Patient Preference and Adherence

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ORIGINAL RESEARCH

A Chinese and Western medication adherence scale in patients with Chronic Kidney Disease

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Objective: The self-reported scale is a widely used method to assess patients' medication adherence in clinical practice, but there is still a lack of medicine adherence measurement scale for patients with Chronic Kidney Disease (CKD). Therefore, this study aimed to develop a medication adherence measurement scale of traditional Chinese medicine and Western medicine, providing a tool for evaluating medicine adherence of CKD patients.

Methods: In the preliminary stage, we formed the prediction scale after three rounds Delphi method and it was filled by 20 patients, who were selected randomly. After pre-investigation and language adaption, we adjusted the prediction measurement scale which included 31 items based on Knowledge-Attitude-Belief Theory. Then, 222 CKD patients in Guangdong Hospital of traditional Chinese Medicine were investigated by this 31-item scale. We screened 31 items by Items analysis theory, including critical ratio, item correlation analysis, internal consistency analysis, principal component analysis and other methods. The left 26 items made up a formal scale. We collected and analyzed data of the 26-item scale and Chinese version of MGL scale, and took their scores correlation analysis as the criterion validity of the 26-item scale. At the same time, we evaluated content validity, Cronbach alpha coefficient and retest reliability of the 26-item scale.

Results: We developed a scale with 26 items and 5 dimensions finally. In the validation analysis, the scale had good construct validity and content validity. The Pearson relation index between respective scores of the scale and Chinese version of MGL scale was 0.426, $P<0.01$. The scale also had good reliability as its 0.915 in Cronbach alpha, 0.753 in retest reliability and $P<0.01$.

Conclusion: The scale revealed great reliability and validity, which could be used as a measurement tool to evaluate the medication adherence of patients with CKD.

Keywords: chronic kidney disease, traditional Chinese medicine, adherence medication, scale, Delphi method

Background

CKD is an important global public health problem. According to related literatures, the prevalence of CKD is about 11%.[1] Professor Wang Haiyan's team[2] carried out a large-scale epidemiological investigation of chronic kidney disease (CKD) in China, and the results showed that the prevalence of CKD among Chinese adults reached 10.8%, meaning the estimated number of existing CKD patients in China reached 120 million. CKD is a progressive disease. If it progresses to end-stage renal disease (ESRD), renal replacement therapy, including hemodialysis, peritoneal dialysis and kidney transplantation, is required to maintain life. Therefore, it is essential to find effective and conservative treatment methods to delay the progression of CKD. CKD is also a

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chronic non-communicable disease, and conservative treatment requires a long-term standardized medication. Previous studies have found that the medication adherence of patients with chronic diseases[3] is worse than that of patients with acute diseases. The medication adherence of patients with chronic diseases gradually declines[4] after 6 months of treatment generally. Clinical researches have reported that their medicine adherence rate is only about 43–78%.[4]

CKD patients, especially those in stage 3–5, are often associating with other diseases such as hypertension, diabetes, cardiovascular disease, metabolic bone disease and anemia. Complication will make the regimen more complex, more drugs and higher cost, resulting the reducing medication adherence.[5–7] Because of the special condition, patients with CKD are faced with more problems in medication,[8,9] such as the dosage forms of diversity (such as oral, subcutaneous injection, intravenous drip, etc.), drug side effects (such as hormone and immune inhibitors, etc.), frequency of variability (such as the hormone and the reduction taking after next day, etc.), which makes adherence less positive. According to the literature, the rate of low drug adherence in CKD patients is about 26–28%.[5] In China, prescriptions for CKD patients often include proprietary of Chinese medicine and traditional Chinese medicine decoction.[10] Traditional Chinese medicine has varied dosage forms, decoction and taste, leading to lower adherence rate.[11,12,13] On the one hand, the little positive adherence rate of medication affects the clinical efficacy of patients; on the other hand, it also affects the accurate judgment on drug effect of clinical research. It is necessary to find effective methods to measure the medication adherence and noncompliance reasons of CKD patients accurately, so as to accurately evaluate the effectiveness of treatment programs and make evaluation of clinical treatment measures and the outcome of scientific research programs more objective. On the other hand, timely measures should be taken to reduce the rate of noncompliance, so as to improve the clinical efficacy of CKD patients.

Currently, there are a variety of methods for measuring patients' medication adherence, which can be roughly divided into non-self-report and self-report.[14] Non-self-reporting methods include electronic monitoring, pill counting, drug level testing, etc. Self-report methods include interview, medication diary and patient self-reported scale. Among them, the patient self-reported scale is the most widely used evaluation method at present.[15,16] However, there is no suitable scale which concentrates on the medication characteristics of CKD or traditional Chinese medicine.

"Knowledge-Attitude-Belief Practice (KABP)" is a behavioral theory that changes human health behavior. It divides the change of human behavior into three consecutive processes: knowledge acquisition, belief generation and behavior formation.[17] By learning knowledge and skills, people will gradually form positive beliefs and attitudes, which will lead to healthy behaviors. We believe that creating the medication adherence scale based on this theory might provide a more thorough judgment of patients' medication adherence. Based on the guidance of KABP theory and clinical treatment and medication of CKD, we learned from foreign-validated scales and integrated domestic experts' nephropathy knowledge and experience. We construct a medication adherence measurement scale which is suitable for CKD patients in China.

Methods

Preparation

Items of the scale

This scale was constructed as three processes based on the KABP Theory. In the preliminary study, we used Delphi method three times from March to July in 2017 and experts' opinions were gradually unified. We finally formed the prediction scale which included 31 items from August to December in 2017. In order to adjust the prediction scale, we randomly selected 20 CKD patients from the chronic disease management department of nephropathy in Guangdong Hospital of Traditional Chinese Medicine for pre-investigation and language adaptation. The adjustments were according to the questions below: Could patients understand the items? Could they answer the scale by themselves? How did they comprehend the item content? Were the items ambiguous? Did it take too long in time? Patients' opinions and suggestions on the scale were collected and discussed again by researchers. The ambiguous sentences, reading difficulties, unclear references and suggestive sentences were modified, and finally, the prediction scale was developed. The prediction scale has 31 items in total, as shown in Supplementary materials.

Scoring rules of prediction scale

The options (A, B, C, D, E) in each question were scored according to 5 grades. The respective score of A–E options in 1–16, 22–31 question is 5, 4, 3, 2, 1 but in 17–21 question it is inverse. The total score was the summation

of scores of 31 items. Its full mark is 155. The higher the summation, the better the patients' medication adherence.

Clinical investigation

Case source

CKD patients who kept long-term follow-up in the chronic disease department of Guangdong Hospital of Traditional Chinese Medicine were recruited from January to March in 2018.

CKD diagnostic criteria

Refer to the 2012 clinical practice guidelines for improving prognosis of global kidney disease (K/DIGO).[18]

Inclusion criteria

Made a definite diagnosis according to CKD diagnostic criteria; aged 18–80; consent and willingness to cooperate with investigators.

Exclusion criteria

Pregnant or lactating women; patients with severe heart, brain, liver or hematopoietic diseases; illiterate or dyslexic; having serious mental illness or being unable to consent due to dyslexia for other reasons; hospitalizations due to acute complications.

Sample size estimation

According to the principle that the proportion of sample size and number of variables shall be more than 5:1, more than 200 patients were planned to be included for investigation.

Survey methods

The scale investigators were trained uniformly. Before the investigation, investigators shall explain the purpose and method of this research to patients, and obtained the informed consent of the patient. The scales shall be filled out by patients themselves. Scales needed to be handed out, inspected and taken back timely. The investigator shall immediately modify and supplement the items with missing or wrong fillings on the spot.

Items analysis

Critical Ratio (CR) method and homogeneity test were used to explore the differences between high and low score in each item, and conducted homogeneity test among items. Items with large differences would be screened or modified.

Correlation analysis was adopted to analyze the relevance between each item and a collection of other items. The higher the correlation between a single item and the total score of the scale, the higher the homogeneity between them. If the Pearson correlation coefficient between the scale items and the total score of the scale was very small, the items shall be deleted.

Cronbach's alpha was tested to evaluate the internal consistency of the scale. If an item reduced the overall Cronbach's alpha, it might be deleted. Factor analysis was used to identify the correlation between the items and the attributes. If the correlation between an item and the main factors have little correlation, it would be deleted.

Reliability and validity test

After screening items by analysis methods above, we formed the formal measurement scale and then we tested its reliability and validity.

Validity means obtaining the degree of psychological or behavior which scales aimed to measured.[19] Construct validity, content validity and criterion-related validity were used to evaluate the formal scale validity. The most widely used medication adherence scale, the Morisky, Green and Levine (MGL) scale,[20] has only 4 items, simple evaluation content, but good reliability and validity. Its Chinses version could be used as the preliminary judgment of adherence.[19,21]

Reliability referred to the stability and consistency of the scale results. The better the reliability of the scale, the smaller the measurement standard error.[22] Cronbach's alpha and retest reliability of each factor and the total scale were measured to test the reliability.

Data entry and statistical analysis

The returned questionnaires were input by a professional person assigned in pairs. If they found wrong data during the period, they shall check the original scale immediately for correction and modification. Missing data would be statistically treated according to their properties.[22,23] SPSS17.0 was used to analyze the data. The main methods of statistical analysis included descriptive analysis, independent sample *t*–test, exploratory factor analysis, correlation analysis, etc.

Result

General situation

226 questionnaires were issued in total and 222 were returned, with a recovery rate of 98%. The filling time of the scale was 7.3±1.2 mins.

Results of items analysis

We carried out exploratory factor analysis, correlation analysis, items analysis, reliability and validity test on prediction scale of traditional Chinese and western medication adherence in CKD patients. The results are shown in Table 1. And the indicators which were more than five would be deleted, and eventually 5 items were deleted, including Item17 "Less hospitalization after taking drugs", Item18 "Symptoms improvement after taking drugs", Item22 "Don't want to take medicine in fact", Item 29 "Often same Chinese medicine prescription in the past month", Item30 "Changed the number of drugs in prescription on one's own in the past month"; then, we formed the formal scale and named it Measurement Scale, see Supplementary materials.

The options (A, B, C, D, E) in each question were scored according to 5 grades. The respective score of A–E option in 1–16, 20–26 item is 5, 4, 3, 2, 1 but in 17–19 item it is inverse. The total score was the summation of scores of 26 items. Its full mark is 130. The higher the summation, the better the patients' medication adherence.

Scale validity analysis results

Construct validity

Exploratory factor analysis was conducted to determine whether the retained 26 items could reflect the scale structure correctly. In Bartlett sphericity test, X^2=2967.731, P<0.001, KMO=0.891, showed good quality and suitability for factor analysis. By the principal component analysis, the linear rotation shaft with the maximum variation method is carried out on the variance. We got 7 elements which were more than 1 in initial eigenvalues. The 7 shared elements were more suitable as the theoretical structure of the scale, and the explanation rate of the cumulative variance of 7 elements is 68.85%. See Table 2 and Figure 1. Linear rotation of 7 elements was carried out on the 26 items to obtain the component matrix, as shown in Table 3. As can be seen from the component matrix after the rotation axis, shared element 1 covered items 4, 6, 7, 8, 9, 10, 11 and 12; shared element 2 covered items 13, 14, 15 and 16; shared element 3 covered items 1, 2, 3 and 5; shared element 4 covered items 22, 23, 24 and 25; shared element 5 covered items 17, 18 and 19; shared element 6 covered items 20 and 21; and shared element 7 only covered item 26. The elements obtained by exploratory factor analysis were the same as the structure of the prediction scale, indicating that the measurement scale had stable construct validity. According to the theoretical structure of the initial scale, combined with the exploratory factor analysis results, the shared element 5 revealed positive belief in drug taking, and the shared element 6 revealed negative belief in drug taking. Because the two elements consisted of few items, we combined them into an element: medication beliefs. There was only item 26 in shared element 7, so we added it to shared element 4 and named as medication behavior. Item 4 is semantically similar to the item in share element 3, so it was added to shared element 3 and named as basic knowledge of taking medicine. As a result, the final five elements were, respectively, named: basic knowledge on medication (5 items, items 1–5), knowledge about Chinese medicine decoction (item 7 and items 6–12), knowledge about taking Chinese medicine (4 items, items 13–16), medication beliefs (item 5 and items 17–21) and medication behavior (5 items, items 22–26).

Content validity

The scale was reviewed and investigated by 23 experts in 3 rounds of expert consultation, and modified appropriately according to the experts' opinions. According to the experts' opinions, the items reflected the medication adherence of traditional Chinese and western medicine in CKD patients clearly, and the language was clear and easy to understand, without logic confusion, revealing its good content validity.

Calibration correlation validity

222 patients finished the Chinese version of MGL scale while filling the measurement scale. We carried out correlation analysis between the total score of the 26 items and that of the MGL scale, and took it as the calibration validity of the scale. See Table 4. The mean score of the measurement scale was 92.44, and the standard deviation was 14.95. The mean score of the MGL questionnaire was 17.37, and the standard deviation was 2.48. The Pearson correlation coefficient between the scale score and the MGL questionnaire score was 0.426, indicating that there was a correlation between them (see Table 4).

Scale reliability analysis results

Internal consistency reliability

The results showed that the total Cronbach's alpha of 26 items was 0.915, and the Cronbach's alpha of 5 elements was 0.439–0.930. The internal consistency of the scale was acceptable (See Table 5).

Table 1 Items analysis result

Item	Critical ratio	Item and total score correlation	Calibration item and total score correlation	α (after deleting items)	Inter-community	Factor loading	Sub-standard index	Remark
1	13.1	0.66	0.62	0.889	0.44	0.66	0	R
2	7.06	0.48	0.42	0.893	0.23	0.48	0	R
3	9.90	0.61	0.56	0.890	0.38	0.62	0	R
4	10.95	0.63	0.58	0.889	0.42	0.65	0	R
5	8.37	0.55	0.50	0.891	0.31	0.56	0	R
6	12.4	0.71	0.67	0.888	0.57	0.75	0	R
7	16.23	0.76	0.73	0.887	0.65	0.81	0	R
8	16.28	0.76	0.72	0.886	0.63	0.80	0	R
9	15.53	0.75	0.71	0.887	0.63	0.80	0	R
10	15.7	0.75	0.72	0.887	0.65	0.81	0	R
11	15.89	0.78	0.74	0.886	0.68	0.82	0	R
12	13.48	0.72	0.68	0.887	0.57	0.75	0	R
13	11.72	0.65	0.60	0.889	0.46	0.68	0	R
14	14.66	0.70	0.66	0.888	0.52	0.72	0	R
15	13.39	0.70	0.65	0.888	0.51	0.72	0	R
16	12.29	0.61	0.56	0.890	0.39	0.62	0	R
17	1.49*	0.09*	0.03*	0.899*	0.00*	0.01*	6	D
18	1.68*	0.11*	0.07*	0.897*	0.00*	0.05*	6	D
19	3.18	0.24*	0.19*	0.896	0.03*	0.18*	4	R
20	3.63	0.27*	0.23*	0.896	0.05*	0.22*	4	R
21	5.14	0.36*	0.31*	0.895	0.10*	0.32*	4	R
22	2.91*	0.18*	0.11*	0.900*	0.01*	0.10*	6	D
23	3.53	0.25*	0.20*	0.896	0.04*	0.21*	4	R
24	6.00	0.40	0.35*	0.894	0.12*	0.35*	3	R
25	6.33	0.43	0.38*	0.893	0.12*	0.35*	3	R
26	4.89	0.35*	0.3*	0.895	0.08*	0.29*	4	R
27	3.68	0.28*	0.23*	0.896	0.05*	0.21*	4	R
28	3.26	0.30*	0.25*	0.895	0.06*	0.24*	4	R
29	1.07*	0.09*	0.00*	0.904*	0.00*	0.01*	6	D
30	2.52*	0.196*	0.17*	0.896	0.02*	0.16*	5	D
31	3.00	0.263*	0.24*	0.895	0.06*	0.23*	4	R
Criteria	≥3.00	≥0.400	≥0.400	≤0.896#	≥0.20	≥0.45		

Notes: #0.896 represents the total alpha ecoefficiency of the scale. *Represents the substandard items that can be deleted.
Abbreviations: R, Reserved; D, Deleted.

Retest reliability

During filling in the scale, we selected 33 patients from the 222 patients randomly and asked them to refill in the scale within 3 weeks in order to retest reliability statistics. The results showed that the total retest reliability coefficient of the scale was 0.753, and the retest reliability coefficient of each element was 0.472–0.780, indicating that the scale had good stability in retesting, as shown in Table 6.

Discussion

Related literatures revealed that adherence had influences on clinical outcomes. An excellent scale of adherence could predict medication adherence accurately, and had correlation with clinical outcomes. For example, the Mediterranean diet score (MDS) on Tehranian adults, which was carried out by Golaleh Asghari's team, revealed that there was obvious negative correlation between MDS and risk of incident of CKD.[24]

There were a number of factors which influenced adherence of patients. In summary, it could be divided into three aspects: Knowledge, Belief and Behavior. The measurement scale adopts the Knowledge–Attitude–Belief Practice theory as the theoretical basis to measure the medication knowledge, attitude and behavior of CKD patients, so as to evaluate their medication adherence. For medication knowledge, preliminary construction was

Table 2 Cumulative variance interpretation rate in elements analysis

Elements	Initial eigenvalue			The amount of square and load		
	Total	Variance (%)	Accumulation (%)	Total	Variance (%)	Accumulation (%)
1	8.753	33.664	33.664	5.653	21.742	21.742
2	2.377	9.141	42.805	2.764	10.632	32.374
3	1.729	6.649	49.454	2.722	10.468	42.842
4	1.399	5.380	54.834	2.458	9.454	52.297
5	1.328	5.109	59.943	1.622	6.239	58.535
6	1.247	4.796	64.739	1.459	5.612	64.148
7	1.070	4.116	68.855	1.224	4.708	68.855

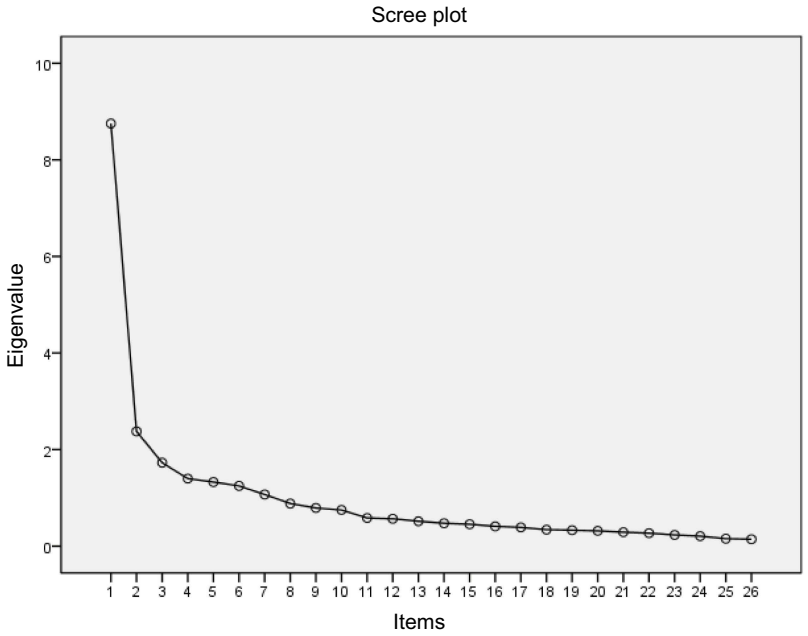

Figure 1 Scree plot of the scale.

mainly referred to the research content before, which was related to the analysis of influencing factors of medication adherence of CKD patients. For medication belief, it was mainly referred to the mature scales, which were based on the health belief model. For medication behavior, modification, which combined features of Chinese and western medicine, was made based on MGL scale. Then, we invited 23 domestic experts in relevant fields to discuss and analyze the preliminary scale, and initially formed a preliminary draft of a 31-item prediction scale. This scale was constructed based on mature theory, previous classic scales, extensive literature research and clinical experience of researchers.

In clinical investigation part, 222 effective scales were collected. We conducted critical ratio method, correlation analysis, Cronbach's alpha method, factor analysis and other methods; finally, we deleted 5 items and formed a measurement scale with 26 items. 26 items were included in the final scale in total, and it took short time to filling, indicating that the number of items in the scale was appropriate and acceptable.

Then, we carried out validity and reliability analysis. For construct validity, according to the exploratory factor analysis results, the cumulative variance interpretation rate of the 7 elements was 68.855%, and its structure was consistent with the original design, indicating that the three subscales of knowledge, belief and behavior had better construct validity. For calibration correlation validity, the Pearson correlation coefficient of the two was 0.425, $p<0.001$. Although it indicated an exist correlation, the correlation degree was not good

Table 3 Elements matrix after rotation axis

Items	Elements						
	1	2	3	4	5	6	7
6	0.827	0.095	0.142	0.084	0.035	0.101	−0.024
7	0.807	0.178	0.172	0.106	0.110	0.166	−0.038
10	0.791	0.313	0.174	−0.051	0.057	0.065	0.002
8	0.783	0.241	0.140	0.126	0.014	0.047	0.097
9	0.780	0.262	0.125	0.090	0.080	−0.048	0.142
11	0.734	0.400	0.156	0.035	0.085	0.136	−0.006
12	0.588	0.506	0.157	0.040	0.080	0.126	−0.065
4	0.541	−0.019	0.491	0.156	0.051	−0.183	0.325
14	0.354	0.753	0.227	0.091	0.107	0.017	0.041
15	0.449	0.672	0.079	0.081	0.108	0.035	0.170
13	0.473	0.618	0.086	0.092	0.018	0.060	−0.102
16	0.267	0.590	0.340	−0.053	0.088	0.000	0.256
2	0.095	0.216	0.788	0.027	−0.028	0.114	−0.078
5	0.158	0.325	0.739	0.026	−0.069	0.147	0.013
1	0.401	0.096	0.713	0.126	0.089	0.019	0.011
3	0.553	−0.118	0.594	0.065	0.015	−0.141	0.203
23	0.035	0.061	0.146	0.813	0.022	0.175	−0.085
22	0.107	−0.030	0.207	0.797	0.168	0.226	−0.097
24	0.080	0.005	−0.061	0.714	0.068	−0.087	0.271
25	0.114	0.163	−0.079	0.649	−0.011	−0.320	0.223
18	0.100	0.022	−0.038	−0.023	0.775	0.099	0.256
17	−0.071	0.267	0.106	0.069	0.652	−0.246	−0.044
19	0.275	−0.015	−0.070	0.240	0.617	0.184	−0.105
21	0.210	−0.004	0.128	0.126	0.168	0.764	0.033
20	0.042	0.220	0.012	−0.060	−0.234	0.619	0.410
26	0.036	0.087	0.033	0.167	0.117	0.153	0.735

Table 4 The correlation between the scale and Morisky, Green and Levine (MGL) Scale

	N	Mean	Standard deviation	Pearson correlation coefficient	*P*
Scale	222	92.44	14.95	0.426	0.00
MGL		17.37	2.48		

Table 5 The internal consistency of the scale (n=222)

Elements	Cronbach's alpha	Item
Basic knowledge on medication	0.831	5
Knowledge about Chinese medicine decoction	0.930	7
Knowledge about taking Chinese medicine	0.835	4
Medication beliefs	0.439	5
Medication behavior	0.732	5
Total table	0.915	26

enough. The MGL scale consisted of 4 questions, which covered 3 kinds of behaviors: drug omission, drug inattention and drug withdrawal. But there was lack of medication in traditional Chinese medicine. The measurement scale contained knowledge, belief, behavior and other contents of traditional Chinese medication, which were much more abundant than the MGL scale. Therefore, they were correlated with each other but with low correlation coefficient. The contents included in our scale might be our advantages.

For reliability test, the total Cronbach's alpha of the final draft of the scale was 0.915, which was better and more reliable than the widely used 2008 MMAS-8 scale with the Cronbach's alpha of 0.83. However, the Cronbach's alpha and retest reliability of medication belief were lower. We considered that the condition might relate to the two contrary constructs including positive belief and

Table 6 The total and the other factors

Elements	*r*
Basic knowledge on medication	0.711**
Knowledge about Chinese medicine decoction	0.780**
Knowledge about taking Chinese medicine	0.667**
Medication beliefs	0.472**
Medication behavior	0.578**
Total table	0.753**

Notes: **$P<0.01$. Retest Reliability Coefficient of the Scale (n=33).

negative belief in this dimension. Because the two constructs were inverse, the internal consistency coefficient was low. On the other hand, both contents belonged to the same medication belief, the reliability of the scale could be considered acceptable, and it was a more reliable measurement tool for the medication adherence of CKD patients in traditional Chinese and western medicine.

Limitations and prospects of the study

The medication adherence scale of traditional Chinese and western medicine for non-dialysis CKD patients was preliminarily developed. It was inevitable to have deficiencies in the research process because of limited time and knowledge, which were mainly in the following aspects:

First, based on Knowledge–Attitude–Belief Practice theory, the scale was not consistent with scales that were commonly used in health belief theory, and the final form of the scale had a larger proportion of knowledge of medicine but a relatively smaller proportion of behavioral aspects. The results of the survey might not comprehensively reflect the patient's medication behavior whereas it had a better understanding of the patient's refusal of medication.

Second, it is a cross-sectional study and without constant follow-up after verifying reliability and validity of the scale. The correlation between good adherence measured by this scale and clinical outcomes is difficult to analyze. We wish to explore more in further study.

Third, chronic disease outpatients of Guangdong Hospital of Traditional Chinese Medicine and urban population took the larger proportion of objects. And the proportion of taking Chinese medicine or proprietary of Chinese medicine was larger, revealing limited population representation. The applicability of the scale needed more researches and more different groups of people for verification.

Conclusion

The measurement scale included 26 items finally, which consisted of 3 dimension (Knowledge, Beliefs, Behavior) and 5 elements. Its 5 elements included basic knowledge on medication (5 items, items 1–5), knowledge about Chinese medicine decoction (item 7 and items 6–12), knowledge about taking Chinese medicine (4 items, items 13–16), medication beliefs (item 5 and items 17–21) and medication behavior (5 items, items 22–26), see Supplementary materials. The content validity, construct validity and calibration correlation validity of the scale achieved benign results. The total Cronbach's alpha of the scale was 0.915, and the total retest reliability coefficient was 0.753, indicating that the scale had good stability.

Ethics approval

The patients' consent was written informed consent, and this study was conducted in accordance with the Declaration of Helsinki. It was approved by Ethics Committee of Guangdong Provincial Hospital of Chinese Medicine. Petition Number: B2016-93.

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Disclosure

The authors report no conflicts of interest in this work.

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