



Revista Brasileira em Promoção da Saúde

ISSN: 1806-1222

ISSN: 1806-1230

rbps@unifor.br

Universidade de Fortaleza

Brasil

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Revista Brasileira em Promoção da Saúde, vol. 33, 2020, , pp. 1-10

Universidade de Fortaleza

Brasil

DOI: <https://doi.org/10.5020/18061230.2020.9906>

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Self-medication in chronic kidney disease patients on hemodialysis

Automedicação em pacientes renais crônicos hemodialíticos

Automedicación de pacientes renales crónicos en hemodiálisis

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ABSTRACT

Objective: To analyze self-medication in chronic kidney disease patients on hemodialysis. **Methods:** A quantitative descriptive cross-sectional study was conducted at a hemodialysis center in Southwestern Bahia in March 2015 using a form to collect sociodemographic, clinical and drug therapy data from 170 patients in March 2015. The sample comprised patients undergoing chronic hemodialysis treatment for over one year aged 18 years or older. Epidata 3.1 was used as a database. Descriptive analysis was performed and binary logistic regression was used to check for associations between self-medication and independent variables using the SPSS software version 21.0. **Results:** In all, 64.1% (109) of the participants were men and the mean age was 50.5 years (± 14.9). 57% (98) of the participants earned less than one minimum wage, 20% (34) had never studied, 48.2% (82) had been on dialysis for one to five years, and 92.9% (158) had no health insurance. We confirmed self-medication of 104 drugs, particularly calcitriol (9.6%) and clonidine (6.7%). Patients with higher levels of education ($OR=1.32$; $95\%CI=1.32-28.72$) and those who use leftover drugs at home ($OR=22.48$; $95\%CI=6.53-77.38$) were more likely to self-medicate. **Conclusion:** The rate of self-medication in chronic kidney disease patients is low and it is associated with the use of drugs stored at home and low levels of education.

Descriptors: Renal Dialysis; Pharmacoepidemiology; Nonprescription Drugs; Drug Utilization; Outpatients; Renal Insufficiency, Chronic.

RESUMO

Objetivo: Analisar o uso de medicamentos por automedicação em pacientes renais crônicos hemodialíticos. **Métodos:** Estudo quantitativo, descritivo e transversal, realizado em um centro de tratamento hemodialítico, na região Sudoeste da Bahia, em março de 2015, por meio da aplicação de formulário contendo variáveis sociodemográficas, clínicas e farmacoterapêuticas de 170 pacientes. A amostra compôs-se de pacientes em tratamento hemodialítico crônico há mais de um ano, com idade maior ou igual a 18 anos. Utilizou-se o Epidata 3.1 como banco de dados. Realizou-se análise descritiva e empregou-se o método de regressão logística binária, usado para avaliar a associação entre automedicação e variáveis independentes, utilizando o programa SPSS, versão 21.0. **Resultados:** Dos participantes, 64,1% (109) eram homens, com idade média de 50,5 anos ($\pm 14,9$); 57% (98) possuíam renda menor que um salário mínimo; 20% (34) nunca estudaram; 48,2% (82) estavam dialisando em período de um a cinco anos e 92,9% (158) não possuíam plano de saúde. Contabilizaram-se 104 medicamentos utilizados por automedicação, com destaque para o calcitriol (9,6%) e a clonidina (6,7%). Verificou-se que pacientes com maior escolaridade ($OR=1,32$; $IC95\%=1,32-28,72$) e que usam sobra de medicamentos em casa ($OR=22,48$; $IC95\%=6,53-77,38$) têm mais chances de se automedicar. **Conclusão:** Há baixa frequência de automedicação na população de renais crônicos investigada, sendo associada ao uso de medicamentos guardados em casa e à baixa escolaridade.

Descritores: Diálise Renal; Farmacoepidemiologia; Medicamentos Sem Prescrição; Uso de Medicamentos; Pacientes Ambulatoriais; Insuficiência Renal Crônica.



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Received on: 09/02/2019

Accepted on: 01/30/2020

RESUMEN

Objetivo: Analizar el uso de medicamentos por automedicación de pacientes renales crónicos en hemodiálisis. **Métodos:** Estudio cuantitativo, descriptivo y transversal realizado en un centro de tratamiento de hemodiálisis de la región Sudoeste de Bahía en marzo de 2015 a través de la aplicación de un formulario con variables sociodemográficas, clínicas y de tratamiento farmacológico de 170 pacientes. La muestra ha sido de pacientes en tratamiento de hemodiálisis desde hace más de un año con edad mayor o igual a 18 años. Se utilizó el Epidata 3.1 para el banco de datos. Se realizó un análisis descriptivo y se utilizó el método de regresión logística binaria para evaluar la asociación entre la automedicación y las variables independientes con el programa SPSS, versión 21.0. **Resultados:** Entre los participantes, el 64,1% (109) era hombres con edad media de 50,5 años ($\pm 14,9$); el 57% (98) tenía renta de menos de un sueldo mínimo; el 20% (34) nunca ha estudiado; el 48,2% (82) realizaba la hemodiálisis desde el periodo entre uno y cinco años y el 92,9% (158) no tenía seguro de salud. Se ha contabilizado 104 medicamentos utilizados por la automedicación con énfasis para el calcitriol (9,6%) y la clonidina (6,7%). Se verificó que los pacientes con mayor escolaridad ($OR=1,32$; $IC95\%=1,32-28,72$) y los que usan lo que queda de los medicamentos que tienen en casa ($OR=22,48$; $IC95\%=6,53-77,38$) tienen más oportunidades para la automedicación. **Conclusión:** Hay baja frecuencia de automedicación en la población de renales crónicos investigados y la misma se asoció con el uso de medicamentos almacenados en casa y las personas de baja escolaridad.

Descriptores: Diálisis Renal; Farmacoepidemiología; Medicamentos sin Prescripción; Utilización de Medicamentos; Pacientes Ambulatorios; Insuficiencia Renal Crónica.

INTRODUCTION

Chronic kidney disease (CKD) is epidemic worldwide with an important and representative social and economic burden for the population in the context of public health⁽¹⁾. Systemic arterial hypertension (SAH) and diabetes mellitus (DM) stand out as the main primary causes of CKD – 34% and 31%, respectively⁽²⁾. Knowledge of the epidemiological and clinical aspects of dialysis patients can assist managers in planning safe care and promoting quality of life with reduced morbidity and mortality⁽²⁻⁴⁾.

In 2016, 124,675 new patients started dialysis treatment in the United States and a cost of approximately US\$ 3.7 billion was estimated for drugs for patients with end-stage renal disease (ESRD) enrolled in the Medicare Part D program, including dialysis and transplant patients⁽⁵⁾. In Brazil, 40,307 new patients started dialysis treatment in 2017, that is, an estimated incidence rate of 194 patients per million inhabitants (PMP). The estimated prevalence rate of patients on chronic dialysis increased globally from 475 PMP in 2011 to 610 PMP in 2017 (28.4%)⁽²⁾. Thus, it is evident that the best option for promoting the health of this population is prevention through early diagnosis of CKD in one of its five stages and maintenance of renal function⁽³⁾.

It should be noted that patients with ESRD have higher mortality and morbidity rates compared with the general population⁽⁶⁾, with an annual mortality rate of 19.9% in Brazil in 2017⁽²⁾. These patients usually need a high number of medications due to aging, dialysis and its characteristics related to their chronic inflammatory state, hyperparathyroidism, anemia, malnutrition, and presence of multiple comorbidities, such as diabetes, dyslipidemia and arterial hypertension⁽⁶⁾. In addition, there is a greater probability of occurrence of adverse events in these patients; therefore, the real need for using several medications should be reviewed⁽⁷⁾.

Knowledge of the pharmacotherapeutic profile of patients is a very useful tool in the identification of drug-related problems (DRP) and one of its risk factors: self-medication⁽⁸⁾, which is defined as the selection and use of drugs by individuals to treat self-recognized illnesses or symptoms, including the purchase of over-the-counter drugs, the use of leftover doses of old prescriptions and drugs shared with other family members or social groups, and the inappropriate use of a medical prescription by prolonging it, interrupting it or changing the dosage and the period of administration⁽⁹⁾.

Some of the risks related to self-medication include the dangers of polypharmacy and various drug interactions, as well as the chance of overdosing and intoxication, which can be intensified in the population of CKD patients due to their peculiar characteristics in relation to pharmacokinetics⁽¹⁰⁾. Thus, drug utilization studies (DUS) in this population provide important data to assist managers in the elaboration of public health policies⁽¹¹⁾ as more serious diseases or chronic conditions can lead to the use of prescription drugs⁽¹²⁾ and the presence of these chronic diseases can be one of the determining factors for self-medication⁽¹³⁾. In view of these data, the objective of this study was to analyze self-medication in chronic kidney disease patients on hemodialysis.

METHODS

This quantitative descriptive cross-sectional study was carried out at a hemodialysis treatment center in the Southwest region of Bahia, Brazil, in March 2015. We selected 189 out of 250 patients at the center for they met the following inclusion criteria: chronic hemodialysis patients with treatment duration of more than one year⁽¹⁴⁾ and aged 18 years or older. Only 170 of the pre-selected patients completed the form administered. The loss of 10% of the sample was for reasons such as refusal, death, transfers to other services or changes in treatment modality.

For adjustment of the data collection instrument and calibration of the interviewers, we conducted a pilot study with patients included in the sample selected from the same treatment center since there was no need to change the structure of the form built by a multidisciplinary health team. The participants completed the study form after giving their written informed consent.

The data collection instrument comprised questions addressing sociodemographic data (sex, age, race, education, monthly household income, religion, marital status, occupation, cohabitation) and other specific issues related to the participant's health and health services, such as: the date of the last medical appointment, presence of comorbidities (such as DM and SAH) concomitant with kidney disease, lifestyle habits (regardless of hemodialysis treatment) and data on medications, such as the name of the drugs they were taking, origin of the recommendation for their use (medical prescription or from other professionals), number of times the participants self-medicated and characteristics associated with self-medication. With regard to the date of the last consultation with a doctor, we considered only that when the patient was seen in a doctor's office.

When the term self-medication involved some temporal variable in the question, a 30-day recall period was used, as in the study conducted in Pereira, Colombia⁽¹⁵⁾.

In addition, regarding the drugs taken, we took into account whether labels, packages or prescriptions were presented, as in a study carried out in the Federal District⁽¹⁶⁾, but self-report was also included. Prescribed drugs were defined as those listed in medical prescriptions and when these were not presented, but the patient reported the use or brought labels or packages, it was checked whether these drugs were prescribed in the patient's electronic medical record, with a subsequent check by the researcher. Thus, when these criteria were not met, drugs were classified as non-prescribed or as self-medication, even if the prolonged use of a previously prescribed drug could have occurred due to an alleged failure in communication between the medical team and patients.

The drugs were also classified as for use at the clinic or at home. Doubts, inconsistencies and form items not filled in during the first contact were supplemented by the participant in a second contact, both having been previously scheduled. During the dialysis session prior to the day of the interview, patients and/or companions received a printed reminder containing instructions, which were carefully explained.

The drugs being taken and their respective active ingredients in each specialty were classified according to the World Health Organization's Anatomical Therapeutic Chemical (ATC) classification system⁽¹⁷⁾.

The Epidata software, version 3.1, was used to tabulate the collected data and the Statistical Package for the Social Sciences (SPSS), version 21.0, was used to process and analyze the data. Descriptive analyses were presented as frequencies (absolute and relative), means and standard deviation. Univariate and multivariate associations between self-medication and the selected independent variables were checked using the binary logistic regression model. The magnitude of the association was measured using odds ratios (OR) with 95% confidence intervals and a significance threshold of 0.05.

The independent effect of variables on self-medication was checked by multivariate analysis, and the model-building strategy consisted in deleting variables until the final model was reached and contained only those associations with $p < 0.05$. The goodness of fit was tested by the Hosmer-Lemeshow test.

The study complied with the ethical standards involving research with human beings, as provided for in Resolution No. 466/12 of the National Health Council/Ministry of Health. The study was approved by the Research Ethics Committee of the State University of Southwestern Bahia under Approval No. 957.553.

RESULTS

Of the 170 participants in the present study, 74 (43.5%) declared themselves *Pardos* (mixed-race Brazilians) and 54 (31.8%) declared themselves Black. With regard to marital status, 62 (36.5%) participants were married and 31 (18.2%) were cohabiting. A total of 97 (71.3%) of the literate participants had graduated from primary school. In

addition, 164 (96.5%) participants lived in urban areas and 144 (84.7%) lived with their families. The participants' age ranged 20 to 86 years, with a mean age of 50.5 years (± 14.9). The mean duration of hemodialysis treatment was 61.5 months (± 61.3), as shown in Table I.

Table I - Characteristics of the study population according to sociodemographic and clinical variables and access to health services. Jequié, Bahia, Brazil, 2015.

Variables	n	%
Sex		
Men	109	64.1
Women	61	35.9
Marital status		
Single	56	32.9
Other.	114	67.1
Race/ Color		
White	40	23.5
Non-White**	130	76.5
Living with		
Family	144	84.7
Alone+ other	26	15.3
Monthly household income		
Up to 1 wage	98	57.6
Up to 2 wages or more	72	42.4
Education		
Illiterate	34	20.0
Literate***	136	80.0
Health insurance		
Yes	12	7.1
No	158	92.9
Current health		
Very good and good	73	42.9
Fair	78	45.9
Very poor and poor	19	11.2
Hemodialysis duration		
1-5 years	82	48.2
Over 5 years	88	51.8
DM and/or SAH		
Yes	136	80.0
No	34	20.0
Last appointment		
Up to one month	41	24.1
Over one month	129	75.9
Impaired transfer		
Yes	29	17.1
No	141	82.9

*Other: married, divorced, cohabitating, widowed; **Non-White: *pardo*, Black and Yellow; ***Literate: primary education, secondary education and higher education; DM: diabetes mellitus; SAH: systemic arterial hypertension

Of the participants who said they used medications without guidance or a prescription, only 3 (1.8%) self-medicated for fear of going to the doctor. There were 30 (17.6%) patients who reported having used medications stored at home - 19 (63.3%) of these used leftovers from previous prescriptions. Regarding attitudes considered self-medication, those participants who failed to take any prescribed medication on their own in the last 30 days described the following reasons: price (n=2; 14.3%), medication was sold out (n=3; 21.4%), lack of transportation to get it (n=1; 7.1%), not liking to take the medication (n=2; 14.3%), and not feeling well when taking the medication (n= 6; 42.9%). Also, 53 (75%) participants who used medications on their own reported knowing how to use them and said that they got better after using them, as described in Table II.

Among the participants who reported having self-medicated at some point in their life, only 2 (3%) reported having been influenced by media advertisements and 13 (19.4%) by the price of the medication. Although 152 patients acknowledged that they had been instructed to avoid self-medication, 11 (6.4%) said they had used medication on their own during the hemodialysis session, as shown in Table II.

Table II - Characteristics of self-medication in chronic kidney disease patients on hemodialysis. Jequié, Bahia, Brazil, 2015.

Characteristics of self-medication	n (%)	Self-medication n (%)	n (%)
Do you what self-medication is?	Yes 58 (34.1)	No/ Maybe 112 (65.9)	-
Have you used medications without medical guidance or prescription?	Yes 67 (39.4)	No/ Can't remember 103 (60.6)	-
If no, did CKD influence you to avoid it?	Yes 73 (70.9)	No 30 (29.1)	-
If yes, do you remember when you used it?	> 30 days 29 (43.3)	< 30 days 14 (20.9)	Can't remember 24 (35.8)
Who recommended its use?	Myself 59 (88.0)	Others* 8 (12.0)	-
Have you stopped taking the medications prescribed to you in the last 30 days?	Yes 14 (8.2)	No 156 (91.8)	-
Have you increased the dose for any reasons?	Couldn't get better 1 (0.6)	Never increased 169 (99.4)	-
What signs or symptoms led you to self-medicate?	Headache 38 (56.7)	Other** 29 (43.3)	-
How did you get the medication?	Alone 61 (91.0)	Help from others 6 (9.0)	-
Were they medications that compulsorily required prescription?	No 70 (98.6)	Don't know 1 (1.4)	-
How was your health after taking them?	Improved 53 (74.6)	Got worse/ did not change 18 (25.4)	-

*Others: family, drugstore clerk, pharmacist, neighbor; **Other: coughing, tiredness/fatigue and other; CKD: chronic kidney disease

A total of 103 drugs were used by the participants who self-medicated in the last thirty days (n=51; 30%), with a mean of 2.04 (± 1.40) drugs. Although the main reason for self-medication was headache, drugs with analgesic properties, such as nimesulide and dipyrrone, ranked third and fourth in frequency of use among those classified as non-prescription or self-medication, behind calcitriol and clonidine, as shown in Table III.

Table III - Distribution of medications classified as non-prescription drugs according to the anatomic therapeutic chemical classification. Jequié, Bahia, Brazil, 2015.

Non-prescription drugs by therapeutic subgroup (ATC)	n	%
A- Digestive system and metabolism		
Calcitriol	10	9.7
Other	20	19.4
B- Blood and blood forming organs		
Iron hydroxide	3	2.9
Other	4	3.9
C- Cardiovascular system		
Clonidine	7	6.8
Other	19	18.4
M- Musculoskeletal system		
Nimesulide	6	5.8
Other	11	10.7
N- Nervous system		
Dipyrone	6	5.8
Other	4	3.9
R- Respiratory system		
Dropropizine, expector mel®, resfryneo®	3	2.9
V- Various		
Sevelamer hydrochloride	6	5.8
Other	1	1.0
Other*	3	3.0
Total	103	100

®: registered trademark; HCl: hydrochloride; Other*: J - anti-infectives, L- antineoplastic agents, H- systemic hormonal preparations; ATC: Anatomic Therapeutic Chemical

The univariate analysis checked for associations of self-medication with education, use of drugs stored at home and the identification of the medication by its name. The variables education and use of drugs stored at home were independently associated with self-medication, as shown in Table IV.

Table IV - Outcomes of the multivariate analysis for comparison of the selected variables and self-medication. Jequié, Bahia, Brazil, 2015.

Variables	Self-medication		Multivariate analysis	
	Yes n (%)	No n (%)	OR/ CI	p-value*
Use of medications stored at home				
No	41 (29.3)	99 (70.7)	22.48 (6.53-77.38)	<0.01
Yes	26 (86.7)	4 (13.3)	1	
Education				
Illiterate	4 (11.8)	30 (88.2)	6.15 (1.32-28.72)	0.021
Literate	63 (46.3)	73 (53.7)	1	
Hosmer-Lemeshow test				0.596

Med: medication; *Binary logistic regression, $p < 0.05$

DISCUSSION

Studies like the present one, which addresses self-medication, often have divergent results due to different methodological approaches and recall periods used, a fact that has also been addressed in a study conducted in the Federal District⁽¹⁶⁾. Despite the difficulties, such studies are important strategies for health promotion and avoid drug-related problems, thereby improving patients' quality of life^(2-4,11).

The frequency of self-medication found in the present study is similar to those found in other studies, such as a study with adults in Colombia⁽¹⁵⁾ and one with students from Palestine⁽¹⁸⁾ – both used a 30-day recall period. In a study carried out in Campinas with a group of men using a 3-day recall found a rate of 11.2%⁽¹²⁾.

A prevalence rate of 53.2% was found in a study carried out in Nigeria with Pharmacy students when the recall period was not determined⁽¹⁹⁾. The characteristics of the populations, their health status, the use of health services, the health care model and the sociodemographic and cultural characteristics related to the use of medication can partially designate differences in the prevalence of the use of certain medications and self-medication⁽¹²⁾, thus making knowledge about this practice necessary to direct public policies to this population.

A total of 104 non-prescription drugs were used by the participants in the present study, with a mean of 2.04 (± 1.4) drugs. In a study carried out with university students in Palestine⁽¹⁸⁾, the mean number was 2.63 (± 1.38). The low frequency of self-medication, added to the low mean of drugs used, reinforces the reports of patients who denied self-medication considering the fact that they have CKD, thus corroborating data from the literature that mention that the frequency of self-medication is usually lower in patients with chronic diseases^(11,20).

Chronic hemodialysis patients, particularly the population studied herein, have access to the health service at least three times a week. Furthermore, comorbidities such as DM and SAH are prevalent and make them look for medications and tests more often, which put them in contact with their doctors more often, thus favoring the use of prescription drugs⁽¹²⁾. However, the literature shows a positive association between chronic disease and self-medication⁽¹³⁾.

A study conducted with university students in the state of Santa Catarina found a controversial association between self-medication and access to health services, which was at times more frequent among those who used health services. It was even referred to as an indicator of the replacement of formal health care for self-care and an aid in recovering from minor ailments capable of slightly alleviating the burden of medical services⁽²¹⁾.

The main non-prescription drugs used by the participants in the present study were calcitriol and clonidine. There might have been an error in medication agreement - especially in relation to the first drug - between what was seen in the electronic prescription and what the patient reported using. In such case, the medication could have recently been suspended from the most current monthly prescription and the patient had not yet received the prescription. The alleged failure in communication between prescribers and users in case the physician discontinues the medication and the patient is not communicated or does not understand the treatment is considered a patient safety problem⁽²²⁾. It should be noted that communication problems in health care facilities are among the most common problems found in root cause analysis of sentinel events⁽²²⁾. Therefore, professionals should be concerned with confirming that the patient understood the proposed treatment and/or its alteration, thereby mitigating the risks related to self-medication⁽⁸⁾ and promoting an improvement in quality of life⁽³⁾.

There are several studies showing a positive association of self-medication with less serious diseases – often of spontaneous remission^(13,18) - and minor and more acute signs and symptoms, such as headache and fever⁽²⁰⁻²¹⁾. In the present study, most of the respondents who self-medicated reported the predominance of headache as an unpleasant symptom and most of them reported using dipyrone when asked if they remembered the name of the medication they used on their own. The same was found in other studies^(12,23).

The use of analgesics by chronic hemodialysis patients is extremely important for the control of the various pain situations they face on a daily basis as the disease can worsen the quality of sleep, facilitate physical and functional worsening, and even trigger depressive disorders⁽²⁴⁾. As reported in other studies^(15,23), non-steroidal anti-inflammatory drugs (NSAIDs) were also among the most frequently used non-prescription drugs. These drugs should be avoided by patients who still have good residual diuresis⁽²⁴⁾ due to their considerable potential for drug interactions and adverse reactions and the increased cardiovascular risk⁽²³⁾. It should be noted that although dipyrone and some NSAIDs are non-prescription drugs, that is, over-the-counter drugs, both can be harmful to health^(18,19,23,25), which leads to questions about the real benefit and health promotion of these self-care practices or compliance with treatment in patients with chronic diseases, particularly CKD.

We found that all the patients who used medications on their own did not need to present a prescription at the time of purchase, which suggests non-compliance with the regulations. Despite the increased risk of complications in face of such practice, most interviewees in the current study who self-medicated said they knew how to use the medications and that they got better after using them. In addition to the deficit in public health structure, which fails to meet the demands of a needy society, such behavior makes self-medication an option for self-care, as reported in another study⁽¹⁵⁾.

Most of the participants who reported having stopped using prescribed medications on their own claimed malaise when they took them and said they had informed the doctor of such decision. It is assumed that when the patient behaves as such, i.e., he/she suspends the medication that he/she believes to be the cause of a harm, he/she does not usually communicate the decision to the health team for fear of not being understood or of receiving a new prescription for another medication that he/she believes might cause the same side effects⁽²⁶⁾.

Although most of the participants in the present study had a household income of no more than two minimum wages, spending on medications did not seem to be a cause for concern since the price of the medicine purchased to self-medicate did not influence the purchase in 80% of the situations. Agreeing with these data, the literature shows that income is not a major factor in the decision to self-medicate⁽²¹⁾. It is also known that self-medication is a low-cost alternative and a first option of response to the disease for people of low economic status⁽²³⁾.

A statistical association of self-medication with education and use of medications stored at home was observed in the current study. Additionally, most of the medications stored at home and used by the patients were leftovers from previous prescriptions, a practice that has also been commonly found in other studies^(13,19,23). This practice can contribute to increasing antimicrobial resistance and treatment failures and worsening the quality of medicines⁽²¹⁾. It can even lead to the use of expired medicines. It should be noted that 73% of the participants in the present study said they usually checked the expiration date of the medicines.

Self-medication is associated with education, i.e., the higher the level of education, the more frequent self-medication is⁽¹²⁾. Supposed explanations for this would be that knowledge, skills and access to information make patients more confident to choose the medication even without a medical prescription⁽²⁷⁾.

Despite the methodological difficulties found (information bias and impossibility of validating the respondents' answers; memory bias regarding the use of medicines; difficulties involved in the concept of self-medication), which are similar to those faced by other studies on the theme^(12,20,23), the results achieved in the present study are relevant for the adoption of strategies aimed at a more rational use of medications, the improvement of care and safety of this population, especially considering the lack of studies involving chronic hemodialysis patients. Programs aimed at the therapeutic management of medicines by pharmacists that reduced costs with medicines, the rates and duration of hospitalization and even mortality among chronic renal patients on dialysis have already been reported in the literature⁽²⁸⁾.

CONCLUSION

The frequency of self-medication among the chronic kidney disease patients analyzed was low and it was associated with the use of medications stored at home, low levels of education, problems such as failure in communication, non-compliance with marketing rules and use of leftover medicines, which can cause treatment failures and aggravate comorbidities.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

CONTRIBUTIONS

Lucas Brasileiro Lemos and **Adriana Alves Nery** contributed to the study conception and design, acquisition, analysis and interpretation of data, and writing/revision of the manuscript. **Gabriela Silva Moraes** contributed to the study conception and design and writing/revision of the manuscript. **Gisele da Silveira Lemos** contributed to the acquisition, analysis and interpretation of data and writing/revision of the manuscript.

Manuscript originated from the master's dissertation titled: "Use of medications by chronic kidney disease patients on hemodialysis: pharmacoepidemiological characteristics". State University of Southwestern Bahia, 2015, 97 pages.

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How to cite: Lemos LB, Moraes GS, Lemos GS, Nery AA. Self-medication in chronic kidney disease patients on hemodialysis. *Rev Bras Promoç Saúde*. 2020;33:9906.
