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Medications Not Dosed Within Recommended Range for Renal Function in Patients With Chronic Kidney Disease Identified upon Hospice Admission; a Retrospective Chart Review

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Abstract

Background: Hospice-eligible patients are vulnerable to adverse medication effects given their advanced illnesses and general older age. It is not known how often medications are not renal dose adjusted in hospice-eligible patients and which are frequently problematic. This study aims to identify commonly prescribed medications with significant renal clearance that are dosed too high and patient characteristics that increase the likelihood of occurrence. **Methods:** This is a retrospective chart review of adult patients admitted to hospice care. Data collected included clinical/demographic data, renally cleared medications taken at time of hospice admission, and calculated renal function using several formulas. Descriptive statistics and binomial logistic regression were used to analyze data. **Results:** Of 283 included charts, 27% had ≥1 medication dosed too high for renal function. The most common medications prescribed and not renal dose adjusted included tramadol, gabapentin, duloxetine, loratadine, cetirizine, famotidine, apixaban, rivaroxaban, metformin, trospium, and most antimicrobials. Increasing serum creatinine values and increasing number of renally cleared medications were associated with a higher likelihood of a medication dosed too high [OR, 1.702, 95% CI (1.257, 2.305), $P < 0.001$] and [OR, 1.856, 95% CI (1.517, 2.271), $P < 0.001$] respectively. Residing at home vs a facility was associated with a reduced likelihood of having a medication dosed too high [OR, 0.30, 95% CI (0.134, 0.673), $P = 0.003$.]. **Conclusions:** Hospice-eligible patients frequently have renally cleared medications prescribed and at doses too high for their renal function. Analgesics, over-the-counter antihistamines, anticoagulants, anticholinergics have potential for significant adverse effects and higher vigilance is needed.

Keywords

polypharmacy, renal, dose adjustment, hospice, palliative, medication, symptom management

Background

Patients with impaired renal function often receive medications that are not renal dose adjusted. An early study looking at medication dosing in ambulatory care patients with impaired renal function found that 70% of patients were prescribed at least 1 medication with a high rate of renal elimination and 25% of those medications were dosed too high.[1] Since then, several studies have found similar concerns regarding dosing of medications in chronic renal impairment.[2,3] Likewise, hospitalized patients frequently have medications dosed outside of the recommended range for their renal function. A recent meta-analysis including 20 studies in hospitalized patients with chronic kidney disease (CKD) found a dose error prevalence ranging from 23%–73%.[4] Amongst the collective ambulatory care and inpatient studies, the most common medications not dose adjusted for renal function are metformin, antibiotics, histamine type-2 receptor antagonists (H2RAs) allopurinol, and gabapentin.

Renal function deteriorates with age and the Centers for Disease Control and Prevention (CDC) report the incident of CKD in those over 65 to be almost 40%.[5] As most patients enrolled in hospice are over the age of 65[6] and may have advanced illnesses associated with impaired renal function

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(end-stage renal disease (ESRD)/dialysis dependence, congestive heart failure, end-stage liver disease) it would not be surprising if the rates of renal impairment are concentrated in hospice patients. One study measuring prevalence of abnormal renal function in 332 patients receiving palliative care found elevated serum creatinine in over 20% of patients. Between 35% and 51% had an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2. Just over 10% had an eGFR of less than 30 mL/min/1.73 m^2. Additionally, they found that between 19% and 40% of patients with a normal serum creatinine had an eGFR less than 60 mL/min/1.73 m^2.[7]

Hospice-eligible patients are particularly vulnerable to adverse drug effects given their advanced illnesses and generally older age. Polypharmacy is a concern for these patients as they receive medication for end-of-life symptoms as well as their co-morbid conditions. Many medications prescribed near end-of-life, such as opioids, antibiotics, anticonvulsants, anticoagulants, and antidepressants, have significant renal clearance. Admission to hospice represents a transition of care and an opportunity to reconcile and re-evaluate medication use to reduce the risk of adverse effects and additive symptom burden. Despite the extensive data that shows renally cleared medications are often dosed too high in patients with CKD, it is not known how often this occurs in hospice-eligible patients and which medications are uniquely problematic.

The purpose of this study is to identify commonly prescribed medications with significant renal clearance prescribed to hospice-eligible patients with documented renal impairment and the frequency at which they are prescribed at a dose above the recommended dose range for their renal function. Secondary aims are to describe the incidence of discordance between methods of estimating renal function and identify variables that increase risk for having a medication dosed too high.

Methods

This is a retrospective chart review of patients enrolled in hospice ≥ age 18 admitted to hospice care from January 1, 2021 to June, 30, 2021. Charts were included if they contained an International Classification of Diseases 10th Revision (ICD10) code in the diagnosis list indicating any type of renal dysfunction. Typically, ICD10 codes are entered in the patient's electronic medical record following review of their previous medical records from their primary care physician, hospitalizations, or specialists and are treated as a known chronic medical condition. Charts were excluded if there was narrative documenting renal dysfunction, but no associated ICD10 code. Data collected included patient demographics, primary terminal diagnosis, Palliative Performance Scale score (PPS),[8] renal ICD10 codes, last known lab reported serum creatinine and eGFR, recentness of lab report, height, weight, and medications with renal clearance. Only medications that were present at time of admission were recorded (the transition point to hospice care.) Creatinine clearance (CrCl) was calculated using the Cockroft-Gault equation and eGFR with the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 equations. CrCl and eGFR were also adjusted for body mass index (BMI) and body surface area (BSA), respectively. Medication dose recommendations supplied in the manufacturer package insert and UpToDate® Lexidrug™ were compared to the renal function calculations and laboratory reported renal function.

This study was approved by the University at Buffalo Institutional Review Board (STUDY00007372).

Statistical Analysis

Descriptive statistics were used to summarize the patient characteristics, demographics, and renally cleared medications identified. Univariate analysis of clinical and demographic variables was conducted to identify variables independently associated with having ≥1 medication dosed above recommended range using chi square, Kruskal-Wallace H, and Mann-Whitney U where appropriate. This was followed with a binomial logistic regression. Prior to analysis, all assumptions associated with binomial logistic regression had been tested and/or met. Significance was set to $P < 0.05$. Data was analyzed using IBM SPSS Statistics, version 29 (2022).

Results

From January 1, 2021 through June 30, 2021, there were 1456 patients admitted to hospice care. Of these, 290 (19.9%) had a renal related ICD10 code documented. Seven charts were excluded; 4 had no labs for review and 3 had no height/weight for CrCl calculations. The final analysis included 283 charts.

Most patients were over the age of 80 (>75%), Caucasian (91%), and female (58%). Heart failure, cancer, and ESRD were the most frequent primary hospice diagnoses. Most patients received care at home (70%) and were a PPS of 30% or higher (80%) at time of admission. The most frequent ICD10 codes (>75%) were those for stage 3 and stage 4 CKD. The majority of patients had labs drawn within 30 days of hospice admission (78%). Patients received on average 3.2 ± 1.9 medications with renal elimination (range 0-9). Almost 30% of patients had 1 or more medications that were dosed higher than recommended for their renal function. The calculated CrCl was less than the eGFR value by ≥ 10 mL/minute in 30% of patients. (Table 1)

Medications ordered frequently and dosed above the recommended range for renal function level were tramadol (82% of orders not adjusted), duloxetine (42%), metformin (31%), most antibiotics/anti-infectives, cetirizine (100%), famotidine (19%), loratadine (70%), memantine (41%), trospium (67%), apixaban (17%), rivaroxaban (50%), and gabapentin (16%). Various other opioids and mirtazapine were frequently

Table 1. Patient Characteristics With Univariate and Multivariate Analysis, Odds of Having Medication Dosed Outside of Recommended Range.

	Univariate Analysis		Multivariate Analysis	
Total n = 283	n (%)	*P*-value	OR (95% CI)	*P*-value
Sex				
Male	118 (42)			
Female	165 (58)	0.464	1.662 (0.871, 3.172)	0.124
Age (years)				
<50	0 (0)			
51-60	5 (2)			
61-70	17 (6)			
71-80	41 (14)			
81-90	120 (43)			
≥91	100 (35)	0.354	1.323 (0.946, 1.850)	0.101
Race/Ethnicity				
African American	17 (6)			
Caucasian	258 (91)			
Hispanic	4 (1.4)			
Middle Eastern	2 (0.7)			
Native American	2 (0.7)	0.832	0.926 (0.419, 2.050)	0.850
Hospice Diagnosis				
Cancer	72 (25)			
Cardiac	84 (30)			
Dementia	45 (16)			
ESLD	5 (2)			
ESRD	32 (11)			
Neurologic[a]	5 (2)			
PCM	8 (3)			
Respiratory[b]	19 (7)			
Other[c]	13 (5)	0.340	0.994 (0.861, 1.148)	0.934
Location of Care				
Home	197 (70)			
Nursing home/ALF	86 (30)	0.792	***0.300 (0.134, 0.673)***	***0.003***
PPS on Admission (%)				
10	12 (4)			
20	44 (16)			
30	66 (23)			
40	109 (39)			
50	42 (15)			
60	9 (3)			
70	1 (0.4)	***0.035***	1.294 (0.951, 1.761)	0.101
Renal ICD10 Codes[d]				
E11.2, I12.9, I13.0, K76.7	4 (1)			
N17.9	11 (4)			
N18.2	4 (1)			
N18.30, N18.3, N18.31, N18.32	140 (49)			
N18.4, N18.41	78 (28)			
N18.5	21 (7)			
N18.6	19 (7)			
N18.9	7 (2)	0.236	0.800 (0.569, 1.123)	0.197
Labs drawn PTA (days)				
0-10	155 (55)			

(continued)

Table 1. (continued)

Total n = 283	Univariate Analysis n (%)	*P*-value	Multivariate Analysis OR (95% CI)	*P*-value
11-20	38 (13)			
21-30	27 (10)			
31-60	36 (13)			
61-90	8 (3)			
>90	19 (7)	0.755	1.066 (0.868, 1.309)	0.541
Serum Creatinine (mg/dL)				
≤1.0	22 (8)			
>1.0, ≤1.5	94 (33)			
>1.5, ≤2.0	60 (21)			
>2.0, ≤2.5	32 (11)			
>2.5, ≤3.0	25 (9)			
≥3.0	51 (18)	***0.006***	***1.702 (1.257, 2.305)***	***<0.001***
Body Mass Index (kg/m^2)				
<18.5	28 (10)			
18.5-24.9	141 (50)			
25-29.9	70 (25)			
≥30	44 (16)	0.442	1.071 (0.725, 1.583)	0.730
Calculated CrCl less than eGFR by ≥ 10 mL/minute				
Yes	84 (30)			
No	199 (70)	0.181	0.754 (0.292, 1.947)	0.559
Number of medications with renal clearance per patient				
Mean ± SD	3.2 ± 1.9			
Median	3	***<0.001***	***1.856 (1.517, 2.271)***	***<0.001***
Range	0-9			
Number of patients with medication dosed outside FDA/PI defined parameters for renal function	76 (27)	---	---	---

OR- odds ratio; CI - 95% confidence interval; ESLD- end stage liver disease; ESRD- end stage renal disease; PCM-protein calorie malnutrition; ALF- assisted living facility; PPS- Palliative Performance Scale; ICD10- International Classification of Diseases 10th Revision; PTA- prior to admission; CrCl- creatinine clearance; eGFR- estimated GFR; FDA- United States Food and Drug Administration; PI- package insert.
[a]Neurologic = multiple sclerosis, Parkinson's disease, cerebrovascular accident.
[b]Respiratory = chronic obstructive lung disease, pulmonary fibrosis, respiratory failure.
[c]Other = anoxic brain damage, COVID infection, dermatomyositis, encephalopathy, pressure ulcers, peripheral vascular disease.
[d]Total >100%, some patients had more than 1 renal ICD10 code.

ordered, however do not have clearly defined renal function dose recommendations to be able to categorize them (eg, "Clearance is reduced. Monitor closely" or "Not studied.") Bowel protocol standard order sets for magnesium-based laxatives and sodium phosphate enemas were prevalent mainly for facility-dwelling patients. (Table 2) In all cases where the CrCl and eGFR differed by ≥ 10 mL/minute, the medications were dosed above recommended range regardless of which renal function estimate was evaluated.

In the univariate analysis, there was a statistically significant association between admission PPS score (30%–50%), increasing SCr (≥2.0 mg/dL), and increasing number of prescribed medications with renal clearance with having a medication dosed above recommended range for renal function. The logistic regression model was statistically significant, $\chi 2\ (12) = 64.290$, $P \leq .001$. Increasing Scr [OR 1.702, 95% CI (1.257, 2.305), $P < 0.001$] and increasing number of prescribed medications with renal clearance [OR 1.856, 95% CI (1.517, 2.271), $P < 0.001$] were significant for an increased likelihood of having a medication dosed above recommended range for renal function. Patients residing at home were 70% less likely than patients living in a nursing home or assisted living facility to have a medication dosed above recommended range for their renal function [OR 0.300, 95% CI (0.134, 0.673), $P = 0.003$.] (Table 1)

Discussion

Similar to ambulatory care and inpatient studies, antibiotics, gabapentin, metformin, and H2RAs were identified as frequently being dosed above recommended range for renal function in hospice-eligible patients with renal impairment. Newly identified problematic medications include factor Xa inhibitor anticoagulants, opioids, antidepressants, bladder anticholinergics, over-the-counter (OTC) antihistamines, and cognitive enhancers.

Table 2. Medications With Renal Clearance and Frequency of Doses Above of Recommended.

	#patients	#Dosed too High (%)		#patients	#Dosed too High (%)		#patients	#Dosed too High (%)		#patients	#Dosed too High (%)
Opioid Analgesics			*Anticoagulation*			*Cardiovascular*			*Cognitive Enhancers*		
hydrocodone	19	DR	apixaban	48	8 (17%)	atenolol	4	1 (25%)	memantine	17	7 (41%)
hydromorphone	46	DR	enoxaparin	1	0	cilostazol	1	ND			
morphine	60	DR	rivaroxaban	8	4 (50%)	clonidine	3	DR	*Anti-gout*		
oxycodone	17	DR				digoxin	5	DR	allopurinol	16	1 (6%)
tramadol	17	14 (82%)	*Antimicrobial*			fenofibrate	1	1 (100%)	colchicine	1	0
			acyclovir	2	0	HCTZ	7	1 (14%)	febuxostat	3	1 (33%)
APAP/NSAIDs			amoxicillin	3	2 (67%)	lisinopril	7	DR			
APAP (oral)	114	ND	cefdinir	4	0	lovastatin	2	ND	*Genitourinary*		
facility SO	49	ND	cefpodoxime	2	1 (50%)	magnesium oxide	4	ND	methenamine	1	0
not facility SO	65	ND	ceftriaxone	1	0	metolazone	7	ND	mirabegron	2	0
butalbital	1	ND	cephalexin	1	0	midodrine	2	DR	silodosin	2	2 (100%)
celecoxib	4	1 (25%)	ciprofloxacin	2	2 (100%)	pentoxifylline	1	1 (100%)	solifenacin	1	0
diclofenac (oral)	1	1 (100%)	famciclovir	1	1 (100%)	potassium	12	ND	tamsulosin	3	ND
ibuprofen	3	1 (33%)	fluconazole	1	1 (100%)	ranolazine	5	1 (20%)	trospium	6	4 (67%)
meloxicam	4	1 (25%)	levofloxacin	3	2 (67%)	sacubitril/ valsartan	1	DR			
naproxen	4	1 (25%)	metronidazole	1	0	spironolactone	7	DR	*Anticonvulsants/ Antispastics*		
			nitrofurantoin	2	2 (100%)	triamterene/ HCTZ	1	ND	baclofen	2	DR
Diabetes			SMX/TMP	3	2 (67%)	valsartan	1	ND	gabapentin	25	4 (16%)
alogliptan	1	1 (100%)	valacyclovir	1	0				levetiracetam	1	0
empaflagozin	2	0							oxcarbazepine	2	DR
glimepiride	2	DR	*Antidepressants/ Antipsychotics*						pregabalin	4	0
glipizide	6	DR	bupropion	2	DR				tizanidine	1	DR
metformin	13	4 (31%)	buspirone	1	ND	*Antihistamine*			topiramate	1	DR
sitagliptin	4	1 (25%)	citalopram	7	ND	cetirizine	7	7 (100%)			
			clozapine	1	ND	famotidine	16	3 (19%)	*Miscellaneous*		
Gastrointestinal			desvenlafaxine	1	0	fexofenadine	1	0	alendronate	1	0
bismuth SS	2	ND	duloxetine	12	5 (42%)	hydroxyzine	9	DR	hydroxychloroquine	1	ND
fleets enema	30	ND	escitalopram	1	DR	loratadine	10	7 (70%)	PP/SP	1	0
$Al(OH)_3/MgCO_3$	1	ND	mirtazapine	22	DR	meclizine	2	ND	pramipexole	2	0
metoclopramide	2	DR	paroxetine	2	1 (50%)				ropinirole	2	0
MOM	71	ND									
$Al(OH)_3/$ $Mg(OH)_2$	32	ND									
naloxegol	1	0									

ND, DR means unable to categorize the medication order due to non-specific nature of the dose recommendation found in UpToDate® Lexidrug™. Medications with recommendations to "avoid" below a particular renal function level were counted as a definitive dose recommendation; ND, no specific dose adjustments, use with caution and monitor; DR, initial dose reduction, careful titration, and monitor; APAP, acetaminophen; NSAID, non-steroidal anti-inflammatory drug; SO, standard order; $Al(OH)_3/MgCO_3$, aluminum hydroxide/magnesium carbonate (Gaviscon®); MOM, magnesium hydroxide (Milk of Magnesia®); $Al(OH)_3/Mg(OH)_2$, aluminum hydroxide/magnesium hydroxide (Mylanta® or Maalox®); Bismuth SS, bismuth subsalicylate; PP/SP, potassium phosphate/sodium phosphate.

Duloxetine and tramadol are frequently used for symptom management both in primary care and palliative/hospice care. The FDA supplied information for duloxetine recommends avoiding use with an eGFR less than 30 mL/min as the C_{max} (maximum concentration) and AUC (area under the curve) of a single 60 mg dose are 100% greater in patient with ESRD, and the AUC of the major metabolites is 7 to 9-fold higher with expected accumulation with repeat dosing.[9] The duloxetine orders dosed outside of recommended range consisted entirely of patients with an eGFR less than 30 mL/min.

Tramadol may be more appealing to prescribers given its federal schedule-IV controlled substance classification and presumed safety compared to schedule-II opioid analgesics. Both tramadol and its active M1 metabolite are excreted via the kidneys. For CrCl less than 30 mL/min, it's recommended to increase the dose interval to every 12 hours, with a maximum total daily dose not to exceed 200 mg.[10] For all tramadol orders, it was the dose interval that was not adjusted. Most were prescribed 25-50 mg every 6-8 hours as needed, but the maximum total daily dose was under 200 mg. Although manufacturer defined renal dose cut-offs do not exist for most other opioids, morphine, codeine, tramadol, meperidine, and hydrocodone are not clinically recommended for use in those with significant renal impairment. Preferred opioids include hydromorphone, fentanyl, buprenorphine, tapentadol, and methadone.[11]

Cetirizine, loratadine, and famotidine are generally considered safe and are available OTC for patients to self-medicate. Although higher than OTC approved doses can be used in certain clinical situations, the dosing exceeded recommended dose for the indication listed in the chart, of which nearly all were environmental allergies (loratadine and cetirizine) or reflux (famotidine). Antihistamine and anticholinergic side effects are well known to be problematic in older patients, often leading to altered mental status, decline in clinical condition, and falls.[12] Famotidine, despite histamine type-2 receptor selectivity, has been associated with the development of delirium in patients receiving palliative care as well as cognitive impairment in older adults.[13,14]

There is considerable debate over the best method for determining renal function for the purpose of medication dosing, particularly in older, frail patients. CrCl and eGFR are not the same, but often treated interchangeably. The full merits of CrCl vs eGFR for medication dosing are outside the scope of this paper, however this study found that the calculated CrCl was less than the eGFR by ≥ 10 mL/min in 30% of patients. The study by Deskur-Smielecka et al[15] found discrepancy between calculated CrCl and MDRD eGFR calculation averaging 18.6 mL/min and the magnitude of discrepancy increased with lower SCr values, lower BMI, and increasing age.

Most drug manufacturer dose adjustment recommendations are based on CrCl, but some newer medications have recommendations based on eGFR. Currently, eGFR is the value frequently reported on labs, but GFR estimates have not been validated for use in drug dosing and are intended for CKD staging.[16,17] At the time of this study, the reviewed lab reports provided renal function using either the modified 4-variable MDRD or CKD-EPI 2021 equations and did not report CrCl. Additionally, the eGFR reported on labs is the indexed eGFR (mL/min/1.73 m^2). The use of the non-indexed eGFR (ml/min) by adjusting for BSA would lead to more accurate dosing when used.[18,19] If the provider fails to adjust for BSA in an underweight patient, it would lead to higher medication exposure. Frailty and cachexia are commonly seen near end-of-life. It would be beneficial for labs to report both CrCl and eGFR so these discrepancies may be easier identified and evaluated for medication dosing.

For this study, the patients' renal function was compared to the method used to dose the medication in the package insert or listed in Lexidrug™; if dose recommendations were based on CrCl, the patient's CrCl was used to determine dose appropriateness. Likewise, if dose recommendations were based on eGFR in ml/min/1.73 m^2, the patient's indexed eGFR calculation was used to create an "apples-to-apples" comparison. The medication dose recommendations were also compared to all 3 renal function estimates for completeness, recognizing that prescribers frequently use the eGFR from the lab report to determine dosing rather than CrCl.[20] The inconsistency in medication dosing recommendations (eGFR indexed vs eGFR non-indexed vs CrCl) further contributes to variances in renal dose adjustment. However, even when the CrCl and eGFR differed significantly, the medications were still dosed above recommended range regardless of the renal function estimate evaluated.

This study found 27% of patients had at least 1 medication dosed higher than recommended for their renal function with increased likelihood as SCr increased and number of renally cleared medication orders increased. The findings are analogous to that of the systematic review including 20 studies of hospitalized patients[4] and a subsequent study by Sedaghat et al[21] which found association between lower eGFR values and polypharmacy with medications not being dose adjusted. In contrast, the study by Getachew et al[22] showed elevated SCr prompted physicians to adjust medications. In the ambulatory care setting, Yap et al[1] found that 31% of patients received a higher than recommended dose of medication for at least 1 medication and Chang et al[3] found 13% of patients with CrCl 30-49 mL/min and 29% of patients with CrCl 15-29 mL/min had at least 1 medication that was contraindicated or dosed too high. Chang et al also found that polypharmacy was the strongest risk factor for a medication being dosed above recommended range. Reasons presented in these studies for this pattern of risk include lack of prescriber knowledge on which medications require dose adjustment, admitted lack of attention to renal function, and inability for the study to account for clinical decision making and therapeutic responses to medications considered inappropriately dosed.

Limited data exist on the state of medication dosing for those residing in a long-term care setting. The study by

Papaioannou et al[23] found that 43% of residents received at least 1 medication inappropriately dosed for their renal function. In this study, 24 of 86 patients (30%) receiving care in a nursing home or assisted living facility had 1 or more medications dosed above recommended range for their renal function which is similar to the incidence found for the whole group. The reasons residing in a long-term care facility is associated with a higher risk of a medication being dosed higher than recommended in this study are unclear but may be related to the aforementioned reasons.

Deprescribing, frequent medication evaluation, and monitoring closely for changes in clinical condition is crucial to patient outcomes. Many of the medications with renal clearance identified in this study are common and used in combination in patients that are hospice eligible. The side effect profiles of opioids, anticoagulants, antihistamines, and antidepressants can be significant and dangerous. In a case report by Whalen et al,[24] a 93-year-old patient in hospice with advanced dementia and severe renal impairment underwent significant polypharmacy reduction of medications that were not dose adjusted for renal function (famotidine, mirtazapine, memantine), lacking indication (inhalers and montelukast), and cause sedation or cognitive impairment (mirtazapine, zolpidem, alprazolam, famotidine). Following the medication changes, the patient's cognition and renal function improved over 2 months, and she was no longer considered to be nearing end-of-life. This report exemplifies the impact medications and polypharmacy can have on a patient's diagnoses, prognosis, and quality of life. An additional interesting feature of this case was the role of memantine, which was dosed above range for the patient's renal function, associated with somnolence, and thought to be a potential cause of the patient's renal impairment due to post-marketing reports of nephrotoxicity. Famotidine, memantine, and mirtazapine were all concerning medications found in this study and frequently used together in practice.

Several limitations for this study exist. The current findings likely underrepresent the scope of the problem, and the study population overall lacks diversity. The included charts were 19% of the total admissions over the 6-month window, which is lower than the previously estimated prevalence of renal impairment in palliative care of 35%–51%.[7] Only patients with a documented ICD10 code were included, which is unlikely to capture those who have age related renal function decline, diagnoses that are less associated with poor renal function, or where there was only narrative mention of poor renal function. The medications reviewed were only those present at time of hospice admission. Any medications that were discontinued immediately preceding hospice admission are unknown. It is common for the authors to see a hospice referral prompt sweeping discontinuation of medications before the actual hospice admission occurs, particularly at hospital discharge. The choice of medication reference for dosing may also contribute to the findings of this study. The package insert is the most basic of sources, while Lexidrug™ provides additional recommendations based on current literature. Other sources of medication dosing information used by prescribers may differ in depth of information. Finally, clinical outcomes were not assessed in correlation with dosing and is a critically important area which should be further explored to determine the impact on patient outcomes.

Conclusion

Hospice-eligible patients are at high risk of medication related adverse effects due to advanced illness, older age, and polypharmacy. It is common to see renally cleared medications dosed above recommended range in these patients. An additional set of medications has been identified that should prompt additional scrutiny and evaluation for safe and appropriate use.

Author Contributions

Primary author NL contributions include study concept and development, data collection, analysis and interpretation, primary manuscript development and submission process. Author KL contributions include statistical analysis, data analysis and interpretation of results, and manuscript development and revision.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The primary author NL is a member of the editorial board for the American Journal of Hospice and Palliative Medicine. Primary author NL declares no other potential conflicts of interest. Author KL declares no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Statement

Ethical Considerations

This study received ethical approval from the University of Buffalo Institutional Review Board on May 31, 2023, STUDY00007372. This is an IRB-approved retrospective study, all patient information was de-identified and patient consent was not required. Patient data will not be shared with third parties.

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