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Should Children With Constipation Undergo Blood Lead Level Screening?

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Abstract

This study aimed to compare the prevalence of elevated blood lead level in children with constipation to the population prevalence. We reviewed the charts of 441 children who were screened with a blood lead level on presenting to the gastroenterology clinic at UPMC Children's Hospital of Pittsburgh for evaluation of constipation. The prevalence of blood lead level greater than 5 µg/dL was 1.36% (6/441; 95% confidence interval = 1.23% to 1.49%), which is significantly lower than the 4.01% prevalence in the population reported by the Center for Disease Control and Prevention. No patients had a blood lead level greater than 10 µg/dL. Age under 5 years old showed an increased odds of lead level greater than 5 µg/dL (odds ratio = 7.5; 95% confidence interval = 1.2 to 47.3, $P < .05$). We concluded that children seen in the gastroenterology clinic for constipation are unlikely to have an elevated blood lead level on routine screening.

Keywords

constipation; lead poisoning; diagnosis; retrospective studies; pediatrics

Introduction

Affecting approximately 10% of children in the United States, constipation is one of the most common patient complaints in general pediatric and pediatric gastroenterology offices.

¹ Based on limited data to date, a minority of these children have an organic cause of constipation.^{2,3}

In 2014, the European Society of Pediatric Gastro- enterology, Hepatology, and Nutrition and the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition recommended against screening for an organic cause of constipation, albeit based only on expert consensus due to a lack of convincing evidence.⁴ Similar guidelines produced by the

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Author Contributions

VKR participated in study design, data collection, data analysis, manuscript preparation, and manuscript editing. AJN participated in study design, data collection, and manuscript editing. AIS participated in study design and manuscript editing while providing supervision for data collection and analysis.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

National Institute for Health and Care Excellence also reported a lack of sufficient evidence to support or refute such screening.⁵ A 2013 economic study provided evidence that screening for celiac disease, hypothyroidism, and hypercalcemia was not cost-effective.³ Notably, only 3 patients were screened for lead toxicity, and all had normal levels. Despite the lack of evidence, children continue to undergo this type of screening.

In 2015, the Centers for Disease Control and Prevention (CDC) surveillance data of US children aged 1 to 5 years reported a prevalence of 4.01% for blood lead level greater than 5 µg/dL.⁶ These toxic levels have been linked to poor neurodevelopmental outcomes and are associated with gastrointestinal symptoms. Children with constipation were found to have elevated blood lead levels compared with normally stooling controls in an Iranian study.⁷ However, their high level of environmental exposure makes this result difficult to generalize to the population in the United States.

Thus, the current study aimed to establish the prevalence of elevated lead level in a cohort of children with constipation, encopresis, or irritable bowel syndrome (IBS) while investigating factors that could guide screening. Given current screening practices, we hypothesized that children with constipation would have a higher prevalence of elevated blood lead level than the reported population prevalence in all children.

Methods

This study was a retrospective chart review of outpatient encounters at the gastroenterology clinic at UPMC Children's Hospital of Pittsburgh approved by the University of Pittsburgh's Institutional Review Board (PRO16010546). Patients age 1 year to 18 years were included if they had a lead level analyzed by the hospital laboratory from January 1, 2013, until June 30, 2015, and had an International Classification of Diseases Version 9 (ICD-9) code indicative of constipation, fecal impaction, encopresis, or IBS.

Patients were excluded if they carried a previous diagnosis of thyroid disease, celiac disease, lead toxicity, Hirschsprung's disease, inflammatory bowel disease, any metabolic disorder, spinal cord disorder, or previous abdominal surgery.

Results of lead level screening were collected in addition to diagnosis codes, demographic information, and any diagnostic orders placed. Prevalence in the sample was calculated based on the number of patients with a blood lead level greater than 5 µg/dL during the study period. This result was compared with the prevalence in children aged <72 months from 2013 and 2014 as reported by the CDC.⁶ Using the entire cohort, descriptive statistics and odds ratios given demographic data were calculated using Microsoft Excel.

Sample size was based on a larger study examining screening laboratory values for multiple organic causes in pediatric constipation. Power analysis performed at the completion of the study for the primary outcome using STATA v14 showed a statistical power of 93% in identifying a true difference between elevated blood lead level in this sample of children with constipation compared with the population prevalence.

A nested case-control study was performed with cases defined using the CDC criteria of a blood lead level greater than 5 µg/dL.⁶ Each such patient was matched with 3 controls based on age, gender, race, diagnosis, and timing of encounter. Cases and controls had the following additional data abstracted: diagnostic criteria for constipation (stool frequency, consistency, and quality and physical examination findings), symptoms (abdominal pain, weight loss, nausea, emesis, hematochezia, and encopresis), and comorbid conditions (behavioral health diagnoses or developmental delay). For the purposes of these analyses, data that could not be found on chart review were regarded as a negative response. Odds ratios were calculated using conditional logistic regression analysis for the matched cases and their respective controls. This analysis was completed using SPSS v23.

Results

A total of 10 892 encounters that involved 7211 unique patients who presented to the outpatient gastroenterology clinic at Children's Hospital of Pittsburgh were identified over the study period. Of these, 8125 encounters were excluded because they were not associated with any laboratory testing at the study institution, and an additional 887 encounters were excluded due to the patient having a previous diagnosis consistent with an organic cause of constipation. Of the remaining patients, 443 encounters of 441 unique patients involved testing for lead level. All 441 patients were included in the analysis. Table 1 contains the demographic data of these patients. Of these 441 patients, 426 had a diagnosis code of constipation, unspecified. A complete list of diagnostic codes can be found in Table 2.

Six out of the 441 patients had lead levels elevated to greater than 5 µg/dL. No patients had a lead level greater than 10 µg/dL. Figure 1 shows the distribution of patients with each lead level result. The majority of patients had a lead level of 1 µg/dL.

The calculated prevalence of elevated lead level was 1.36% (95% confidence interval = 1.23% to 1.49%), which is lower than the 4.01% population estimate by the CDC. In the children included in the current study aged 1 to 5 years, the age range used in the previously referenced data published by the CDC, the prevalence of elevated lead level was 2.27% (95% confidence interval = 1.97% to 2.57%).

Table 3 shows the relative risk of lead level greater than 5 µg/dL given race, gender, age, and diagnosis. Age under 5 years old showed a significantly increased odds of elevated lead level (7.5, $P < .05$). The increased odds associated with male gender and decreased odds of Caucasian race were not statistically significant. No diagnoses were associated with increased or decreased odds of elevated lead level.

The 6 patients with lead levels greater than 5 µg/dL were further reviewed. All 6 patients carried a diagnosis code of unspecified constipation and one was further characterized as having full incontinence of feces with a palpable fecal mass in the rectum. No patients carried a diagnosis code of IBS. Five of the 6 patients had symptoms that met at least 2 of the 6 Rome III criteria for functional constipation, while the additional patient had hard stools and stoolled 3 times per week.⁸ All 6 patients had hard or painful stools.

All 6 patients were treated for constipation with polyethylene glycol. Three of the 6 patients were instructed to improve hand hygiene while the other 3 patients were told that their levels were normal. Only 1 patient had a follow-up lead level, which had normalized.

In the case-control analysis, cases and controls were matched exactly with regard to age (mean of 3.3 years) and gender (83% male). Fifty percent of cases were Caucasian while 61% of controls were Caucasian ($P = .67$) as one case was reported as multiracial. Conditional logistic regression analysis was unable to identify any additional historical factors that were significantly correlated to a positive lead screening. Table 4 contains the calculated odds ratios and respective confidence intervals for the univariate regression analysis. In this analysis, no clinical data were found to have significance in increasing the odds of an elevated lead level. Since no univariates showed significance, multivariate analysis was not performed.

Discussion

Patients presenting to the gastroenterology clinic with constipation most often are presenting with a purely functional disorder.^{2,3} However, it continues to be the difficult task of the provider to determine which of the large number of patients with constipation warrant additional evaluation for an organic etiology. This often leads to widespread screening for conditions associated with constipation.

The current study represents the first attempt to stratify patients presenting to the gastroenterology clinic based on their risk of an elevated blood lead level. The prevalence of elevated blood lead level in patients with constipation in this study is significantly lower than the reported prevalence in the general population. Moreover, even in the 6 patients identified with some elevation of lead level, all 6 were treated with polyethylene glycol for their constipation. None of the 6 required further management specifically for the elevated lead level.

In the attempt to find other historical clues that could identify patients at higher risk, the current study was only able to suggest that age under 5 years increased the odds of a positive test. It may be that with a larger sample, African American race and male gender would also show statistical significance in increasing the odds of a positive test result, but this cannot be confirmed with the current study. No other historical facts or examination findings could conclusively be identified as suggestive or not suggestive of lead toxicity. Perhaps these historical clues could be used as a guide to which patients have a higher likelihood of having an elevated lead level and thus warrant testing.

As with any retrospectively collected data, this study is limited by an inability to determine whether the patients with constipation were being tested for elevated blood lead level solely because of the constipation. The sample may represent a heterogeneous group of abdominal complaints being tested for elevated lead level although they were primarily classified as having constipation. Our decision to use ICD-9 codes creates a heterogeneous population that may not all meet Rome criteria for functional constipation. However, in practice, many

providers make diagnostic and therapeutic decisions without strict adherence to the Rome criteria, which improves the external validity of this study.

While this study did attempt to stratify patients by race, other known associations with lead level such as socioeconomic status and geography were not included in the study. This may limit our interpretation of the results compared with national data since there may be a bias toward private insurance and higher socioeconomic status in the pediatric gastroenterology clinic data when compared with CDC data. In addition, national CDC data may have a selection bias toward reports from higher prevalence areas.

Currently, there is some controversy regarding what constitutes an unsafe lead level with levels as low as 3 µg/dL correlating to adverse neurological outcomes.⁹ A prospective study of patients with confirmed functional constipation being screened for elevated lead level may further elucidate the appropriate time to screen and provide insight into whether treating the elevated level aids in the management of constipation.

Based on CDC recommendations, many pediatricians screen high-risk children for elevated blood lead levels at 12 and 24 months of age.¹⁰ This may have identified some patients who had constipation related to lead toxicity prior to coming to the gastroenterology office. However, this practice further limits the utility of screening; it is likely that the 2 study patients detected at age 1 would have been identified regardless in their primary pediatrician's office. The deleterious effects of lead toxicity make it difficult to suggest children with constipation should not be screened, but perhaps this practice is best left to the general pediatrician who is already performing routine screening.

In summary, while elevated lead level has a widely accepted association with many abdominal complaints, lead level screening in children with constipation identifies patients at a lower rate than the general population. There may be some demographic and historical factors, such as age under 5 years, that increase the odds of having an elevated level, but the overall prevalence in constipated children is low. Further work integrating the practices of the general pediatrician and the subspecialist may help identify cost-effective strategies for screening at-risk children.

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Figure 1.

Histogram of blood lead level of patients in the sample (n = 441). Blood lead level of 0 µg/dL corresponds to any value reported as “<1 µg/dL.”

Table 1.Demographic Data of Included Patients (N = 441)^a.

Age	
Average age (years)	6.0 ± 3.7
Race	
Caucasian	356 (81%)
African-American	46 (10%)
Gender	
Male	235 (53%)
Female	206 (47%)
Diagnosis	
Constipation	429 (97%)
Encopresis	146 (33%)
IBS	3 (1%)
None of the above	1 (<1%)

Abbreviation: IBS, irritable bowel syndrome.

^aData expressed as mean ± standard deviation or frequency (percent of sample).

Table 2.

Number of Included Patients With Each ICD-9 Diagnosis Code.

ICD-9 Diagnosis Code	Diagnosis	Number of Patients (%)
564.00	Constipation, unspecified	426 (97%)
564.01	Slow transit constipation	2 (<1%)
564.09	Other constipation	7 (2%)
560.32	Fecal impaction	47 (11%)
787.7	Abnormal feces	2 (<1%)
787.60	Full incontinence of feces	73 (17%)
787.63	Fecal urgency	2 (<1%)
307.7	Encopresis	82 (19%)
564.1	Irritable bowel syndrome	3 (1%)
787.62	Fecal smearing	1 (<1%)

Abbreviation: ICD-9, International Classification of Diseases, Version 9.

Table 3.

Odds Ratios of Blood Lead Level Greater Than 5 µg/dL Given Demographic Data and Diagnostic Category (N = 441).

	Lead >5 µg/dL (n = 6), n (%)	Lead <5 µg/dL (n = 435), n (%)	Odds Ratio (95% CI)	P
Male gender	5 (83%)	230 (53%)	4.5 (0.62–32.1)	.222
Caucasian race	3 (50%)	353 (81%)	0.23 (0.05–1.03)	.089
Age < 5 years	5 (83%)	174 (40%)	7.5 (1.2–47.3)	.043
Constipation	6 (100%)	423 (97%)	-	1.000
Encopresis	1 (17%)	145 (33%)	0.40 (0.05–3.46)	.669
IBS	0 (0%)	3 (1%)	-	1.000
Other	0 (0%)	1 (<1%)	-	1.000

Abbreviations: CI, confidence interval; IBS, irritable bowel syndrome.

Table 4.

Conditional Logistic Regression Analysis of Clinical Data in Patients With and Without Elevated Blood Lead Level^a.

	Odds Ratio (95% Confidence Interval)	P
2 bowel movements per week	3.9 (0.4–39.6)	.25
Stool incontinence	31.5 (0–2.6 × 10 ⁷)	.62
Withholding behavior	0.4 (0.05–4.2)	.48
Hard bowel movements	105 (0.005–2.1 × 10 ⁶)	.36
Blood in stools	2.6 (0.44–16)	.29
Large diameter stools	1.7 (0.10–31)	.71
Emesis	0.7 (0.06–8.0)	.76
Abdominal pain	0.33 (0.053–2.1)	.24
Developmental delay	2.6 (0.38–18)	.33
Behavioral health diagnoses	1 (0.04–25)	1
Constipation before 1 month of age	3 (0.25–36)	.39
Poor weight gain	0.02 (0–3900)	.53
Abdominal distension	1.5 (0.14–17)	.74
Fecal mass in rectum	0.38 (0.04–3.4)	.39
First gastroenterology visit	0.55 (0.10–3.1)	.50
Functional constipation criteria met	1.2 (0.22–6.6)	.83
Irritable bowel syndrome criteria met	1.3 (0.17–9.8)	.80

^aData represent odds ratios for blood lead level greater than 5 µg/dL with corresponding confidence interval and *P* value calculated using conditional logistic regression in IBM SPSS v23.