (0.7)	29 (0.9)	9 (0.5)	0 (-)	10 (1.1)	4 (0.5)	8 (0.6)	27 (1.4)
Gastritis	1568 (11.7)	302 (9.3)	232 (13.4)	75 (6.8)	86 (9.5)	163 (18.2)	165 (12.1)	319 (16.6)
Appendicitis	221 (1.7)	36 (1.1)	32 (1.9)	11 (1.0)	6 (0.7)	22 (2.5)	24 (1.8)	68 (3.5)
IBD	62 (0.5)	8 (0.3)	5 (0.3)	4 (0.4)	4 (0.4)	2 (0.2)	8 (0.6)	26 (1.4)
IBS	25 (0.2)	6 (0.2)	8 (0.5)	0 (–)	3 (0.3)	0 (–)	1 (<0.1)	7 (0.4)
NEC	6 (<0.1)	2 (<0.1)	0 (–)	0 (–)	0 (–)	1 (0.1)	1 (<0.1)	0 (–)
Pancreatic issues	245 (1.8)	31 (1.0)	12 (0.7)	12 (1.1)	32 (3.5)	12 (1.3)	8 (0.6)	115 (6.0)
Gallbladder issues	237 (1.8)	11 (0.3)	11 (0.6)	9 (0.8)	29 (3.2)	14 (1.6)	11 (0.8)	51 (2.7)
Anal/rectal issues	751 (5.6)	119 (3.7)	254 (14.7)	25 (2.3)	39 (4.3)	37 (4.1)	56 (4.1)	149 (7.7)
Peritonitis	362 (2.7)	30 (0.9)	6 (0.4)	78 (7.0)	64 (7.0)	29 (3.2)	3 (0.2)	55 (2.9)
Mucositis	3436 (25.7)	551 (16.9)	722 (41.7)	116 (10.4)	93 (10.2)	345 (38.5)	369 (27.0)	821 (42.7)
GI infection	1650 (12.3)	414 (12.7)	210 (12.1)	118 (10.6)	76 (8.4)	195 (21.8)	101 (7.4)	305 (15.8)

*Administration of constipation medications without the presence of a constipation diagnosis.

Abd, abdominal; CNS, central nervous system; GI, gastrointestinal; GORD, gastro-oesophageal reflux disease; HL, Hodgkin's lymphoma; IBD, irritable bowel disease; IBS, irritable bowel syndrome; NEC, necrotising enterocolitis; NHL, non-Hodgkin's lymphoma.

Constipation management and opioid use

A constipation medication was administered in 45.8% (n=36 444) of all admissions (table 4). Among admissions with constipation, 50.2% received at least one opioid, whereas 43.8% of admissions without constipation received at least one opioid.

These medications were used in the setting of a constipation diagnosis in 73.1% (n=11 912) of admissions, while 38.8% (n=24 532) of admissions used a constipation medication without the presence of a constipation diagnosis code. Among admissions with a constipation diagnosis, 21.9% (n=3568) required two different constipation medications, with 18.2% of admissions requiring three or more unique constipation medications. In admissions without the presence of a constipation diagnosis, a single agent was used 24.1% of the time, whereas 13.3% (n=8413) received a combination of two or more different medications. The most commonly used constipation medication, regardless of the presence of a constipation diagnosis, was polyethyl glycol (n=25 175, 31.7%), followed by docusate (n=11 297, 14.2%), senna (n=10 325, 13.0%) and lactulose (n=5501, 6.9%). These medications were used for a median of 2 to 3 days. A total of 45% (n=35 903) of encounters received an opioid at some point during an admission: 4.5% (n=3598) received fentanyl only, 15.2% (12 068) received ≤2 days of a non-fentanyl opioid and 25.4% (n=20 237) received >2 days of a non-fentanyl opioid. The extended use of non-fentanyl opioids (>2 days) was more common in admissions with a constipation diagnosis compared with those without a constipation diagnosis (33.1% vs 23.5%; p<0.0001). Constipation management and opioid use in specific solid tumour diagnoses are detailed in online supplemental files 2 and 3.

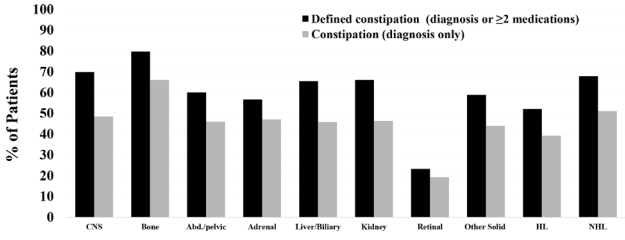

Figure 1 Prevalence of constipation among hospitalised patients with solid cancers. Abd, abdominal; CNS, central nervous system; HL, Hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma.

DISCUSSION

We identified 13 375 unique patients with 79 530 unique admissions in this study of paediatric patients with solid tumours admitted at 48 children's hospitals. A majority of children received constipation medications regardless

Table 3 Characteristics of paediatric patients with solid tumour admissions with constipation

	Constipation admits N=24 719	No constipation N=54 811	P value
Median age (IQR)	10.6 (5.0–15.5)	10.1 (4.1–15.1)	<0.0001
Age at admit (years)			<0.0001
<1	504 (2.0)	2733 (5.0)	
1–4	5712 (23.1)	13 373 (24.4)	
5–12	8901 (36.0)	18 730 (34.2)	
13–17	7221 (29.2)	15 708 (28.7)	
≥18	2381 (9.6)	4267 (7.8)	
Male sex	13 358 (54.0)	31 391 (57.3)	<0.0001
Race			<0.0001
White	15 991 (64.7)	35 070 (64.0)	
Black	3180 (12.9)	6678 (12.2)	
Asian	1157 (4.7)	2635 (4.8)	
Other	4391 (17.8)	10 428 (19.0)	
Ethnicity			<0.0001
Hispanic/Latino	5263 (21.3)	11 504 (21.0)	
Non-Hispanic/Latino	18 284 (74.0)	40 254 (73.4)	
Other/unknown	1172 (4.7)	3053 (5.6)	
Median LOS (IQR)	5 (3–10)	3 (2–5)	<0.0001
Insurance type			0.0002
Public	11 347 (45.9)	25 177 (45.9)	
Private	11 912 (48.2)	26 165 (47.7)	
Other	882 (3.6)	2293 (4.2)	
Unknown	578 (2.3)	1176 (2.2)	
Use of narcotic	14 044 (56.8)	21 859 (39.9)	<0.0001
OR charges	7236 (29.3)	10 240 (18.7)	<0.0001
TPN	2592 (10.5)	3661 (6.7)	<0.0001
Abdominal/pelvic imaging			
US	2044 (8.3)	2209 (4.0)	<0.0001
CT	2999 (12.1)	3385 (6.2)	<0.0001
MRI	741 (3.0)	800 (1.5)	<0.0001
X-Ray	4517 (18.3)	4014 (7.3)	<0.0001

LOS, length of stay; OR, operating room; TPN, total parental nutrition; US, ultrasound.

of having a billed diagnosis or not. The prevalence of constipation identified in our study (64.7%) is impressively greater than the prevalence reported in the general paediatric population (ranging from 0.7% to 29%[10 11]).

For unclear reasons, paediatric females have been demonstrated to have a higher prevalence of constipation than males in healthy children and the paediatric ALL patient population.[9 12] Similarly, our data demonstrated that females with solid tumours are at higher risk for experiencing constipation during hospitalisation. In addition, our finding that opioids are associated with constipation has been well studied in adult and paediatric cancer literature.[13] Opioids lead to constipation through their action on opioid receptors in the GI tract, leading to reduced GI propulsion and increased fluid absorption.[13] Unfortunately, opioids are commonly a necessity for cancer-related visceral or bone pain. In addition, patients with solid tumours can undergo surgical interventions for tumour, staging or central line placement, involving anaesthesia and post-procedure pain control. Certain immunotherapies, such as dinutuximab in patients with neuroblastoma, may require continuous intravenous pain medications, leading to prolonged opioid use. Non-Hodgkin's lymphoma treatment is notoriously intense and can often result in prolonged mucositis resulting in lengthy opioid use for pain control, which likely correlates with the high rates of constipation we identified. Similarly to patients with ALL in induction, we demonstrated a wide variability in constipation medications prescribed, regardless of a constipation diagnosis, further evidence of the lack of standard practice on how to manage constipation in the paediatric oncology setting.[9]

Previous studies have shown that children with a constipation diagnosis have a significant increase in healthcare utilisation compared with children without constipation.[14] Although constipation in healthy children develops insidiously over time and fortunately is almost always secondary to functional constipation, paediatric oncology patients have psychological stressors as a result of their diagnosis and receive chemotherapy and other

Table 4 Constipation medical management and opioid utilisation in paediatric patients with solid tumours during inpatient admission (Pediatric Hospital Information System, 2015–2019)

Medication	All admissions N=79 530	Constipation admissions N=16 306	No constipation admissions* N=63 224
Anti-Constipation	36 444 (45.8)	11 912 (73.1)	24 532 (38.8)
Polyethyl glycol–electrolyte	25 175 (31.7)	8874 (54.4)	16 301 (25.8)
Senna	10 325 (13.0)	4384 (26.9)	5941 (9.4)
Lactulose	5501 (6.9)	2272 (16.7)	2774 (4.4)
Docusate	11 297 (14.2)	4139 (25.4)	7158 (11.3)
Electrolyte laxatives	865 (1.1)	559 (3.4)	306 (0.5)
Glycerin	1745 (2.2)	641 (3.9)	1104 (1.7)
Mineral oil	834 (1.0)	312 (1.9)	522 (0.8)
Bisacodyl	2094 (2.6)	888 (5.4)	1206 (1.9)
Laxative combination†	806 (1.0)	400 (2.5)	406 (0.6)
Total different laxatives taken			
0	44 229 (55.6)	4679 (28.7)	39 550 (62.6)
1	20 359 (25.6)	5098 (31.3)	15 261 (24.1)
2	9433 (11.9)	3568 (21.9)	5865 (9.3)
3 or more	5509 (6.9)	2961 (18.2)	2548 (4.0)
Opioid group			
None	43 627 (54.9)	8120 (49.8)	35 507 (56.2)
Fentanyl only	3598 (4.5)	485 (3.0)	3113 (4.9)
≤2 days of other opioids	12 068 (15.2)	2304 (14.1)	9764 (15.4)
>2 days of other opioids	20 237 (25.4)	5397 (33.1)	14 840 (23.5)
Duration of medication (when used) (IQR)			
Median polyethyl days	2 (1–4)	3 (2–5)	2 (1–4)
Median senna days	3 (1–5)	3 (2–6)	2 (1–5)
Median docusate days	3 (2–6)	4 (2–6)	3 (2–5)
Median lactulose days	2 (1–4)	2 (1–5)	2 (1–4)

Percentages may not sum to 100% due to rounding.
*Administration of >2 constipation medications without the presence of a constipation diagnosis.
†Excludes combinations with iron.

interventions which predispose them to constipation. While symptoms of constipation go unnoticed or underreported due to patient embarrassment and/or anxiety with the medical team, symptoms and risks of constipation can worsen. Stool withholding, caused by hard, painful bowel movements, anal fissures and mucositis, can disrupt brain-colonic signalling leading to increased stretch and stool burden, and progressively worsen stool build-up.[15] The disruption of this signalling may be complicated by mucositis, anorexia and poor nutritional intake resulting in decreased peristalsis. The majority of bowel regimens are readily available and affordable for patients to take in the hospital or at home. In addition, there are minimal to no interactions between constipation medications and cancer-directed therapy.[16] Preventative measures and attention to constipation symptoms could eliminate chemotherapy delays and decreases due to severe constipation or chronic constipation habits following chemotherapy. Finally, children with haematological malignancies and constipation have increased abdominal imaging exposure.[9] Multiple paediatric subspecialist organisations, including the Children's Oncology Group, have previously published that increasing ionising radiation exposure from X-ray and CT should be avoided as much as possible due to risks of secondary malignant neoplasms.[17] Although in a general paediatric setting, constipation is a clinical diagnosis that rarely requires imaging, children undergoing chemotherapy can have underlying pathophysiology or life-threatening diagnoses such as typhlitis that may necessitate further work-up when presenting with abdominal imaging or nausea. Decreasing the physical symptoms of abdominal pain, nausea and bloating that accompany many patients with constipation could result in decreased abdominal radiograph exposure and in turn, decrease unnecessary ionising radiation exposure.

The causative mechanisms of constipation vary, and a uniform approach to management should be avoided. Best practices for constipation management in children with cancer should target the dominant pathophysiology causing symptoms. Personalised constipation treatment should consider the chemotherapeutic agent, opioid use, mobility status, and patient's ability to tolerate oral intake and medications. Children receiving opioids should receive stimulant medications due to reduced GI propulsion, with literature supporting senna as a first line to both

prevent and reduce problematic constipation.[18] Refractory vincristine-induced constipation has demonstrated improvement with lactulose, which is hypothesised to correlate with the possible damage to myenteric plexus.[19] Magnesium oxide should be avoided as a treatment option in children requiring antacids due to negative drug interactions.[20] Patients suffering from mucositis or difficulties with taking oral nutrition should avoid Miralax, as the volume could be problematic. Future research should focus on prospective trials across all paediatric oncology patients to identify the best personalised prophylaxis and treatment approach for children at risk for constipation.

Limitations

These findings should be interpreted in light of the strengths and limitations of our study design and data source, as outlined in our previous study.[9] These limitations acknowledge that PHIS is a large-scale database that provides multi-institutional, geographically diverse representation of a large number of subjects. Relying on accurate coding and diagnoses using ICD-10 codes is an inherent limitation of PHIS. We cannot assess with certainty how often constipation medications were used to prevent, rather than treat, constipation; however, we attempted to account for this conservatively by requiring a diagnosis of constipation before considering the intent to be treatment. It is certainly possible that patients receiving constipation medications for 'prevention' by our definition could have been experiencing signs or symptoms of constipation, in which case we have underestimated the true prevalence of constipation in this patient population. Similarly, in patients who received constipation medications, we are unable to comment on whether the number and type of medication prescribed were appropriate for their needs. In those patients receiving an opioid, we are unable to assess if this was used for sedation/anaesthesia purposes or pain control. In an attempt to account for this, we placed patients into four opioid groups of presumed increased constipation risk. We are limited to ICD-10-CM coding to define the specific cancer groups based on location of tumour and have no detail regarding the specific tumour classification, stage, histology or specific treatment regimen. Finally, the PHIS data set does not allow us to assess the extent of constipation or use of medications after discharge.

CONCLUSIONS

In summary, constipation is highly prevalent in children with solid tumours receiving chemotherapy and is likely multifactorial in nature, and most children receive a variety of medications to treat it. Clinical practice guidelines and additional supportive care recommendations for constipation are lacking in paediatric oncology. This report demonstrates the high frequency of constipation in paediatric patients with solid tumours and supports the need for increased attention to prophylaxis and management in this population to prevent patient discomfort, minimise potential impact on cancer treatment, as well as reduce exposure to expensive and potentially harmful radiological testing for evaluation of GI symptoms. Supportive care guidelines are sorely needed in this area, particularly for high-risk populations such as patients with solid tumour, and future prospective studies should seek to determine the most effective standardised treatment regimens.

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