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Research Article

The Impact of Implementing a Pharmacist-led Deprescribing Program on Medication Adherence among Hemodialysis Patients

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Abstract

Background: One way to target polypharmacy and inappropriate medication in hemodialysis (HD) patients is with medication deprescribing. ***Objective***: To assess the impact of implementing a pharmacist-led deprescribing program on medication adherence among HD patients. ***Method***: A prospective interventional, one-group pretest-posttest-only design study was conducted at a hemodialysis center in Wasit Governorate, Iraq. Medication reconciliation followed by medication review based on the deprescribing program was done for all eligible patients, and the patients were monitored for three months for any possible complications. ***Results***: Two hundred and seventy patients were screened for eligibility. Only one hundred and eighteen were enrolled in the deprescribing program. The median age was 51.5 years, 56.8% were males, and hypertension was the most common etiology for their chronic kidney disease (CKD); 78% had comorbidities. After deprescription, there was a significant reduction in the number of medications from 6.0 to 4.0 and a reduction in the number of pills from 7.0 to 5.0. Medication adherence accessed using the Arabic version of Morisky, Green, and Levine's (MGL) adherence scale also had a significant reduction from 2.0 to 1.0. ***Conclusion***: A pharmacist-led deprescribing program is a successful strategy for decreasing the number of medications and daily pills prescribed while simultaneously improving hemodialysis patients' adherence to their regimens without compromising the patient's safety.

Keywords: Adherence, Chronic kidney disease, Deprescribing practice, Hemodialysis, Iraqi patients.

تأثير تنفيذ برنامج تقليل الأدوية بأشراف الصيدلي على الالتزام الدوائي بين مرضى غسيل الكلى الدموي

الخلاصة

الخلفية: مرضى غسيل الكلى لديهم أعلى الوصفات الطبية من بين جميع المرضى المصابين بأمراض مزمنة مما يعرضهم لخطر كثرة الادوية واستخدام الأدوية الغير المناسبة. في المتوسط ، يستخدم مرضى غسيل الكلى ما بين 10 إلى 14 دواءً مختلفًا يوميًا. وهذا يزيد من خطر الاستخدام غير الضروري للأدوية، والآثار الضارة، والتفاعلات الدوائية ويقلل من جودة الحياة المرتبطة بالصحة والالتزام الدوائي. تتمثل إحدى طرق استهداف تعدد الأدوية والاستخدام غير الملائم للأدوية في عملية تقليل الادوية لمرضى غسيل الكلية بشكل ممنهج وآمن. **الهدف:** تقييم تأثير تنفيذ برنامج تقليل الادوية بقيادة الصيدلاني على على عدد الادوية والالتزام الدوائي بين مرضى غسيل الكلى. **الطريقة:** تم إجراء دراسة تداخلية مستقبلية، أحادية المجموعة بالاختبار الاولي والمراجعة اللاحقة فقط في مركز غسيل الكلى، محافظة واسط، العراق. تم إنشاء قائمة دوائية دقيقة تحوي جميع الأدوية التي يتناولها المرضى وكيفية استخدامها متبوعة بمراجعة الأدوية بناءً على برنامج تقليل الادوية لجميع المرضى المؤهلين، وتم مراقبة المرضى لمدة 3 أشهر بحثًا عن أي مضاعفات محتملة. **النتائج:** تمت معاينة مئتان وسبعون مريضا لغرض ادخالهم في برنامج تقليل الادوية ولكن شروط الادخال توفرت في مائة وثمانية عشر مريضا فقط. كان متوسط العمر 51.5 سنة، كان 56.8٪ من الذكور، وكان ارتفاع ضغط الدم أكثر المسببات شيوعًا لمرض الكلى المزمن، وكان 78٪ منهم يعانون من أمراض مصاحبة غير ارتفاع ضغط الدم ومرض الكلى المزمن. بعد تنفيذ البرنامج، كان هناك انخفاض معنوي في عدد الأدوية من 6.0 إلى 4.0 وانخفاض في عدد الجرع اليومي من 7.0 إلى 5.0. الالتزام الدوائي الذي تم قياسه باستخدام النسخة العربية لمقياس الالتزام مورسكي كان له أيضًا انخفاض معنوي من 2.0 إلى 1.0. **الاستنتاج:** يعد تنفيذ برنامج تقليل الادوية الذي يقوده الصيدلاني استراتيجية ناجحة من حيث تقليل عدد الأدوية والجرع اليومية الموصوفة مع تحسين التزام مرضى غسيل الكلى في الوقت نفسه بأنظمتهم الدوائية دون التعرض لخطر المساس بسلامة المريض.

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INTRODUCTION

A significant proportion of individuals diagnosed with end-stage renal disease (ESKD) also suffer from hypertension, diabetes, and cardiovascular disease, among others. Furthermore, there is an elevated likelihood that these individuals will develop numerous complications, including hyperlipidemia, hypocalcemia, hyperphosphatemia, hyperkalemia, metabolic acidosis, and anemia [1]. The intended purpose of the medications is to treat or prevent these conditions. As a result, hemodialysis (HD) patients are at an increased risk for polypharmacy [3] due to their prescription loads being the greatest among chronically ill patients [2]. HD patients take, on average, fourteen to ten distinct medications daily. Patients who routinely use eleven medications frequently ingest nineteen tablets per day; this reduces health-related quality of life and adherence and increases the risk of adverse effects, drug interactions, and unnecessary medication use [4]. As "the use of multiple medications or the use of more medications than are medically necessary" [5] is an alternative definition of polypharmacy that lacks consensus. A decreased adherence to prescribed regimens, an elevated risk of adverse effects, hospitalization, and mortality are all associated with it [6]. Among patients undergoing hemodialysis for ESKD, medication nonadherence is a relatively prevalent issue, with an average prevalence rate of 52.5%. [7]. There are two types of medication nonadherence: deliberate and inadvertent. Intentional nonadherence transpires when patients disregard treatment recommendations by prolonging, altering, or excluding prescribed medication dosages. Conversely, unintentional nonadherence may arise due to factors such as a patient misinterpreting instructions, neglecting to communicate with healthcare providers, or negligence. [8] Nonadherence to prescribed medications, whether deliberate or negligent, hinders patients from attaining the full potential of the therapeutic advantages associated with those medications. Furthermore, there is a correlation between medication nonadherence and a heightened likelihood of mortality, hospitalizations, comorbidities, and diminished quality of life among patients with ESKD [9]. Medications deprescribing is one strategy for addressing polypharmacy and improper medication use. Deprescribing is a method that is deliberately and under supervision reduced or discontinued medication usage (or discontinuation of medications that may be harmful or no longer beneficial) in order to improve outcomes, decrease polypharmacy, and preserve or enhance quality of life. [10,11] In 2002, the expression "deprescribing" was initially documented in the medical literature. Deprescribing effectively reduces unnecessary medications and mitigates adverse drug effects, resulting in decreased healthcare expenditures, improved adherence and quality of life, and decreased hospitalizations and mortality rates, according to the available evidence [10]. A multitude of deprescribing instruments have been created with the intention of aiding healthcare practitioners in the reduction of inappropriate medication use and polypharmacy among the elderly [12]. The utilization of these tools has yielded substantial favorable results, including reduced expenditures on medications, a diminished need for transfers to long-term care facilities, decreased mortality rates, and an enhanced perception of overall health. Significantly, the aforementioned advantages were realized while mitigating the potential for enduring detrimental outcomes. It is important to note, however, that the development of these tools was predicated on safety and efficacy data pertaining to the geriatric population and that their applicability may be limited to hemodialysis patients, for whom their validation has not yet been established [2]. Despite the existence of several recommendations concerning the deprescribing of medications among hemodialysis patients, there is a paucity of research on this particular subject [13]. Numerous studies on patients with chronic illnesses, including persistent asthma [14–17], diabetes mellitus [18–21], and ESKD [22–26], have been conducted in Iraq. Additionally, medication adherence has been evaluated among various patient populations [27,28]. As far as our understanding goes, there is a dearth of research examining the impact of deprescribing on medication adherence in the dialysis patient population. Thus, the purpose of this research is to assess the effect of a proactive deprescribing program conducted by a pharmacist on medication adherence among hemodialysis patients.

METHODS

Study design and setting

This prospective interventional, one-group pretest-posttest-only design study was conducted at the Wasit Center for Hemodialysis, Wasit Governorate, Iraq, from November 2022 to April 2023.

Study population

Patients who were at least 18 years old, on hemodialysis for at least three months, and gave oral consent to participate in the study were screened for eligibility. Inpatient hemodialysis patients admitted to the hospital during data collection, those who were not willing to participate in the study, and those with hearing, speech, or cognitive impairments that would hinder their ability to comprehend the study questionnaires are excluded. Figure 1 shows the patients' recruitment flow chart.

Data collection

A data collection document was formulated by the researcher in order to amass the necessary information for the present study. The following information was gathered from each participant in the study via a self-administered questionnaire: Fundamental demographic attributes: Mature and female Disease and comorbidity information: etiology of chronic

kidney disease (CKD), presence of other chronic diseases besides CKD, and hypertension; medication usage details for patients, including quantity, name, dosage, and frequency of tablets. Additional details include the need for a caregiver, the cycle number of dialysis, and the timetable.

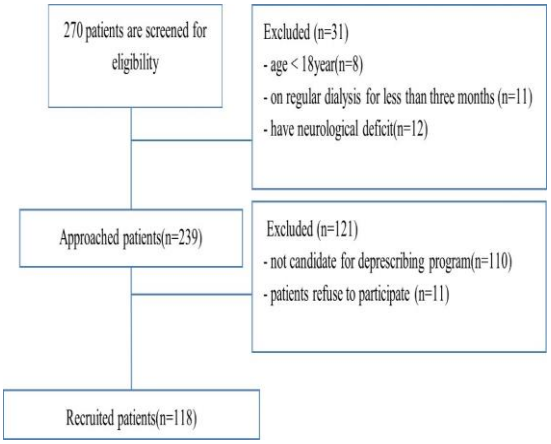

Figure 1: Patients' recruitment flow chart.

Assessing patient's adherence

The Arabic version of the Morisky, Green, and Levine Medication Adherence Scale (MGL) was used to assess how well patients on hemodialysis adhered to their prescribed medication. MGL is a 4-item generic medication-adherence tool that was developed in 1986. It was first tested on 290 patients with hypertension and proved to be consistent and reliable. Since then, it has been used for assessing non-adherence to several health conditions [29]. The MGL Medication Adherence Scale employs a scoring system where a response of "yes" is assigned a value of 1, while a response of "no" is assigned a value of 0 for each item question. The total score on this scale can range from 0 to 4. The aggregate of "yes" responses provides an overall measure of non-compliance. Lower scores indicate a greater level of adherence. The total patient scores can be categorized as high adherence level (zero items answered "yes"), moderate adherence level (one to two items answered "yes"), or poor adherence level (three to four items answered "yes") [30]. It is common to use a dichotomous adherence definition based on the MGLS, where 0 indicates perfect adherence while 1+ represents some degree of non-adherence [31].

The deprescribing program

The program was developed based on comprehensive literature reviews and all the latest guidelines and recommendations for the treatment of patients on hemodialysis. The program was made up of the deprescription tools as shown in Box 1.

Deprescribing protocol

A list was made of all medications a patient was taking, including prescription drugs, over-the-counter drugs, herbal remedies, and supplements. It involved the following information: name, indication, duration of use, dosage, and frequency. Then, the medication list is reviewed to determine the eligibility of each medication to be deprescribed (based on the deprescribing program).

Box 1: Deprescription tools used in the study

1. Patients should stop diuretics when their daily urine output falls below 200 ml. Patients were asked to monitor their urine output on the day before HD.
2. Justify the use of proton pump inhibitors (PPIs) and prokinetics medication and stop using them when there are no current indications to begin or continue.
3. Allopurinol and febuxostat (Uric acid lowering drugs) should be stopped when serum uric acid is less than 12 mg/dl, and the patient has no history of nephrolithiasis or gout.
4. Stop taking oral iron supplements. Instead, intravenous Iron is used to treat iron deficiency. It is unnecessary to stop using iron-containing binding agents when they are used as a reduction agent for phosphate.
5. Sodium bicarbonate supplements should be stopped when serum bicarbonate equals or exceeds 24 mEq/L.
6. When available, fixed-dose combinations (FDC) are used rather than multi-pills to reduce the pill number.
7. Recommend extended-release drug formulations (when available) to reduce the medication dosage frequency.
8. Stop using calcium supplements and calcium-based phosphate-binding drugs if total serum calcium levels exceed 9.5 mg/dl.
9. When serum calcium is more than 9 mg/dl. Calcium supplements and calcium-containing phosphate binders should be stopped.
10. When serum phosphate falls below 5 mg/dl and PTH within the range of 150-600 pg./ml. Phosphate binders should be stopped.
11. Ensure all medications are administered with the correct renal dose adjustments.
12. Patients with benign prostate hyperplasia on alpha-blockers should be stopped if they are anuric.
13. All contraindicated and poor evidence drugs in hemodialysis patients should be stopped.
14. If a patient is taking both OADs and insulin and has not achieved an acceptable glycemic level, the OADs should be stopped.

Issues identified during the medication review were communicated to the nephrologist to decide whether the medication has to be deprescribed or a specific action is needed. The patients were monitored weekly by in-person interviews for any potential adverse effects and to ensure that a deprescribed medication was restarted. The patients were followed up for three months to identify any possible complications. Figure 2 summarizes the steps of the deprescribing process.

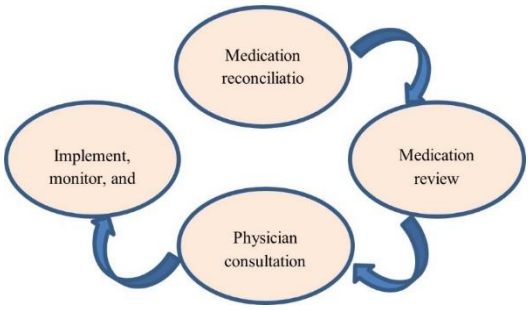

Figure 2: The steps of the deprescribing process.

Study outcomes

Primary outcomes are the average number of pills and medications per patient and the adherence of patients before and three months after the implementation of the program. Patient safety is the secondary outcome.

Ethical approval

The Scientific and Ethical Committee at the "College of Pharmacy, University of Baghdad" approved the

study after the researcher submitted a proposal describing the study's objectives and methods in detail. In addition, Ministry of Health authorization was obtained. Patients' consent to participate in the investigation was verbally obtained.

Statistical analysis

The IBM SPSS Statistics version 25 software for Microsoft Windows was used for the statistical analysis. The distribution of data was assessed using the Shapiro-Wilk test. Because they are not normally distributed, continuous variables are presented as medians (interquartile ranges), while categorical variables are presented as frequencies and percentages. The Mann-Whitney test was used to determine the influence of continuous variables on medication adherence, while the Pearson chi-square was used to assess the association between categorical variables. In addition, differences between the medians of pairs of measurements made before and after the deprescription were compared with the Wilcoxon signed-rank test. A P-value of less than 0.05 was considered statistically significant.

RESULTS

One hundred and eighteen patients were enrolled in the deprescribing program. The median age of patients was 51.5 years (IQR 39–62). Male patients constituted 56.8% of them, while female patients constituted 43.2%.

Table 1: Baseline characteristics of participants

Characteristics	*n*=118
Age-years	
Median (IQ)	51.5(39-62)
Gender *n*(%)	
Male	67(56.8)
Female	51(43.2)
Etiology of CKD *n*(%)	
Diabetic nephropathy (DN)	36(30.5)
Hypertension (HT)	59(50)
Others	23(19.5)
Dialysis vintage (months)	
Median (IQ)	24(11-48)
Dialysis schedule *n*(%)	
Twice weekly	52(44.1)
Thrice weekly	66(55.9)
Comorbidities other than CKD and HT *n*(%)	
Yes	92(78)
No	26(22)
Need for care giver *n*(%)	
Yes	45(38.1)
No	73(61.9)
Number of medications	
Median (IQ)	6(4.75-7)
Number of pills	
Median (IQ)	7(6-9)

Hypertension was the most prevalent etiology for CKD (50%), followed by diabetic nephropathy (30.5%) and renal disease (19.5%) for others. The median number of medications and pills was 6 (4.75-7) and 7 (6-9), respectively. All enrolled patients' baseline characteristics are shown in Table 1. Based on participants' responses to Morisky, Green, and Levine's (MGL) adherence scale, twenty-seven patients (22.9%) adhered to their prescribed medication regimen effectively. This means patients took their medications exactly as prescribed, without missing or stopping doses on their own unless they consulted their physician. Fifty-two patients (44.1%) had some difficulty adhering to their prescribed medication regimen. This means they may occasionally ignore taking their medication or omit doses without calling their physician. Thirty-nine patients (33.1%) adhered poorly to their prescribed medication regimen (Figure 3).

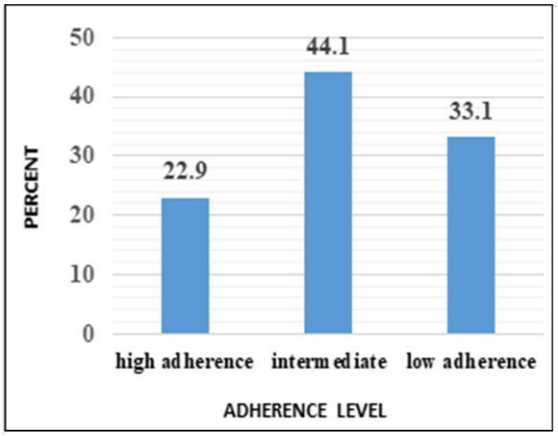

Figure 3: Patient's distribution according to adherence level

The participants reported that forgetfulness and stopping medication use when they felt worse or better were the two main causes of nonadherence to medication regimens. Carelessness regarding medication use was also documented in lesser proportions of participants (Table 2).

Table 2: Patient's responses to Morisky, Green, and Levine (MGL) adherence scale

Questions	*n*(%)	
	Yes	No
Do you ever forget to take your medicine?	81(68.6)	57(48.3)
Are you careless at times about taking your medicine?	19(16.1)	99(83.9)
When you feel better, do you sometimes stop taking your medicine?	61(51.7)	37(31.4)
Sometimes, if you feel worse when you take the medicine, do you stop taking it?	60(50.8)	58(49.2)

In terms of the influence of age, dialysis vintage, number of medications, and number of pills on medication adherence, there was a significant difference in adherence according to five parameters: age, dialysis vintage, number of medications, and number of pills (Table 3). Patients with comorbidities or those who do not have a caregiver are more likely to be nonadherent. Patients with comorbidities or who did not have a caregiver, in other words, were more likely to have poor medication adherence (Table 4).

Table 3: The relationship between patient characteristics and medication adherence

Parameters *n*(%)		Medication adherence		*p*-value
		Adherent	Nonadherent	
Gender	Male	14(20.9)	53(79.1)	0.556
	Female	13(25.5)	38(74.5)	
Etiology of CKD	HT	14(23.7)	45(76.3)	0.172
	DN	5(13.9)	31(86.1)	
	Others	8(34.8)	15(65.2)	
Presence of comorbidities	Yes	14(15.2)	78(84.8)	0.000*
	No	13(50)	13(50)	
Dialysis schedule	Twice weekly	15(28.8)	37(71.2)	0.171
	Thrice weekly	12(18.2)	54(81.8)	
Presence of a caregiver	Yes	44(97.8)	1(2.2)	0.000*
	No	47(64.4)	26(35.6)	

*Mann-Whitney U test

Table 4: Influence of continuous variables on medication adherence

Parameters	Medication adherence	*n*	Median rank	*p*-value*
Age	adherent	27	40	0.001
	nonadherent	91	55	
Dialysis vintage	adherent	27	18	0.029
	nonadherent	91	36	
Number of medications	adherent	27	4	0.000
	nonadherent	91	6	
Number of pills	adherent	27	5	0.000
	nonadherent	91	8	

* Chi-Square test

After implementing the deprescribing program, there was a significant decline in the median of the measured outcomes before and after conducting the deprescribing program, as shown in Table 5. At the end of the 3-month follow-up period after deprescribing, there were two mortality cases (a 74-year-old male due to acute coronary syndrome and a 68-year-old male due to hemorrhagic stroke). In the first patient, three medications were deprescribed (oral iron, vitamin D supplement, and PPI); in the second one, two medications were deprescribed (domperidone and calcium supplements). In addition, three patients were hospitalized—two for respiratory tract infections and one for pulmonary congestion resulting from a missed dialysis session.

Table 5: Number of medications and pills and MGL scores before and after conducting the deprescribing program

Outcome variables	Pre	Post	*p*-value*
	Median (IQR)	Median (IQR)	
Number of medications	6.00 (4.75-7.00)	4.00 (3.00-5.00)	0.000
Number of pills	7.00 (6.00-9.00)	5.00 (4.00-6.00)	0.000
MGL adherence scale	2.00 (1.00-3.00)	1.00 (0.00-2.00)	0.000

* Wilcoxon signed-rank test

DISCUSSION

Nonadherence is a significant issue among ESRD patients due to both its prevalence in the population and its influence on health outcomes. By increasing the efficiency of adherence interventions, the population's health will be positively impacted more than any medical treatment [8]. In our study, nonadherence to the prescribed medication was highly prevalent among participants. Based on the MGL adherence scale, more than three-quarters (77.2%) of enrolled patients had poor medication adherence before deprescribing. This finding was higher than those reported in previous studies [27,32]. The high prevalence of multimorbidity among the participants provides a potential explanation for this observed poor adherence. Approximately 78% of patients had multiple health conditions, which necessitated the use of multiple medications to manage these comorbidities, and this was evident in our study, as a substantial number of participants reported taking five or more medications (75.3%) and seven or more pills (61.8%) on a daily basis. There is strong evidence indicating that the risk of medication nonadherence increases as the number of medications prescribed or the frequency of administration increases [1,33]. A meta-analysis by Ghimire *et al*. reported that the prevalence rates of medication nonadherence among hemodialysis patients ranged from 12.5% to 98.6%. [9]. This wide variation in the prevalence of nonadherence among hemodialysis patients may be attributed to the diverse methods used to assess medication adherence and the different definitions employed to estimate nonadherence rates. Our data also revealed significant differences between adherent and nonadherent groups in terms of age, dialysis

vintage, and quantity of drugs and pills. When compared to the adherent group, the nonadherent patients typically consume more pills and drugs, are older, and have had dialysis for a longer period of time. These findings were consistent with the findings of previous studies conducted in hemodialysis settings [34–38]. This can be explained by the fact that older age is frequently associated with multiple chronic health conditions that require various medications to manage. This increases the risk of polypharmacy, drug interactions, adverse effects, a complex medication regimen, and a greater perceived medication burden, which makes nonadherence more possible [39,9]. Furthermore, there was a significant association between having comorbidities, having a caregiver, and medication adherence. Patients with fewer comorbidities or who have a caregiver are more likely to adhere to their medications. This was in line with previous studies, which showed that patients with multimorbidity are more likely to have poor medication adherence [40,41]. Multimorbidity is tightly linked with polypharmacy, and it has already been shown that the risk of medication non-adherence can increase as additional medication is prescribed to patients [42]. Berglund *et al*. and Bouldin *et al*. evaluated the role of informal caregiving on medication adherence; their findings showed that patients with caregivers were less likely to be nonadherent to their prescribed medications compared with those who didn't [43,44]. Informal caregivers are crucial in ensuring that their relative patients consume prescribed medications. They can improve medication adherence by providing medication reminders, assisting with medication administration, and monitoring adverse effects. In addition, they can help organize medications and communicate with healthcare providers regarding medication-associated problems [45]. The most common reason for nonadherence reported by the participants was forgetfulness. This was in line with the findings of previous studies, which showed that the most prevalent reason for medication non-adherence was forgetting a dose [1,46]. Forgetfulness can cause undesirable effects due to underdosing, and a recurrence of symptoms contributes to the worsening of the patient's clinical condition and may result in treatment failure [47]. After implementing the deprescribing program, a significant reduction was observed in the number of medications and pills and the MGL adherence scale (Table 5); our findings agreed with previous studies that examined the impact of deprescribing processes to combat medication nonadherence in different health care settings [32,48,49]. Our study provides indirect evidence that reducing the number of medications, daily doses, and administration frequency through deprescribing will positively affect adherence.

Study Limitations

This study was carried out at a single center, potentially limiting the generalizability of the findings across other hemodialysis units. The lack of a control group impedes the judgment to attribute observed improvements in outcomes solely to deprescribing programs and reliance on patients' self-reporting of their medication usage. Due to the absence of electronic medication records, the reliability of reported medication use by patients could be affected due to recall bias.

Conclusion

Pharmacist-led medication evaluation with a deprescribing program is an effective and safe strategy in terms of both decreasing the number of medications and daily pills prescribed while simultaneously improving hemodialysis patient' adherence to their regimens.

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Conflict of interests

No conflict of interest was declared by the authors

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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