Original Article

Comparative Effectiveness of Senna to Prevent Problematic Constipation in Pediatric Oncology Patients Receiving Opioids: A Multicenter Study of Clinically Detailed Administrative Data

Chris Feudtner, MD, PhD, MPH, Jason Freedman, MD, Tammy Kang, MD, MSCE, James W. Womer, BA, Dingwei Dai, PhD, and Jennifer Faerber, PhD

Pediatric Advanced Care Team, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

Abstract

Context. Pediatric oncology patients often receive prolonged courses of opioids, which can result in constipation.

Objectives. Comparing patients who received senna matched with similar patients who received other oral bowel medications, determine the subsequent risk of "problematic constipation," assessed as the occurrence of the surrogate markers of receiving an enema, escalation of oral bowel medications, and abdominal radiographic imaging.

Methods. This was a retrospective cohort study of hospitalized pediatric oncology patients less than 21 years of age in 78 children's and adult hospitals between 2006 and 2011 who were started on seven consecutive days or more of opioid therapy and were started on an oral bowel medication within the first two days of opioid therapy. Clinically detailed administrative data were used from the Pediatric Health Information System and the Premier Perspective Database. After performing propensity score matching of similar patients who started senna and who started a different oral bowel medication, Cox regression modeling was used to compare the subsequent hazard of the surrogate markers.

Results. The final matched sample of 586 patients averaged 11.5 years of age (range 0–20 years); 41.8% ($n = 245$) had blood cancer, 50.3% ($n = 295$) had solid tumor cancer, and 7.9% ($n = 46$) had brain cancer. Initiating senna therapy within two days of starting the prolonged opioid course, compared with initiating another oral bowel medication, was significantly associated with a lower hazard during the ensuing five days for receipt of an enema (hazard ratio [HR], 0.31; 95% CI, 0.11–0.91) or undergoing abdominal radiographic imaging (HR, 0.74; 95% CI, 0.55–0.98), was marginally associated with a lower hazard of oral bowel medicine escalation (HR, 0.78; 95% CI, 0.59–1.03), and overall was significantly

Address correspondence to: Chris Feudtner, MD, PhD, MPH, CHOP North–Room 1523, The Children's Hospital of Philadelphia, 34th and Civic Center Boulevard, Philadelphia, PA 10194, USA. E-mail: feudtner@email.chop.edu

Accepted for publication: September 10, 2013.

0885-3924/$ - see front matter
http://dx.doi.org/10.1016/j.jpainsymman.2013.09.009

associated with a lower hazard of the composite end point of problematic constipation (HR, 0.70; 95% CI, 0.56−0.88).

Conclusion. Initiating senna therapy, compared with other oral bowel medications, diminishes the subsequent risk of surrogate markers of problematic constipation in this population. J Pain Symptom Manage 2013;■:■−■. © *2013 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.*

Key Words

Pediatric, cancer, opioid therapy, constipation, senna, sennosides, prevention, comparative effectiveness

Introduction

Constipation is a distressing and uncomfortable problem, causing pain, discomfort, nausea, vomiting, bowel obstruction, and reduced quality of life.[1−5] Constipation also is associated with increased medical costs and higher utilization of resources including emergency room visits, abdominal imaging, and pharmacotherapy.[5] The prevalence of constipation in the general pediatric population is 8.9%[6] and anywhere from 50% to 60% of pediatric cancer patients experience it at some point during therapy.[1,2] Although many physical, psychological, and pharmacological factors associated with cancer and cancer treatment can cause or contribute to constipation,[6−12] opioid therapy stands out as a major cause.[4,8]

Opioids are a mainstay of treatment for cancer pain; consequently, cancer patients often receive long courses of opioids and can experience constipation as a result.[2,4,5,7,9,13−15] Although changes to diet and fiber intake, increased physical activity, and better fluid intake are helpful for patients with constipation,[1,9] these interventions are not often possible in children with cancer for numerous reasons. There are a multitude of pharmacologic agents available for the management of constipation.[4,7,8,11,13,16] Scant data, however, address which is the most effective in children and young people with cancer.[2,12]

Treatment approaches are often inconsistent, and the few adult studies in this area report conflicting results;[1,16] however, there are multiinstitutional studies that demonstrate lower incidence of constipation in patients who are given prophylactic bowel regimens when started on opioid therapy.[14,15] Given this, guidelines have been developed for adult patients by the National Comprehensive Cancer Network supporting initiation of prophylactic laxative regimens (polyethylene glycol or stimulant laxatives such as senna, with or without stool softeners) when starting any opioid regimen.[15] In children, however, no such guidelines exist. Choice of prophylactic therapy is left to physician preference, often causing delay in treatment, exacerbation of problematic constipation, and greater likelihood of needing multiple agents, and increased utilization of resources to manage constipation effectively. As constipation induced by opioids is predictable and preventable, there is an urgent need to understand how to best proactively manage and provide a prophylactic bowel regimen before constipation becomes problematic.

Because the active metabolites of senna cause both enhanced intestinal peristalsis and increased intestinal secretion, and do not act chiefly as a softening or bulking agent, senna has been cited as an effective pharmacological option to prevent opioid-induced constipation,[17−20] but no rigorous comparative effectiveness study has been performed in children. Therefore, we sought to investigate senna's effectiveness, compared with other prophylactic oral bowel medications, in reducing opioid-induced constipation in pediatric cancer patients.

Methods

Study Design

This retrospective cohort study used propensity score matching analyses to control for observed differences in the likelihood of senna exposure.

Data Sources

All records from inpatient hospitalizations for children 20 years of age or younger in which the child was on a prolonged course of opioid