

Letters

A Prospective Study to Investigate Contributory Factors That Lead to Constipation in Palliative Care Patients

To the Editor:

Despite the prevalence of constipation in hospice/palliative care patients, attributable risk factors remain poorly codified. Although opioids are commonly cited, very little attention has been paid to exploring other variables prospectively and objectively. Thus far, only retrospective reports correlate medications with anticholinergic side effects and opioids,¹ functional status,¹ and overall frailty² with laxative prescription in this cohort. This dearth of data is concerning, especially when compared with the rigor with which other symptoms in palliative care with comparative multifactorial etiologies have been considered. For example, it is well accepted that there are many factors that contribute to breathlessness, and much work details the need to consider objectively such factors when palliating this symptom.

Here, we report the results of a bivariate analysis undertaken to consider whether there are specific clinicodemographic variables that contribute to the prescription of laxatives. Furthermore, this work begins a more in-depth exploration of the constipating effects of medications with anticholinergic effects, which include opioids. This is particularly important, given the number of medications prescribed in palliative care that have anticholinergic properties.³

Methods

With the approval of the responsible Human Research Ethics Committees, on the day consenting cancer patients were admitted to one of two

palliative care units, the following information was sought: demographics (age, gender, and performance status as measured by the Australia-modified Karnofsky Performance Status⁴ and the Eastern Cooperative Oncology Group⁵ scales), medications (opioids, medications with anticholinergic effects, and all other medications), laxatives, and blood tests (albumin and serum anticholinergic activity [SAA]). SAA was calculated using the method outlined by Tune,⁶ which involves a radioreceptor assay using competitive binding. The final result includes the effects of endogenous and exogenous substances (medications and active metabolites) with anticholinergic activity. In addition, each patient's clinician-calculated anticholinergic load (CCAL) from pre-existing tables⁷ was summarized based on current medications. Opioid doses were converted to mean oral morphine equivalents.⁸ Laxative use was coded as yes or no and then subcategorized as stimulant (docusate with sennosides, sennosides, and bisacodyl) or nonstimulant (docusate, paraffin, lactulose, and macrogol) laxatives.⁹ For this work, if people were receiving both types of medications, they were classified as "mixed."

There were two specific aims to this work. The first was to explore if there was a particular clinicodemographic variable associated with a greater likelihood of being prescribed laxatives. The second was to determine whether different classes of laxatives were more likely to be prescribed when SAA or CCAL was higher. This was of interest because of the fact that acetylcholine, which is blocked by anticholinergic substances, is the major excitatory neurotransmitter implicated in colonic activity. It previously has been shown that depletion of this agent may result in delayed colonic transit.¹⁰

Bivariate analysis was undertaken using the Chi-square test for categorical data and Student's *t*-test for continuous variables. Comparisons of

Table 1
Patients' Characteristics by Laxative Use (N = 113)

Variables	Laxative Use		Results
	Yes (n = 83)	No (n = 28)	
Gender, n (%)			
Male	47 (57)	11 (39)	$\chi^2_1 = 2.52, P = 0.112$
Female	36 (43)	17 (61)	
Age, years, mean (SD)	71.2 (0.9)	74.0 (10.5)	$t_{109} = 1.22, P = 0.224$
ECOG, mean (SD)	2.8 (0.7)	3.0 (0.7)	$t_{109} = 1.12, P = 0.265$
AKPS, mean (SD)	47.1 (14.4)	45.4 (15.0)	$t_{109} = -0.55, P = 0.584$
Admitted for symptom control, n (%)	76 (92)	25 (89)	$\chi^2_1 = 0.13, P = 0.716$
Admitted for other reasons, n (%)	7 (8)	3 (11)	
Oral morphine equivalent (mg), mean (SD)	128.4 (173.5)	98.1 (171.4)	Mann-Whitney U-test
	median = 60	median = 30	$P = 0.142$
Benzodiazepines prescribed, n (%)			
Yes	27 (33)	7 (25)	$\chi^2_1 = 0.56, P = 0.455$
No	56 (67)	21 (75)	
Total number of medications prescribed (excluding laxatives), mean (SD)	7.7 (3.2)	7.0 (2.7)	$t_{109} = -1.00, P = 0.319$
Clinician-calculated anticholinergic load, mean (SD)	2.3 (1.4)	1.8 (1.3)	$t_{109} = -1.59, P = 0.114$
Serum anticholinergic activity, mean (SD)	19.0 (13.5)	19.7 (11.6)	$t_{109} = 0.24, P = 0.808$

ECOG = Eastern Cooperative Oncology Group; AKPS = Australia-modified Karnofsky Performance Status.

means with SAA and CCAL also were conducted using *t*-tests. For continuous variables with skew distributions, a nonparametric approach, the Mann-Whitney *U*-test, was applied for comparison of medians.

Results

Data were collected from 113 people; results are summarized in Tables 1 and 2. Laxatives

were prescribed for 70% ($n = 83$). No specific variable significantly contributed more to the prescription of any laxatives, including opioids, medications with anticholinergic effects, albumin (as a measure of cachexia), and Australia-modified Karnofsky Performance Status and Eastern Cooperative Oncology Group scores (as measures of function). When focusing just on opioids and laxatives, it was observed that although 71 people received

Table 2
Comparisons of the Serum Anticholinergic Activity and Clinician-Calculated Anticholinergic Load by Different Laxative Types

Laxative Type	Serum Anticholinergic Activity Median (SD)	Results
Stimulant only		
Yes (n = 39)	22.3 (14.8)	$t_{106} = -1.42, P = 0.157$
No (n = 44)	18.4 (13.8)	
Osmotic only		
Yes (n = 8)	19.9 (13.9)	$t_{106} = 0.71, P = 0.483$
No (n = 75)	16.4 (8.2)	
Mixed		
Yes (n = 36)	16.4 (12.5)	$t_{106} = 1.79, P = 0.077^*$
No (n = 47)	21.3 (13.8)	
	Clinician-Calculated Anticholinergic Load Median (Interquartile Range)	
Stimulant only		
Yes (n = 39)	2.0 (1.0–3.0)	Mann-Whitney U-test $P = 0.108$
No (n = 44)	2.0 (1.0–3.0)	
Osmotic only		
Yes (n = 8)	2.0 (2.0–4.75)	Mann-Whitney U-test $P = 0.856$
No (n = 75)	2.0 (1.0–3.0)	
Mixed		
Yes (n = 36)	2.0 (1.0–3.0)	Mann-Whitney U-test $P = 0.385$
No (n = 47)	2.0 (1.0–3.0)	

*When comparing the medians, there was a significant difference between groups (Mann-Whitney U-test, $P = 0.035$).

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