Medication discrepancies in late-stage chronic kidney disease

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Abstract

Background: Late-stage chronic kidney disease (LS-CKD) can be defined by glomerular filtration rate (GFR) 0–30 mL/min. It is a period of risk for medication discrepancies because of frequent hospitalizations, fragmented medical care, inadequate communication and polypharmacy. In this study, we sought to characterize medication discrepancies in LS-CKD.

Methods: We analyzed all patients enrolled in Northwell Health’s Healthy Transitions in LS-CKD program. All patients had estimated GFR 0–30 mL/min, not on dialysis. Medications were reviewed by a nurse at a home visit. Patients’ medication usage and practice were compared with nephrologists’ medication lists, and discrepancies were characterized. Patients were categorized as having either no discrepancies or one or more. Associations between patient characteristics and number of medication discrepancies were evaluated by chi-square or Fisher’s exact test for categorical variables, and two-sample t-test or Wilcoxon text for continuous variables.

Results: Seven hundred and thirteen patients with a median age of 70 (interquartile range 58–79) years were studied. There were 392 patients (55.0% of the study population) with at least one medication discrepancy. The therapeutic classes of medications with most frequently occurring medication discrepancies were cardiovascular, vitamins, bone and mineral disease agents, diuretics, analgesics and diabetes medications. In multivariable analysis, factors associated with higher risk of discrepancies were congestive heart failure [odds ratio (OR) 2.13; 95% confidence interval (CI) 1.44–3.16; P = 0.0002] and number of medications (OR 1.29; 95% CI 1.21–1.37; P < 0.0001).

Conclusions: Medication discrepancies are common in LS-CKD, affect the majority of patients and include high-risk medication classes. Congestive heart failure and total number of medications are independently associated with greater risk for multiple drug discrepancies. The frequency of medication discrepancies indicates a need for great care in medication management of these patients.

Key words: chronic renal failure, chronic renal insufficiency, CKD, diuretics, medications
Introduction

Medication discrepancies can be defined as a mismatch between a treating physician’s understanding of patients’ current medications (including dose and frequency) and the actual medications that the patient takes. Discrepancies have the potential to impair the effectiveness and safety of medication treatment. Ideally, the physician conducts a medication reconciliation with the patient and educates patients about medications. In addition, the physician should maintain good communication with other medical providers regarding medication changes. In actual practice, however, medication discrepancies are frequent, occurring in 34–95% of patients at the time of admission for acute hospitalizations or psychiatric clinics [1, 2]. When discrepancies occur there may be failure to recognize symptoms and signs as medication side effects and increased risk for adverse events [3]. A systematic review of acute hospitalizations found that 11–59% of medication discrepancies were clinically important and 39% had potential to cause moderate-to-severe patient harm [1].

To date there have been no studies of medication discrepancies in late-stage chronic kidney disease (LS-CKD). LS-CKD can be defined as CKD Stages 4–5, prior to the initiation of renal replacement therapy. There are several reasons to suspect that medication discrepancies may be common in LS-CKD. Patients often take multiple medications, reaching a mean of 11.8 by the time of dialysis need [4]. Polypharmacy and conflicting dosing schedules are never easy for patients to manage. This is probably more true in LS-CKD, where patients are usually older and have comorbidities including cognitive decline. In addition, patients with LS-CKD often have multiple different physicians involved in their care. The result can sometimes be care fragmentation with confusion created by numerous drug and dosing changes. Frequent hospitalizations among patients with LS-CKD result in medication and dose changes, often without adequate reconciliation and communication among providers at hospital discharge. In general, communication problems are a recurring theme throughout the care system, contributing to medication risk.

Since 2012, we have operated the Healthy Transitions care management program for patients with LS-CKD. Nephrologist treatment is supplemented by nursing care management services to patients with LS-CKD, in an effort to facilitate care processes and improve preparation for end-stage kidney disease (all such patients were eligible for participation in the program). The program includes patients with CKD Stages 4–5 defined as estimated glomerular filtration rate (eGFR) 0–30 mL/min, and excludes patients (i) on dialysis and (ii) with significant cognitive impairment, defined as need for assistance with activities of daily living. The program began as a pilot, entered a full implementation phase and subsequently had an imbedded randomized controlled trial (RCT) [7] and a 3-year period of funding by Centers for Medicare and Medicaid Innovation program Health Care Innovations Award.

All patients enrolled throughout all program phases from October 2012 to December 2016 were included in the current analysis except for patients from the RCT control group. The justification for inclusion of all of these program phase patients is that all had exactly the same initial home visit with medication review conducted prior to any other interventions. The program functions and patients were enrolled, from Nassau, Suffolk, Queens, Kings and New York counties of New York State. There have been seven different participating nephrology groups. Three of the offices were private practices, four were academic nephrology practices. There was no standardized method for medication history-taking among the nephrologists.

Medication review

Medication discrepancies were defined from the perspective of the nephrologist. Most patients had a recent visit with the nephrologist at the time of program enrollment. After enrollment, a home visit was conducted by a program nurse. The nephrologist’s medication list was printed from the electronic health record (EHR) prior to the home visit. All program nephrologists’ EHRs prompt for medication reconciliation at all patient visits.

Medication reviews were all conducted by one of the program’s registered nurses. All took place during an initial home visit that occurred prior to any other program interventions. The purpose of the home visit is to begin to build a trusting relationship, to assess the patient’s knowledge regarding their kidney disease, to initiate education regarding modality options for renal replacement therapy and diet and most relevant to the current analysis, to conduct a complete medication review.

The medication portion of the visit begins with the nurse asking the patient and key caregiver where in the home medications are kept, and how the patient carries medications if needed during the day. Next, the patient was asked to remove their currently used medication jars from their medicine cabinet or other storage area. In many cases, the nurse helped the patient with this task. Each medication jar was reviewed individually with attention to accuracy. The patient was questioned on (i) how many pills, (ii) how many times a day and (iv) were there any other medications, including over-the-counter agents, herbs or vitamins, that the patient took. The patient was questioned on other medications that were on the nephrologist’s medication list but that the patient was not taking at that time. For any difference between the nephrologist’s list of medications and the patient’s actual medication consumption, a discrepancy and its characteristics were recorded. Although all patients had subsequent medication reviews as part of the program, only the baseline review was included in the current analysis to avoid potential bias introduced by program interventions.

Materials and methods

Patient population

The Healthy Transitions in Late Stage Kidney Disease program began operation in October 2012. The program provides nursing care management services to patients with LS-CKD, in an effort to facilitate care processes and improve preparation for end-stage kidney disease (all such patients were eligible for participation in the program). The program includes patients with CKD Stages 4–5 defined as estimated glomerular filtration rate (eGFR) 0–30 mL/min, and excludes patients (i) on dialysis and (ii) with significant cognitive impairment, defined as need for assistance with activities of daily living. The program began as a pilot, entered a full implementation phase and subsequently had an imbedded randomized controlled trial (RCT) [7] and a 3-year period of funding by Centers for Medicare and Medicaid Innovation program Health Care Innovations Award.

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Table 1. Patient characteristics

| Characteristic                      | n (% or SD) |
|-------------------------------------|-------------|
| Mean age (years)                    | 67.5 (15.9) |
| Male                                | 403 (56.5)  |
| Race                                |             |
| White                               | 434 (60.9)  |
| Black                               | 174 (24.4)  |
| Other or multiracial                | 67 (9.4)    |
| Asian                               | 38 (5.3)    |
| Hispanic ethnicity                  | 64 (9.0)    |
| Hypertension                        | 662 (92.8)  |
| Diabetes                            | 364 (51.1)  |
| Congestive heart failure            | 181 (25.3)  |
| Primary insurance type              |             |
| Medicare                            | 400 (56.1)  |
| Private                             | 239 (33.5)  |
| Medicaid                            | 67 (9.4)    |
| No insurance                        | 7 (1)       |
| Active smoker                       |             |
| Yes                                 | 41 (5.8)    |
| No                                  | 666 (93.4)  |
| Not specified                       | 6 (0.8)     |
| Mean eGFR (mL/min)                  | 18.6 ± 6.4  |
| eGFR category (mL/min)              |             |
| <10                                 | 52 (7.3)    |
| 10–15                               | 188 (26.4)  |
| 15.1–20                             | 178 (25)    |
| >20                                 | 295 (41.4)  |
| Mean number of medications          | 8.1 (3.4)   |

Statistical analyses

Baseline patient demographics (age, gender, race, ethnicity, hypertension, diabetes, congestive heart failure, insurance type, smoking status and eGFR) were described using categorical or continuous variables as appropriate. In the entire patient cohort, the frequency, proportion and type of medication discrepancy was described. Categorization of medication discrepancy type was determined a priori, and included therapeutic class, and any difference between the nephrologist’s list of medications and the patient’s actual medication consumption (i.e. patient taking medication not on nephrologist’s list, patient not taking medication on nephrologist’s list, different dose and/or different frequency, drug discontinued and patient taking, drug discontinued and still on nephrologist’s list or patient not taking medication as instructed).

To evaluate patient characteristics associated with risk for multiple medication discrepancies, we first divided patients into two categories, one with no medication discrepancies and one with one or more discrepancies. We decided on categorization prior to any inspection of results by category. The variables chosen for study were based on availability and then on those with potential causal pathways. In an initial univariable analysis, we used chi-square or Fisher’s exact test as appropriate for categorical variables, and two-sample t-test or Wilcoxon test as appropriate for continuous variables, to evaluate the association of each patient characteristic with the outcome of number of medication discrepancies (no discrepancies versus one or more). In subsequent multivariable logistic regression analysis, factors that were found statistically significant in the univariable analysis plus age and gender were taken as the candidate variables for the final model. We conducted all analyses using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Table 2. Frequency distribution of number of medication discrepancies per patient

| Medication discrepancies per patient | Number | Percentage |
|--------------------------------------|--------|------------|
| 0                                    | 321    | 45.0       |
| 1                                    | 125    | 17.5       |
| 2                                    | 83     | 11.6       |
| 3                                    | 57     | 8.0        |
| 4                                    | 41     | 5.8        |
| 5                                    | 19     | 2.7        |
| 6                                    | 24     | 3.4        |
| 7                                    | 14     | 2.0        |
| 8                                    | 4      | 0.6        |
| 9                                    | 5      | 0.7        |
| 10                                   | 1      | 0.1        |
| 11                                   | 3      | 0.4        |
| 12                                   | 3      | 0.4        |
| 13                                   | 1      | 0.1        |
| 14                                   | 2      | 0.3        |
| 15                                   | 1      | 0.1        |
| 16                                   | 1      | 0.1        |
| 17                                   | 0      | 0.0        |
| 18                                   | 1      | 0.1        |

Results

A total of 713 patients were reviewed who were enrolled from October 2012 to December 2016. In the entire cohort, the median age was 70 (interquartile range (IQR) 58–79) years, 56.5% were men, 24.4% were black, 60.9% were white, 9% were Hispanic, 51.1% were diabetic and 92.8% had hypertension. Patient characteristics are displayed in Table 1. The distribution of eGFR was <10 mL/min, 7.3%; 10–15 mL/min, 26.3%; 15.1–20 mL/min, 25%; >20 mL/min, 41.4%. Six patients had previously undergone kidney transplantation. The median time from last nephrologist medication reconciliation to nurse visit was 3 (IQR 1–6) days.

There were 392 patients (55.0% of the study population) with at least one medication discrepancy. The total number of discrepancies was 1280, and the median number of discrepancies per patient (in patients with at least 1 discrepancy) was 2 (IQR 1–4). The distribution of discrepancies per patient is displayed in Table 2. There were 321 patients with zero discrepancies (45%), 125 patients with one discrepancy and 83 patients with two discrepancies. There were 12.1% of patients with five or more discrepancies. The most common type of discrepancies were patients taking a medication not on nephrologist’s list (49.1% of discrepancies), patients not taking a medication on the nephrologist’s list (24% of discrepancies), patients not taking medication on nephrologist’s list, different dose and/or different frequency, drug discontinued and patient taking, drug discontinued and still on nephrologist’s list or patient not taking medication as instructed.

When assessing the outcome of multiple medication discrepancies, there were 321 patients with no discrepancies, and 392 patients with one or more discrepancies. In a univariable analysis, the following patient characteristics were found to be associated with medication discrepancies (P < 0.05): congestive
heart failure, white race, hypertension and number of medications taken (Table 3). In subsequent multivariable logistic regression analysis, factors that were found statistically significant in the univariable analysis plus age and gender were taken as the candidate variables for the final model. After backward variable selection, factors in the final model independently associated with higher risk of one or more medication discrepancies compared with zero discrepancy were congestive heart failure [odds ratio (OR) 2.13; 95% confidence interval (CI) 1.44–3.16; \( P = 0.0002 \)] and number of medications (OR 1.29; 95% CI 1.21–1.37; \( P < 0.0001 \)) (Table 4).

**Discussion**

We found that more than half of patients with LS-CKD had at least one discrepancy between the nephrologist’s medication record and the medications actually being consumed. Approximately one-third of patients had two or more discrepancies. Most discrepancies were related to medications being taken that were not on the nephrologist’s list, medications on the nephrologist’s list that were not being taken, and dose and frequency differences.

Effective medication management is achieved by optimizing the benefits and reducing risks of treatment. Ongoing medication review and reconciliation by the provider is essential for longitudinal maintenance of medication safety. When discrepancies develop between the medications that the provider intends for the patient to be taking and those actually being used, there is increased risk for loss of efficacy or adverse events. Discrepancies can be highly relevant, with a recent study finding that in intensive care units, 17.1% of discrepancies were serious or potentially life-threatening [8].

In the treatment of patients with LS-CKD, the medication management process is fraught with polypharmacy, extensive comorbidity and altered medication pharmacology due to reduced renal function, fragmented medical care and frequent hospitalizations. The nephrologist plays a key and often principal role in maintenance of medication safety in these patients.
Our finding of a high rate of medication discrepancies signifies an important gap in performance and opportunity for improvement in LS-CKD. The fact that more than one-third of patients had two or more discrepancies is a strong indicator of the magnitude of the problem.

It is concerning that cardiovascular medications were the most commonly discrepant class of medication and diuretics the fourth most common, because of the hemodynamic and metabolic effects of these agents. This aligns with the finding that congestive heart failure as comorbidity was a key independent predictor of multiple discrepancies. It is likely that concordant cardiac disease creates important vulnerabilities in medication management in LS-CKD. The diseases complicate and confound treatment of each other. Medications such as renin angiotensin aldosterone system inhibitors and diuretics are adjusted frequently in response to cardiac, renal or electrolyte disturbances. When the medications are changed, communication between physicians may often be suboptimal.

| Patient characteristics | Zero discrepancies (n = 321) | >1 discrepancy (n = 392) | P-value |
|-------------------------|-------------------------------|--------------------------|---------|
| Mean number of discrepancies (SD) | 68.0 ± 15.8 | 67.3 ± 16.1 | 0.40 |
| Gender, n (%) | Male 172 (42.7), Female 149 (48.1) | 231 (57.3), 161 (51.9) | 0.15 |
| Race, n (%) | White 177 (40.8), Black 89 (51.2) | 257 (59.2), 85 (48.9) | 0.03 |
| Hispanic ethnicity, n (%) | Yes 33 (51.6), No 288 (44.4) | 31 (48.4), 361 (55.6) | 0.27 |
| Hypertension, n (%) | Yes 289 (43.7), No 32 (62.8) | 373 (56.3), 19 (37.2) | 0.90 |
| Diabetes mellitus, n (%) | Yes 163 (44.8), No 158 (45.3) | 201 (55.2), 191 (54.7) | 0.0004 |
| Congestive heart failure, n (%) | Yes 61 (33.7), No 260 (48.9) | 120 (66.3), 272 (51.1) | 0.82 |
| Current smoker, n (%) | Yes 20 (48.8), No 298 (44.7) | 21 (51.2), 368 (55.3) | 0.23 |
| Insurance status, n (%) | Medicaid 37 (55.2), Medicare 180 (45.0) | 30 (44.8), 220 (55.0) | 0.08 |
| Number of medications | 1.29 (1.21–1.37) | <0.0001 |

Table 3. Univariate association of patient characteristics and number of medication discrepancies

| Variables | Odds ratio (95% confidence interval) | P-value |
|-----------|-------------------------------------|---------|
| CHF (yes versus no) | 2.13 (1.44–3.16) | 0.0002 |
| Number of medications | 1.29 (1.21–1.37) | <0.0001 |

Table 4. Multivariable analysis for medication discrepancy (logistic regression)

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Conflict of interest statement
None declared.

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