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Improving Adherence to Prescribed Antidiabetics and Cardiovascular Medications in Primary Health Care Centers in Nyala City, South Darfur State-Sudan*

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ABSTRACT

Aims: Prospective pharmacist's interventions aimed to improve patient's knowledge and behaviors to adhere to medications in patients with type 2 diabetes with or without cardiovascular medical conditions in primary health care (PHCs) centers in Nyala city, South Darfur State, Sudan. **Methodology and Materials:** 300 patients were enrolled for assessing adherence with the Brief Medication Questionnaire (BMQ) in ten PHCs in Nyala city. We assessed patients' responses to BMQ pre- and post-interventions plan by: complex interventions, humanitarianism and disease outcomes determined by health-related outcomes (SF-36), glycosylated hemoglobin (HbA1c) and blood pressure. **Results:** BMQ scores have improved significantly in four screens (pre- and post-interventions): regimen [4.6 ± 0.2 to 1.8 ± 0.1; $P = 0.001$], belief [1.6 ± 0.3 to 0.3 ± 0.3; $P = 0.007$], recall [1.7 ± 0.2 to 0.6 ± 0.2; $P = 0.043$] and access screens [1.8 ± 0.1 to 0.4 ± 0.1; $P = 0.005$]; which have indicated an improved patients' adherence to medications. Percentage of subjects reaching target of post prandial blood glucose (PPBG) have increased from 28.0% to 49.3%; [$P = 0.02$] post interventions. PPBG mean values have decreased significantly from [11.1 ± 0.6 mmol/L to 8.1 ± 0.8 mmol/L; $P = 0.001$]. Percentage of subjects with improved blood pressure control have increased significantly from [50.3% to 89.0%; $P = 0.001$]. Significant differences existed between baseline and post-baseline scores on four of eight SF-36 sub-domains. **Conclusions:** Pharmacist provided patient education and behavioral interventions were effective in increasing medications knowledge and raising adherence issues in patients with type 2 diabetes with or without cardiovascular chronic medical conditions.

Keywords: Adherence; Darfur; Medications; Nyala; PHCs; Sudan

1. Introduction

According to a medical literature review published recently in the Annals of Internal Medicine, approximately 50 percent of medications for chronic disease are not taken as prescribed. Failure to take prescribed medications was estimated to cause 10 percent of hospitalizations and 125,000 deaths annually. The total cost to the US health system from poor medication adherence was put at $100 billion to $289 billion per year. Several studies have shown a low adherence rate [1]. In Saudi Arabia and Egypt, for example, adherence rates of only 34.2% and 15.9% have been reported, respectively; [2]. A systematic review indicates that adherence to cardiovascular medications in resource-limited countries is sub-optimal and appears very similar to that observed in resource-rich

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countries. Efforts to improve adherence in resource-limited settings should be a priority given the burden of heart disease in this context, the central role of medications in their management, and the clinical and economic consequences of non-adherence [3]. In China, gender difference had been observed for the adherence of antihypertensive medications [4].

The scope of problems due to medications non-adherence is enormously rising. In Sudan, there were very rare scientific articles published about medications adherence. The current needs for medications adherence provide good opportunity to implement an interventional adherence programs in health setup in Sudan. In early 2000, El Zubair and co-workers conducted cross-sectional study of hypertensive patients in Sudan and estimated drug adherence. Factors associated with adherence, status of BP control and occurrence of complications were assessed. Adherence was 59.6% as measured with the pill count method. They found 92.0% of compliant patients had controlled BP in comparison with 18.0% of non-compliant patients, and 30.1% of the compliant patients had complications in comparison with 46.3% of the non-compliant patients. While the adherence rate was reasonable, 36.8% of patients were non-compliant because they could not afford to buy antihypertensive drugs. These patients experienced uncontrolled BP and other complications [5]. We aimed to design approaches (behavioral and educational) that improve patient's knowledge and behaviors as to adhere to antidiabetics and cardiovascular medications. We have imposed continuous structured program for improving adherence to medications and implemented sequentially as a policy in ten primary health care centers (PHC's) in Nyala, South Darfur State, Sudan. The main objective was to promote awareness and explore reasons for non-adherence to antidiabetics and cardiovascular medications. We emphasized pharmacist's role in improving patient's adherence to antidiabetics and cardiovascular medications.

2. Methodology

Study design: A multi-centre prospective intervention (pre and post) clinical trial. It was ethically approved by the Ethics Committee in Faculty of Pharmacy at Gezira University, Ministry of health (MOH) in South Darfur State and director of primary health care clinics (PHC's).

Setting: It was performed in 10 PHC's in Nyala city which is located in the western provinces of Sudan, South Darfur State, Sudan.

Patient enrollment: The eligible randomly selected population was composed of all patients with diabetes type 2 with or without cardiovascular diseases visiting the PHC's in Nyala city. The estimated sample size followed the procedure outlined in similar setting [6].

Outcome measures: The study primary outcome measures were improvements in SF-36, HbA_{1c} and blood pressure. The secondary outcomes were improvement to responses to the BMQ (at baseline, at 3 and 6 months post interventions plan).

2.1. Tools Used to Measure Outcome

The interventions plan was in the form of: behavioral interventions involved the use of tools to change patient's skill, dosage schedule changes, written refill, pill count, communications with healthcare providers and counseling. Educational interventions involved teaching the patients about the medications and diseases through written communications (handouts, brochures, booklets and posters), public campaigns and direct consultations in the clinics by using face-to-face education sessions.

2.2. Brief Medication Questionnaire (BMQ) and SF-36

The validated BMQ is more sensitive in identifying and diagnosing adherence problems [7]. It consists of four sub-scales (regimen, beliefs, recalls and access screens). The tool includes 5-items regimen screen that asks patients how they took each medication in the past week, a 2-items belief screen that asks about drug effects and bothersome features, and a 2-items recall screen about potential difficulties remembering. While 2-item, access screen evaluates the patient difficulty in buying and refilling their medications in time. The higher the score (positive screen) in each aspect indicates an increased potential for adherence problems (or barrier to adherence). Whereas a negative screen indicates that there was decreased non-adherence or non-barrier to adherence. We used SF-36 to determine improvements in health-related quality of life-HRQoL [8].

3. Results

A total of 350 eligible patients with diabetes with or without cardiovascular diseases were enrolled, of which 300 patients 85.7% have successfully completed the study. Thirty patients 8.6% were considered drop outs because of the irregular follow up and twenty patients 5.7% were not reachable. Our results indicated a high participants' response rate of 85.0% and a high number of illiterate 19.7% and unemployed subjects 31.0%. More than two third of patients were either overweight or obese 67.0%. The number of patients with diabetes and coexisting cardiovascular diseases was high 46.0%, while the number of patients with coexisting diabetes and hypertensions exceeds 24.7%. The socio-demographic characteristics were shown in **Table 1**.

Table 1. Socio-demographic characteristics of enrolled population (N = 300).

Parameter	Frequency (N)	Percentage (%)
Age (mean age ± SD, 49.7 ± 1.2 years)		
18 to44	75	25.0
45 to 60	197	65.7*
>60	28	9.3
Gender		
Male (Mean age ± SD 50.8 ± 4.5 years)	148	49.3
Female (Mean age ± SD 49.6 ± 4.4 years)	152	50.7*
Marital status		
Married	276	92.0*
Unmarried	24	8.0
Educational level		
Illiterate	59	19.7
Preliminaryschool	91	30.3*
Secondary school	85	28.3
University graduate	63	21.0
Post university degrees	2	0.7
Occupation/work status		
Government employee	111	37.0*
Private employee	26	8.7
Skilled labor	47	15.7
Business	17	5.6
Unemployed	93	31.0
Retired	6	2.0
Chronic medical condition		
Diabetes	162	54.0*
Diabetes and hypertension	74	24.7
Diabetes and cardiovascular diseases	64	21.3
Income per month (Sudanese Ginaih/Pound)		
1 - 499 (≤6000 per year)	116	38.7
500 - 1000 (≥6000 and <12,000 per year)	152	50.7*
>1000 (>12,000 per year)	32	10.6
Body max index (Kg/m^2)		
Under weight < 22	1	0.3
Normal weight ≤ 25	98	32.7
Over weight > 25 to < 30	186	62.0*
Obesity > 30	15	5.0
Total (at each sub row)	**300**	**(100)**

Key: N = Frequency; (%) = Percentage; *The highest percentage achieved in raw.

3.1. Brief Medication Questionnaire (BMQ) Adherence Measure

At baseline assessment, nearly half of participants 147, 49.7% were able to name their medications. However, at 3rd assessment more than two thirds 241, 80.3%; P = 0.002 have reported that they knew their medications names. The number of patients who reported that they did not missed their medication was increased from 71, 23.7% to 184, 61.3% and to 236, 78.7%; P = 0.001 at stages 1, 2 and 3; respectively. More than 90.0% of respondents have stated that they were aware about their chronic medical conditions; P = 0.459. At baseline 163, 54.3%; P = 0.001 of patients had a concern or doubt when asked how well the medications worked for them. The number of patients who said that their medication bother them, was 48, 16.0%; 25, 8.3% and 8, 2.6%; P = 0.015 at stages 1, 2 and 3; respectively. There were 81, 27.0%; 55, 18.3% and 33, 11.0%; P = 0.03 who admitted that their medications caused side effects (barrier to adherence). 105, 35.0%; 75, 25.0% and 55, 18.3%; P = 0.02 have agreed that it was at least somewhat hard to remember all the doses at assessment 1, 2 and 3; respectively. Results revealed 125, 41.7%; 99, 33.0% and 65, 21.6%; P = 0.04 have indicated that it was at least somewhat hard to pay for their medications at assessment 1, 2 and 3; respectively. There were 106, 35.3%; 72, 24.0% and 36, 12.0% at stages 1, 2 and 3, respectively; have said that it was at least somewhat hard to get their refill in time, this barrier to adherence was decreasing significantly; P = 0.042. Also 120, 40.0%; 143, 47.6% and 136, 45.3% at stages 1, 2 and 3, respectively; have reported that it was at least somewhat hard to read the print on the container; P = 0.285. 226, 75.3% at baseline, 241, 80.4% at 2nd and 280, 93.3% at 3rd assessment, have stated that their dosage times were convenient; P = 0.006. There were 41, 13.6%; 21, 7.0% and 3, 1.0% have stopped taking some of their medications in the past six months during the assessment stages 1, 2 and 3, respectively; P = 0.01. Furthermore, n = 226, 75.3%; 177, 59.5%, and 105, 35.0%, responded that, they did not know how well did their medications worked for them; P = 0.01.

3.2. BMQ Adherence Measure by Scoring Procedure

The responses to each screen were detailed in **Table 2**. To determine correlations between screen and demographic parameters, person correlation coefficient was used at 6 months post interventions, **Table 3**. The percentage of patients achieved controlled PPBG were 28.0%, 37.0% and 49.3%, moderately controlled 21.0%,

Table 2. Comparison of the BMQ mean scores of the four screens at different assessments intervals.

BMQ Screen scores (Mean ± SD) (N = 300)	**Assessment 1**	**Assessment 2**	**Assessment 3**	***P* value**
Regimen Screen	4.6 ± 0.2	2.9 ± 0.1	1.8 ± 0.1	0.001*
Belief Screen	1.6 ± 03	0.9 ± 0.2	0.3 ± 0.3	0.007*
Recall Screen	1.7 ± 0.2	1.1 ± 0.3	0.6 ± 0.2	0.043*
Access Screen	1.8 ± 0.1	1.0 ± 0.2	0.4 ± 0.1	0.005*

Key: *P < 0.05.

Table 3. Correlation between the BMQ screen and demographic parameters at final stage (N = 300).

Patient socio-demographic parameter (final assessment, stage 3)		**Regimen**	**Belief**	**Recall**	**Access**	**Total**
Education	Correlation coefficient	−0.54	−0.11	−0.06	−0.16	−0.4
	P value	0.001*	0.049*	0.329	0.004*	0.001*
Occupation	Correlation coefficient	0.38	0.16	0.08	0.14	0.32
	P value	0.001*	0.007*	0.154	0.017*	0.001*
Body max index	Correlation coefficient	−0.05	0.05	0.13	0.11	0.08
	P value	0.371	0.396	0.026*	0.062	0.145
Income	Correlation coefficient	−0.32	−0.14	0.00	−0.03	−0.2
	P value	0.001*	0.014*	0.961	0.64	0.001*
Age	Correlation coefficient	0.13	0.04	0.05	0.06	0.12
	P value	0.029*	0.521	0.391	0.267	0.036
Total number of study patients (at each sub row)		300	300	300	300	300

Key: *P < 0.05.

27.0% and 31.0%, poorly controlled 18.0%, 15.0% and 12.0% and uncontrolled 33.0%, 21.0% and 7.7% at stages 1, 2 and 3; respectively. A significant decrease in patients PPBG mean values was observed from baseline, at 3 and 6 months 11.1 ± 0.6 mmol/L; 9.4 ± 0.5 mmol/L and 8.1 ± 0.8 mmol/L; $P = 0.001$; respectively. The percentage of patients who reached target PPBG levels (controlled) increased from 28.0% at baseline to 49.3% at 6 months post interventions. At baseline, HbA_{1c} mean was 10.5 ± 1.2 and patients adhered to medications has a mean HbA_{1c} of 7.6 ± 0.2. At baseline, BP levels were SBP 135.7 and DBP 81.8 mmHg, improved to SBP 123.3 and DBP 77.6 mmHg] after 6 months, $P = 0.001$. The percentage of patients with improved BP controlled levels was 50.3% *vs.* 89.0%; $P = 0.001$ at baseline and post baseline; respectively. While the percentage of patients with improved BP adequate levels decreased 22.7% *vs.* 4.7%; $P = 0.01$, inadequate 18.3% *vs.* 4.7%; $P = 0.03$, with markedly poor 8.7% *vs.*1.7%; $P = 0.04$ at baseline and 6 months post baseline; respectively. Analysis revealed that significant differences existed between baseline and post baseline scores on SF-36 domains; **Table 4**.

4. Discussions

The main study findings were significant improved BMQ scores in four screens (pre and post interventions): Regimen, Belief, Recall and Access screens; which have indicated an improved patients' adherence to medications. The percentages of subjects reached target post prandial blood glucose (PPBG) have increased post interventions. PPBG mean values have decreased significantly. The percentages of subjects with improved blood pressure control have increased significantly. Remarkable differences existed between baseline and post baseline scores on four of eight SF-36 sub domains.

4.1. The Participant's Responses to BMQ Adherence Measure

The percentage of patients who knew their prescribed medications names have increased from 50.0% at baseline to more than 80.0% post interventions. There was increase in the number of patients who have reported that they did not miss their medications. Almost all participants indicated that they have previous idea about their disease. Although not tested, but it was anticipated that knowledge test may reveal the precise idea about their knowledge. This finding had been reported in a previous study [9].

The pharmacist's interventions has led to decline in the number of patients who have had a concern or doubt about how well their medications worked for them. The percentage of patients who reported that their prescribed medications worked very well, have improved at 6 months post interventions. This finding strongly supports the sprouting role of pharmacist in patient's medications education. These findings were in line with previous recent study [10] and earlier study [11]. The improved adherence to medications was evident in the decrease in percentage of patients experiencing medications bothersome. More prominent achievement was gained in the declined percentage of patients for those who admitted that their medications caused side effects. The patients expressed their concerns about the cost of medications. However, simplifying the regimen with combinations therapy was offered as a solution to the increased cost. The percentage of patients who have stopped taking their medications in the past six months have reduced from baseline, to 2nd assessment and to final assessment. The percentage of patients who have missed to take their medications decreased at 6 months post interventions. These findings were attributed to continued education,

Table 4. Descriptive statistics and comparison of SF36 mean scores ± SD (N = 300).

SF36 sub domain scale (Mean ± SD)	Stage 1	Stage 2	Stage 3	*P* value
Physical functioning	65.5 ± 25.4	69.0 ± 25.8	74.3 ± 19.9	0.001*
Role limitations due to physical health	53.8 ± 36.0	47.9 ± 41.5	48.7 ± 42.0	0.142
Role limitations due to emotional problems	56.1 ± 38.8	66.7 ± 41.3	58.2 ± 42.6	0.004*
Energy/fatigue	59.8 ± 22.4	59.8 ± 24.1	66.1 ± 20.4	0.001*
Emotional well-being	68.9 ± 23.0	82.7 ± 20.6	86.8 ± 14.1	0.001*
Social functioning	58.1 ± 24.7	60.6 ± 25.6	60.5 ± 24.4	0.387
Pain	61.1 ± 25.0	62.5 ± 26.8	62.0 ± 22.8	0.770
General health	51.3 ± 10.4	49.9 ± 10.2	50.3 ± 10.7	0.252

Key: *$P < 0.05$.

improved skills, available information and discussions with patients as they were involved to ask and talk freely.

4.2. BMQ Adherence Measure by Scoring Procedure

Post pharmacist's interventions, there was a significant $P < 0.05$, improvement in scores in all BMQ four screens [regimen, belief, access and recall screens] from baseline throughout the assessment intervals which have indicated an improved patients' medications adherence. This was a positive finding and supports the fact entailing the importance of pharmacist in patient education tailored to medications adherence. In this respect the study supports the findings drawn in a similar study using the same BMQ instrument [9]. Patients have received a multiple dose regimen (2 or more times/day) and have reported difficulty remembering their medications at the start of the study, which entails the presence of recall barriers. The pharmacist interventions in this respect regarding simplification of regimen, use of combinations and prioritize dispensing chronic medications to patients on chronic diseases as our population facilitated this barrier with resultant improved adherence to medications.

4.3. Barriers to Medication Adherence

The results indicated the presence of side effects to medications among few participants. However, the reported problems in medications decreased significantly post pharmacist's interventions. This finding was in line with many other studies [12-14]. Another barrier to medications adherence was that some patients reported not remembering all the doses of their medications which was consistent with previous study [15]. The issue of medications cost was another barrier to adherence to medications and was increasing throughout the assessment intervals. This finding complies with a previous study [16]. The refill problem was raised by patients as barrier to medications adherence, however; it was in contrast with a previous study [17]. In the latter study patients refill barrier was decreasing. A considerable number of patients find it difficult to read the label on their medications which may be attributed to high number of illiterate patients in the study population. A remarkable finding was the increasing number of patients reporting their dosage times were convenient. These findings dictated the importance of policies for refill, labeling and convenient dosing for improving adherence and to halt medications non-adherence.

Also there was no written policy for non-adherence risk reduction and for assessing any suspected medications non-adherence in all of the surveyed facilities. This might explain why even serious risks of non-adherence to medications were underreported. All these facts taken together would also indicated the decreased level of awareness about medications adherence safety concerns, which were recognized and implemented in most of the developed countries and some of the underdeveloped ones. Medications adherence is important in order to achieve better treatment outcomes in chronic diseases such as diabetes, hypertension and other cardiovascular diseases.

4.4. Post Prandial Blood Glucose (PPBG) and HbA1c

A clinical study by Avignon and co-workers showed that PPBG (post-lunch) is a better predictor of HbA_{1c} than FPG > 7.2 mmol/L before breakfast [18]. Postprandial hyperglycemia has been associated with increased risk of micro vascular [19] and macro vascular complications [20]. In this respect the results revealed a remarkable increase in the percentage of patients who have reached target PPBG levels from 28.0% at baseline to 49.3% after 6 months. Whether or not this has been associated with reduced microvascular or macrovascular complications deserve more attention in future studies in our population. Although the level of HbA_{1c} decreased; but the target was not reached <7.0%. This may be due to the fact that some patients failed to regularly monitor their HbA_{1c} which may have affected the final results.

4.5. Mean Values of Blood Pressure (BP)

The number of patients with controlled BP has increased from 50.0% to 89.0% within the study period. This was in agreement with previously published study [21]. The medications discontinuation rate in our population at the end of the final follow up was very low, 1.0%. This may be attributed to the fact that patients were informed at each clinic visit to adhere to their medications and this was reinforced in each clinic visit. Furthermore, many patients has been switched to combinations therapy and ensured that it contains an ACE inhibitor. Our results lend support to the findings reported few years ago by [22].

4.6. Results of Short Form Health Survey (SF-36)

The largest improvements in HRQoL were for the physical functioning score and the emotional wellbeing scores (improved health). This finding was in concordance with that previously reported [23]. The provision of pharmacist education to patients with type 2 diabetes with or without cardiovascular diseases has resulted in improvement in terms of their HRQoL. The outcome of

the pharmacist's interventions on patient's HRQoL demonstrated the relationship between this outcome measure and adherence to medications. Improvement in HRQoL may in part be attributed to the increased contact of these patients with the pharmacist, improved adherence to medications and resultant clinical improvement in patients' clinical outcomes. The current study lend support for the adoption of assessing HRQoL as an outcome for evaluating health education programs in patients with diabetes type 2 with or without cardiovascular diseases; who were on multiple medications.

4.7. Impact of Education on Adherence

Patient education on medication adherence is one of the main issues of interventions in the literature to enhance medication adherence [24]. In many of the surveyed facilities; health care providers appreciated the importance of education to patients in order to enhance the therapeutic success. The current study results demonstrated that a collaborative approach between the pharmacist and healthcare providers can facilitate implementing medications adherence concepts which were expected to contribute to improved patient outcomes. During the study period, patients were asked to visit their clinic regularly, in order to get controlled (target) blood glucose and BP levels. As patients adhered to see their physicians regularly they showed improvements in the therapeutic outcomes. However, patients have shown significant decrease in the BP and blood glucose levels. This was due to continued pharmacist's interventions and follow up. This was also in agreement with previously published study [25]. This finding dictates the importance of educating and training the patients about the different forms of medications adherence barriers. Non-adherence to long-term medications in chronic diseases is a worldwide problem. It has been estimated that 40.0% to 50.0% chronic disease patients are non-adherence to their prescribed treatment [26]. Non-adherence to medications is a major concern in the management of chronic disease such as hypertension [27,28]. The issue of the risk of medications non-adherence was not been identified in most of the surveyed PHCs facilities. However, most of the PHCs facilities in developed countries have implemented policies for medications adherence. In summary; this improved adherence to medications was associated with good control of blood glucose and BP, coupled with other positive effects observed in patient knowledge and reduction in difficulties in taking antihypertensive medications. The study highlighted that some patients lack knowledge about their medications, their respective disease type and its management as the main reasons for poor adherence. This finding was in concordance with recent published study [29]. This negative attitude places the pharmacist to play more vital role in responding to queries and in raising the awareness about medications adherence among patients and healthcare providers alike.

4.8. Current Study Limitations

There was a limitation with the current study, that medication adherence was measured using BMQ a screening behavioral measure, we anticipate that extent of adherence to medications may not be precisely estimated by this method.

4.9. What Is New

The pharmacist managed medications adherence, significantly improved patients' glycaemia control, blood pressure control and HbA_{1c}. The findings of this study provide evidence of the effectiveness of pharmacists' educational and behavioral interventions in medication adherence.

5. Conclusion

There is a need for further research to highlight medications non-adherence and barriers to patients' adherence, in order to identify the type of interventions that may be needed for improving adherence and to evaluate whether improvements in awareness, knowledge and adherence are sustained in the longer term. We concluded that, the pharmacist's education and behavioural interventions were effective in increasing the medications knowledge and raising adherence issues in patients with type 2 diabetes with or without cardiovascular diseases.

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