Underprescription of Renin–Angiotensin System Blockers in Moderate to Severe Chronic Kidney Disease

Shayan Shirazian, MD, Candace D. Grant, MD, Shanza Mujeeb, MD, Sairah Sharif, MBBS, Pooja Kumari, MBBS, Milind Bhagat, MBBS and Joseph Mattana, MD

Abstract: *Background:* Renin–angiotensin system (RAS) blockers slow the progression of chronic kidney disease (CKD). Despite this, up to 40% of patients with CKD and an indication for RAS blockade do not receive these medications. The purpose of this study was to examine variables associated with the prescription of RAS blockers in patients with CKD and to identify opportunities to increase their use. *Methods:* The electronic medical records of patients with moderate to severe CKD and an indication for RAS blockade were reviewed. For patients with an indication for RAS blockade who were not prescribed these medications, previous notes were reviewed to ascertain reasons why RAS blockade was not prescribed. *Results:* Six hundred twenty-seven patients with moderate to severe CKD and an indication for RAS blockade were identified. Of these patients, 225 (36%) were not prescribed RAS blockade. This group was found to have significantly less diabetes, to be significantly older and to have significantly lower estimated glomerular filtration rate and blood pressure than the group on RAS blockade. For the majority (59%), no documented reason for not being prescribed RAS blockade was found. Among documented reasons, hyperkalemia and a history of acute kidney injury were the most common. *Conclusions:* The authors found that a large proportion of patients with CKD and an indication for RAS blockade were not prescribed these medications. For the majority, there was no provider-documented reason explaining why these medications were not prescribed, and the findings suggest that there may be opportunities to increase RAS blocker prescribing.

Key Indexing Terms: Angiotensin-converting enzyme inhibitor; Angiotensin receptor blocker; Chronic kidney disease; Proteinuria; Electronic medical records. **[Am J Med Sci 2015;349(6):510–515.]**

Renin–angiotensin system (RAS) blockade with an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin receptor blocker (ARB) has been shown to slow progression to end-stage renal disease in patients with diabetes and moderately increased albuminuria and in patients with severely increased albuminuria with or without diabetes.[1–5] Accordingly, the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend that healthcare providers should prescribe RAS blockers for these patients regardless of the stage of chronic kidney disease (CKD).[6]

In the United States and worldwide, 20% to 40% of those patients with CKD and an indication for RAS blockers are not prescribed these medications.[7–12] Past studies aimed at improving rates of RAS blocker prescription using health system interventions, including clinical decision support systems, have failed to improve these rates.[11,13,14] These previous interventions targeted healthcare providers who were unaware of RAS-prescribing guidelines and attempted to prompt these providers to prescribe RAS blockers when appropriate. There are, however, other potential reasons why providers are not prescribing RAS blockade in patients with CKD, including previous development of acute kidney injury (AKI), hypotension, allergy or hyperkalemia, as well as situations like renal artery stenosis and advanced CKD in which the provider may not think RAS blockade is appropriate. Health system interventions may have failed to improve RAS blockade prescription rates not because providers are unaware of CKD treatment guidelines but rather because providers believe RAS blockade is inappropriate and are ignoring prompts to start these medications.

Unfortunately, few studies have examined the reasons why patients with moderate to severe CKD (stage 3–5) are not being prescribed RAS blockade,[15,16] and to the best of the authors' knowledge, no studies have examined reasons why nephrologists, a group that is presumably aware of CKD treatment guidelines, are not prescribing RAS blockade for their patients. To improve provider prescription of RAS blockers, it may be helpful to identify factors affecting the prescription of these medications by nephrologists. The purpose of this study was to determine factors associated with the prescription of RAS blockers and to elucidate descriptive reasons for not prescribing them in patients with CKD and an indication for their use.

METHODS

Patient Population and Setting

In this cross-sectional study, the electronic medical record (EMR) of adult patients with stage 3, 4 or 5 CKD seen at an outpatient academic nephrology practice at least once within a 2-year period from October 2011 to October 2013 was reviewed. Stage 3 to 5 CKD was verified by 2 estimated glomerular filtration rate (eGFR) measurements of <60 mL/min per 1.73 m^2 at least 3 months apart. The eGFR was calculated using the 4-variable Modified Diet in Renal Disease (MDRD) equation.[17]

Albuminuria/Proteinuria Assessment

Patients were considered to have albuminuria/proteinuria if they had (1) a spot urine albumin to creatinine ratio (UACR) greater than 30 μg/mg during the study period, (2) a spot urine protein to creatinine ratio (UPCR) greater than 150 mg/g, (3) a 24-hour urine albumin or protein collection greater than the above values and/or (4) a diagnosis of proteinuria by *ICD-9* coding or medical history regardless of UACR, UPCR or 24-hour testing values. For patients in whom UPCR alone was available but UACR was not, a linear regression equation was used to calculate urine albumin from urine total protein.[18]

From the Division of Nephrology, Department of Medicine, Winthrop University Hospital, Mineola, New York.

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Correspondence: Shayan Shirazian, MD, Division of Nephrology, Department of Medicine, Winthrop University Hospital, 200 Old Country Road, Suite 135, Mineola, NY 11501 (E-mail: sshirazian@winthrop.org).

Study Inclusion

Patient records were chosen for study inclusion if they had stage 3 to 5 CKD and an indication for RAS blockade. These indications included (1) patients with diabetes and albuminuria/proteinuria (UACR >30 μg/mg or UPCR >150 mg/g or equivalent 24-hour values), (2) patients, regardless of the diabetes status, with UACR >300 μg/mg or UPCR >500 mg/g or equivalent 24-hour values, (3) patients with a diagnosis of albuminuria/proteinuria and (4) patients on an RAS blocker regardless of the level of albuminuria/proteinuria (these patients were assumed to have an indication for RAS blockade).

EMR Review

For study patients with an indication for RAS blockade, a review of the EMR was performed to evaluate for ACEi or ARB prescription during the 2-year study period. For study patients not prescribed an ACEi or ARB, the EMR was additionally reviewed to ascertain reasons why their providers did not prescribe these medications. This involved a manual review of all progress notes written by the patient's provider that were available through the outpatient EMR, in some cases going back 10 or more years, to find provider-documented reasons why an RAS blocker was not prescribed. Reviewed notes included handwritten notes before the adoption of the EMR by the practice in 2012 that were scanned into the EMR (free-hand, nontemplate notes) and electronic notes that were written after the adoption of the EMR (notes with areas of free text and structured data entry). The reasons for not being on an RAS blocker were classified into 10 categories as follows: no documented reason found, hyperkalemia, history of AKI, hypotension, discontinued by another physician and chosen not to be restarted by the current physician, allergy, provider documented that RAS blockade was not indicated, renal artery stenosis, advanced CKD and other.

Statistical Analysis

Variables were displayed as mean ± SD for continuous variables and total number (percentage) for categorical variables. Groups receiving and not receiving an RAS blocker were statistically compared to define any differences between the groups. Continuous parametric variables were compared using unpaired *t* tests, and continuous nonparametric variables were compared using Mann-Whitney's *U* tests. Categorical variables were compared using Fisher's exact test.

RESULTS

The EMR of 932 patients with stage 3, 4 or 5 CKD was reviewed, and 627 patients with an indication for RAS blockade were identified. Of the 627 patients with an indication for RAS blockade, 402 patients or approximately 64% were prescribed an RAS blocker during the 2-year study period (Figure 1). Of the patients prescribed an RAS blocker, 9 patients (2%) were prescribed dual blockade with both an ACEi and an ARB. The baseline characteristics of the entire study group including subgroups receiving and not receiving an RAS blocker are listed in Table 1. The mean age of this group was 69 years, 59% were men, 78% were white and 55% had diabetes. The mean eGFR was 32 mL/min per 1.73 m^2, the mean serum potassium level was 4.6 mEq/L and the mean UACR was 909 μg/mg. In the subgroup of 225 patients with an indication for RAS blockade and not on these medications, the majority had stage 4 or 5 disease (55%). This subgroup of patients were found to be significantly older (72 versus 67 years, $P < 0.001$) and were found to have significantly lower eGFR (29 versus 34 mL/min per 1.73 m^2, $P < 0.001$), blood pressure (BP) (129/70 versus 133/73 mm Hg, $P < 0.020$) and body mass index (27.9 versus 30.6 kg/m^2, $P < 0.001$). They were also found to less often have diabetes (60% versus 45%, $P < 0.001$) than the subgroup of patients with an indication for an RAS blocker who were receiving these medications (Table 1).

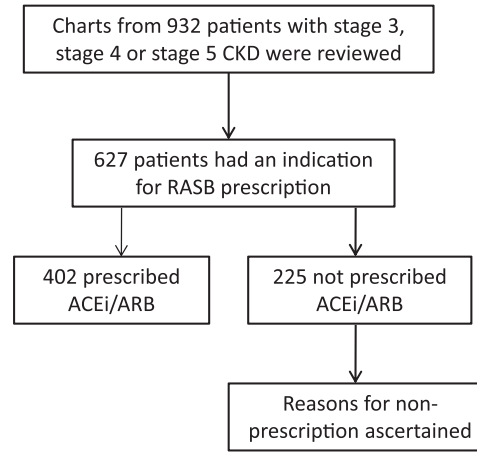

FIGURE 1. Study flowchart. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; RASB, renin–angiotensin system blockade.

In the subgroup of patients who had an indication for an RAS blocker and were not on these medications, a chart review was performed to ascertain provider-documented reasons why these medications were not prescribed and to determine whether RAS blockade was prescribed in the past. The authors found that 96 of the 225 patients (43%) not on RAS blockade at the time of their last study visit had previously been on RAS blockade (review of outpatient charts went back as far as 10 years). For the majority of patients not on RAS blockade (59%), no documented reason was found for not being on these medications. Table 2 lists the frequency of provider-documented reasons for not prescribing RAS blockers. The top 5 most commonly documented reasons included AKI (13%), hyperkalemia (10%), hypotension (6%), allergy to ACEi or ARB (4%) or discontinued by another provider (2%). The authors were able to identify the percent increase in creatinine, which led the provider to stop RAS blockade, in 23 of the 29 patients documented to have AKI. The average percent rise in creatinine for patients with AKI was 55%, with 82% having a rise of greater than 30% and 18% having a rise of less than 30%. For patients with provider-documented hyperkalemia as a reason for not being on RAS blockade, 74% (17 of the 23) developed hyperkalemia while on RAS blockade causing it to be discontinued and 26% (6 of the 23) were not started on RAS blockade because of hyperkalemia. With advancing CKD (stage 4 and stage 5), a larger percentage of patients were not receiving an RAS blocker (43% in stage 4 CKD and 66% in stage 5 CKD), but a reason for not prescribing these medications was more commonly provided (Table 3).

DISCUSSION

In this study, the authors examined RAS blocker prescribing patterns for patients with moderate to severe CKD and an indication for RAS blockade in an academic nephrology practice. They attempted to gain insights into patient variables associated with RAS blockade and reasons documented by