Pharmacist Role in Enhancement of Medication Adherence and Clinical Outcomes in Acute Coronary Syndrome Paitents

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Abstract:

Background: Patients who experience acute coronary syndrome (ACS) are at high risk of having further events in the future. One month after the attack, the average readmission rate was estimated to be approximately 20%. As a result, patients must receive secondary prevention medications to avoid reoccurrence of these cardiovascular events. To get the entire benefit, patients must adhere to the prescribed regimen. However, many studies demonstrated that patients do not adhere to the prescribed medications upon the long term, and this leads to substantial deterioration of disease and consequently death, as well as significant financial burden. This study has the objective of assessing the impact of pharmacist intervention on increasing patients' adherence to ACS medications.

Method: a prospective interventional study was performed from January to October 2018. A total of 70 patients were selected randomly and were divided into those who received the usual care processes offered by pharmacists at discharge, and those who received well-structured clinical pharmacist intervention about the discharge medications and disease. Heart rate (HR), blood pressure (BP) and lipid profile were measured at baseline and after 3 months. Also, patients' level of adherence to the discharge medications was assessed after 3 months. Furthermore, 30-day hospital readmission rate was evaluated.

Results: Regarding patients' medication adherence, 63.3% of the patients in intervention group had high level of adherence compared to only 21.1% of controls. After 3 months of follow up significant reduction in mean scores of outcomes were noticed in intervention group compared to control, where HR (73.6 vs. 80), SBP (129.5 vs. 141), DBP (81.2 vs. 87.5). Also serum cholesterol, triglycerides, and LDL were reduced and HDL increased significantly in the intervention group ($P < 0.05$), while no such changes seen in controls. Moreover, no considerable difference was observed in hospital readmission between the intervention and control group.

Conclusion: This study showed that pharmacist intervention caused notable enhancement in patient' medication adherence with subsequent improvement of heart rate, blood pressure, and lipid profile, but with no improvement in hospital readmission.

Key words: Adherence, Outcomes, Pharmacist, Intervention, ACS.

دور الصيدلاني في تعزيز الالتزام بالأدوية و النتائج السريرية لمرضى متلازمة الشريان التاجي الحاد

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الخلاصة:

المقدمة: المرضى الذين يعانون من متلازمة الشريان التاجي الحاد هم في خطر كبيرلحدوث نوبات اضافية في المستقبل. يقدر معدل عودة الدخول للمستشفى بسبب حدوث نوبات اخرى بعد مرور شهر على النوبة الاولى بحوالي 20٪ ، وكنتيجة لذلك ، يجب أن يتلقى المرضى أدوية وقائية لتجنب تكرار هذه النوبات . لغرض الحصول على الفائدة الكاملة ، يتحتم على المرضى الالتزام بالأدوية الموصوفة. بالرغم من ذلك ، أظهرت العديد من الدراسات أن المرضى لا يلتزمون بالأدوية الموصوفة على المدى الطويل ، وهذا يؤدي إلى تدهور كبير في المرض و بالتالي الوفاة ، ضافة الى أعباء مالية كبيرة. تهدف هذه الدراسة إلى تقييم تأثير التدخل الصيدلي على زيادة التزام المرضى بدواء متلازمة الشريان التاجي الحاد .

طرق العمل: دراسة تدخلية مستقبلية أجريت من يناير إلى أكتوبر 2018. أختير ما مجموع 70 مريضا بشكل عشوائي وتم تقسيمهم إلى أولئك الذين تلقوا عمليات الرعاية المعتادة التي يقدمها الصيادلة عند خروج المرضى ، وأولئك الذين تلقوا توصيات مركزة و مرتبة بشكل جيد من قبل الصيدلي السريري حول علاجاتهم و مرضهم . تم قياس معدل ضربات القلب ، ضغط الدم و مستوى الدهون عند اختيار المرضى وبعد 3 أشهر. تم تقييم مستوى التزام ا لمرضى للمجموعتين بالادوية الوقائية بعد 3 أشهر. علاوة على ذلك ، تم تدوين معدل عودة الدخول في المستشفى خلال 30 يوم.

النتائج : فيما يتعلق بالالتزام بأدوية المرضى ، كان 63.3 ٪ من المرضى في مجموعة التدخل لديهم مستوى عال من الالتزام مقارنة مع 21.1 ٪ فقط من مجموعة السيطرة. بعد 3 أشهر من المتابعة لوحظ انخفاض كبير في متوسط درجات النتائج في مجموعة التدخل مقارنة بمجموعة السيطرة، حيث كان معدل ضربات القلب 73.6)مقابل 80) ، ضغط الدم الانقباضي (129.5 مقابل 141) ، ضغط الدم الانبساطي 81.2) مقابل 87.5). أيضا لوحظ انخفاض نسبة الكولسترول في الدم ، الدهون الثلاثية ، و البروتينات الدهنية واطئة الكثافةLDL)) ، وزيادة البروتينات الدهنية عالية الكثافة HDL)) بشكل ملحوظ في مجموعة التدخل (P <0.05) ، في حين لم تظهر مثل هذه التغييرات في مجموعة السيطرة. علاوة على ذلك ، لم يلاحظ أي فرق كبير في عودة الدخول للمستشفى بين مجموعة التدخل ومجموعة السيطرة .

الخلاصة: أظهرت هذه الدراسة أن التدخل الصيدلي تسبب في تحسين ملحوظ في التزام المرضى بالدواء مع التحسن اللاحق من معدل ضربات القلب ، وضغط الدم ، ومستوى الدهون في الدم ، لكن بدون تحسن في معدل عودة الدخول للمستشفى.

الكلمات المفتاحية: التزام، نتائج، صيدلاني، تداخل ،متلازمة الشريان التاجي الحاد

Introduction:

Cardiovascular disease (CVD) is one of the major causes of death globally. In 2015, it was reported that 17.5 million deaths were caused by CVD, accounting for 31% of all worldwide deaths. ACS was responsible for 7.4 million of these deaths [1]. Patients who experience ACS are at high risk of having further events in the future. One month after the attack, the average readmission rate for ACS was estimated to be approximately 20% [2]. Therefore, patients must receive secondary prevention medications to avoid reoccurrence of these cardiovascular events [1], and reduce morbidity and mortality associated with ACS [3-6]. American college of cardiology (ACC) and American heart associate (AHA) consensus guidelines for management of ACS recommend that these patients should receive antiplatelets, ACE inhibitors or ARBs, β-blockers and statins in absence of contraindications [7]. To get the entire benefit, patients must adhere to the prescribed regimen. Adherence, the extent to which a patient behavior complies with the prescribed regimen, is essential for delivering effective medical treatment. However, many studies demonstrated that patients do not adhere to the prescribed medications upon the long term, and this leads to substantial deterioration of disease, death, and significant financial burden [8]. The WHO reported that only 50% of chronic disease patients adhere to their medications [9]. In particular, the adherence to ACS

secondary prevention therapy is suboptimal worldwide [10]. Medication non adherence causes substantial increase in medical expenditures. In United States, 33% to 69 % of hospital admissions are due to non-adherence to the prescribed regimen [11], with a resultant annual cost of approximately 100 billion dollars [12]. There is a significant association between adherence to medications and clinical outcomes. A study showed that patients who stopped the use of all secondary prevention medications one month after discharge had lower than one-year survival compared to those who were adherent to therapy [13]. Another study illustrated that**;** patients who did not adhere to statin therapy had 3-fold higher mortality rate compared to adherent ones [14]. Numerous factors have been correlated with poor medication adherence. Some patients believe that the medication does not help with their disease [15]. Insufficient communication between patients and caregivers is another factor influencing patients' adherence [16]. Forgetfulness is one more reason for poor medication adherence [17]. About one third of ACS patients suffer from depression, which has an essential contribution to non-adherence [18]. It has been shown that depressed patients have twice the likelihood of being non adherent compared to non-depressed patients [19]. Financial limitation also plays a role. It has been demonstrated that patients with low income are more likely to have poor adherence [20]. Interestingly, patients who underwent invasive procedure demonstrated lower level of adherence compared to those who treated medically, supposed to be due to patients' belief that they were no longer sick if they managed by invasive procedure [21]. Also, complexity of medication regimens contributes to the poor adherence [22]. It has been shown that patients tend to adhere to single daily dosing more than multiple daily dosing [23]. Drug adverse effects are non-modifiable contributors to poor adherence [24,25]. In addition, the presence of multiple comorbidities interferes with patients' adherence. It is evident that non adherent patients have more comorbidities than adherent ones. Moreover, due to the prominent side effects profile demonstrated by elderly patients, they usually have poor adherence to medications [17]. A number of evidence based interventions have been developed to maximize patients' adherence. Of these, a significant proportion can be offered by pharmacist. Along with medication dispensing, pharmacist can deliver an organized counseling at discharge [26] by educating patients about their disease and goals of therapy; giving a thorough review of medications in terms of indication, duration of use, anticipated benefits, adverse effects as well as correct use concerning medication name, dosage schedule, dose, and storage; discussing control of risk factors and lifestyle modification**;** and educating patients about the importance of adhering to their drugs [27,28]**.** To ensure recognition of the provided information, the education process should continue post discharge [29]. This can be achieved by using electronic reminders which involve text messaging (SMS), and telephone calls [30-33]. In addition, applications of mobile phones and tablets that provide information about cardiac health may be used as reminders to improve adherence [22]. This study was designed to assess the role of pharmacist intervention in enhancing patients' adherence to ACS discharge medications.

Patients and Methods

Study Design:

This prospective interventional study was carried out at AnNajaf Center for Cardiac Surgery and Catheterization, Al-Sader Medical City; AnNajaf Province, Iraq during the period of January to October 2018. The follow up period was 3 months. Patients were selected randomly and were divided into those who received the usual care processes offered by pharmacists at discharge, and those who received well-

structured clinical pharmacist intervention which involved educating patients about their disease and goals of therapy; giving a review of medications in terms of indication, duration of use, anticipated benefits, correct use, as well as educating patients about the importance of adhering to their drugs. Heart rate, blood pressure and lipid profile were measured at baseline and after 3 months. Also, patients' level of adherence to the discharge medications was assessed after 3 months. Furthermore, 30-day hospital readmission rate was evaluated. Data were collected by using a purpose designed data collection sheet. Data regarding patients' demographics, contact information, level of education, occupation, diagnosis, medical history, smoking status, date of interview, discharge medications was collected. The 8 items Morisky Medication Adherence Scale (MMAS-8) was used to evaluate patients' level of adherence to the discharge medications. MMAS-8 composed of eight questions with yes or no response for the first 7 items. The last item is of 5-point Likert response. Total score can be achieved by summation of all eight items, and it can range from 0 to 8. According to MMAS, patients' adherence falls in three categories: Low (< 6), medium (6 - <8), and high (8) [34].

Participants: Patients who participated in this study were those admitted to AnNajaf Center for Cardiac Surgery and Catheterization due to ACS. Eligible patients were adults, experienced an ACS for the first time, and were able to complete the study. Excluded patients were those having severe comorbidities such as liver failure, lung failure, and cancer; patients who have communication barriers; those experienced ACS previously; those discharged without prescription; those could not identify their medications; very elderly patients; those could not provide phone number; and patients did not reside in AnNajaf. Verbal consent was obtained from all participants. Of 226 patients assessed for eligibility, 156 patients were excluded because of exclusion criteria, 70 patients were enrolled in the study. Out of the total included patients, 7 patients were lost during the follow up either because not answering phone calls (6 patients) or died (one patient).

Statistical Analysis: Statistical analysis of the current study was performed by using the statistical package for social sciences (SPSS) version 25. Descriptive statistics was presented as percentages, frequencies, mean, and standard deviation. The comparison of variables of the two groups was done using various statistical tests according to the type of variables. For categorical variables, chi-square test and Fisher's exact test (when chi-square couldn't be applied) were used. Independent two samples student's t test was used to compare means of normally distributed continuous variables. The not normally distributed variables were compared using non-parametric Mann-Whitney U test for two independent samples. P value< 0.05 was statistically significant.

Results

Baseline Characteristics of Study Population:

In this study, two groups of patients were enrolled; namely, intervention group and control group included a total of 30 and 33 patients, respectively. As it is shown in (**Table 1**), no statistically significant differences have been found between both groups with regards to their baseline characteristics, in all comparisons of these variables, P.value > 0.05.

Table (1): Baseline characteristics of studied groups

Variables		Group				P. value
		Intervention (n = 30)		Control (n = 33)		
		No.	%	No.	%	
Age (year)	< 65	23	76.7	23	69.7	0.53
	≥ 65	7	23.3	10	30.3	
Gender	Male	23	76.7	25	75.8	0.93
	Female	7	23.3	8	24.2	
Education	Uneducated	7	23.3	15	45.5	0.17
	Primary school	18	60.0	15	45.5	
	Secondary school	5	16.7	3	9.1	
Occupation	Not employed	26	86.6	26	78.8	0.49
	Employee	4	13.3	7	21.2	
Smoking status	Smoker	8	26.7	4	12.1	0.29
	Non-Smoker	10	33.3	11	33.3	
	Ex-Smoker	12	40.0	18	54.5	
Diagnosis	UA	13	43.3	19	57.6	0.49
	STEMI	12	40.0	9	27.3	
	NSTEMI	5	16.7	5	15.2	
Number of comorbidities	Less than two	20	66.7	16	48.5	0.239
	Two and more	10	33.3	17	51.5	
Number of medications	Less than five	7	23.3	12	36.4	0.26
	Five and more	23	76.7	21	63.6	

Data expressed as N: number and %: percent. Analyzed Chi square and P ≤ 0.05 considered significant.UA, unstable angina; STEMI, ST Segment Elevation Myocardial Infarction; NSTEMI, Non-ST Segment Elevation Myocardial Infarction.

Impact of Pharmacist's Intervention on Medication Adherence

The comparison of total Morisky scores between both studied groups shows that the mean Morisky score in intervention group was (7.4 ± 0.2) which was significantly higher than that in controls (5.6 ± 0.3), with a statistically significant difference, patients in intervention group had higher Morisky score; moreover, the effect size of intervention was large (1.18), (**Table 2**). Furthermore, 63.3% of the patients in intervention group had high level of adherence compared to 21.2% of controls. Low adherence level in intervention group was reported in only 2 patients (6.7%) compared to 18 controls (54.5%), (P. value < 0.001), (**Table 3**).

Table (2): Comparison of total Morisky scores of both studied groups

Total Morisky scale	Group		Effect size	P. value
	Intervention (n = 30)	Control (n = 33)		
Mean	7.4	5.6	1.18 (large)	< 0.001
Minimum	5.0	1.3		
Maximum	8.0	8.0		
Standard Error of Mean	0.2	0.3		

Data expressed as Mean ±SEM. Analyzed by Mann-Whitney. P value< 0.05 was statistically significant.

Table (3): Levels of adherence in both studied groups

		Group			
		Intervention (n = 30)		Control (n = 33)	
		No.	%	No.	%
Level of adherence	High	19	63.3	7	21.2
	Medium	9	30.0	8	24.2
	Low	2	6.7	18	54.5
Fisher's exact test= 19.7, P value <0.001					

Data expressed as N Number and % percent analyzed by Fisher's exact test

Impact of Pharmacist's Intervention on Outcomes

Vital Signs and Lipid Profile

Changes in Vital signs in both studied groups indicate that in intervention group, heart rate, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were significantly ,(P value <0.05), reduced after three months than their baseline levels , while no such changes had been reported in control group. The comparison between groups showed that after three months heart rate , SBP and DBP were significantly lower in intervention than control group, (P. value < 0.05), (**Table 4**).Serum Cholesterol, Serum Triglycerides and LDL were significantly reduced after 3 months in intervention group (P<0.05), while HDL was significantly increased in all comparisons (P<0.05). No similar changes occurred among controls,**(Table 5).**

Table (4): Changes in vital signs at baseline and 3 months after intervention

Vital Sign		Intervention (n = 30)		Control (n = 33)		P. value between groups
		Mean	SD	Mean	SD	
Heart rate	Baseline	80.8	12.7	83.0	12.1	0.497
	After 3 months	73.6	9.3	80.0	15.2	**0.048**
	Mean difference	7.2	1.8	3.0	2.3	0.16
	Percentage change	8.9%		3.6%		
	P. value within group	**<0.001**		0.21		
Systolic blood Pressure	Baseline	142.8	21.1	147.2	22.5	0.437
	After 3 months	129.5	16.7	141.0	18.4	**0.012**
	Mean difference	13.3	3.2	6.1	4.5	0.20
	Percentage change	9.3%		4.2%		
	P. value within group	**<0.001**		0.18		
Diastolic blood Pressure	Baseline	87.2	12.3	91.9	12.7	0.141
	After 3 months	81.2	9.8	87.5	12.6	**0.031**
	Mean difference	6.0	2.6	4.4	2.6	0.66
	Percentage change	6.9%		4.7%		
	P. value within group	**0.026**		0.11		

Data expressed as mean ±SD, Standard Deviation. Analyzed by independent two samples student's t test.

Table (5): Changes in lipid profile at baseline and 3 months after intervention

Variable		Group				P. value between groups
		Intervention (n = 30)		Control (n = 33)		
		Mean	SD	Mean	SD	
Serum Cholesterol	Baseline	172.1	58.1	170.5	46.2	0.759
	After 3 months	147.8	54.7	169.2	42.4	0.206
	Mean difference	-24.3	5.5	-1.4	0.6	**0.034**
	Percentage change	-14.1%		-0.8%		
	P. value within group	**0.007**		0.98		
Serum Triglycerides	Baseline	199.2	101.7	191.1	97.5	0.746
	After 3 months	170.6	90.2	181.0	104.0	0.676
	Mean difference	-28.6	9.5	-10.1	0.8	0.21
	Percentage change	-14.4%		-5.3%		
	P. value within group	**<0.001**		0.35		
High density lipoprotein	Baseline	30.8	8.4	33.1	6.7	0.281
	After 3 months	-33.1	7.8	-32.9	7.8	0.909
	Mean difference	-2.3	1.0	0.2	0.5	0.061
	Percentage change	-7.5%		0.7%		
	P. value within group	**0.005**		1.00		
Low density lipoprotein	Baseline	99.4	48.7	101.3	42.8	0.948
	After 3 months	80.8	49.3	100.2	39.0	0.071
	Mean difference	-18.6	7.5	-1.1	2.3	**0.035**
	Percentage change	-18.7		-1.1		
	P. value within group	**0.02**		0.84		

Data expressed as mean ±SD, Standard Deviation. Analyzed by Independent two samples student's t test. P value< 0.05 was statistically significant.

Hospital Readmission As shown in **(Table 6)**, need for re-admission was insignificantly different between both groups.

Table (6): Need for Re-admission in both studied groups

Re-admission	Group			
	Intervention (n = 30)		Control (n = 33)	
	No.	%	No.	%
Re-admitted	1	3.3	3	9.1
No- readmission	29	96.7	30	90.9
Fisher's exact test, P = 0.35				

Data expressed as N Number and % percent analyzed by Fisher's exact test

Discussion

Patients' non adherence to medications is a dilemma. This study tried to find out the role of pharmacist intervention in improving patients' adherence to the lifesaving preventive medications prescribed for patients who experienced ACS for the first time. The current study has shown that pharmacist led intervention through patient education and follow up has considerable impact on optimizing patient' medication adherence as evidenced by the finding that 63.3% of the patients in intervention group had high level of adherence compared to only 21.1% of controls.

This finding is in accordance with a randomized controlled trial done in Vietnam which revealed that pharmacist interventional program via patient education caused remarkable enhancement in adherence to ACS discharge medications [26]. In United States, a randomized controlled trial revealed that pharmacist multifaceted intervention consisting of patient education and follow up by phone calls and voice messages increased medication adherence markedly among patients with ACS [35]. Moreover, A Canadian study stated that pharmacist-initiated intervention by simple telephone calls, dramatically enhances patient' adherence to dual antiplatelet therapy for patients with primary Percutaneous intervention (PCI) [32]. Possible reasons behind this finding are patients' awareness about their disease, and importance of their medications in preventing recurrent events, reducing readmission and enhancing quality of life helped to increase patients' medication adherence. It is important to note that, pharmacist mediated intervention did not only improve patients' medication adherence, but also had positive effect on patient' outcomes among the intervention group, where three months after discharge, heart rate and blood pressure were considerably lower in the intervention group compared to control (Table 4). These findings are in partial agreement with several randomized controlled trials which reported that pharmacist educational intervention caused enhancement of patients' medication adherence, and notable reduction in their blood pressure [36-38] .The most likely justification of such result is that the high level of medication adherence among intervention group caused improvement in patients' outcomes. The current study showed that there was a

considerable reduction in serum cholesterol, serum triglycerides and LDL as well as increased HDL levels among the intervention group after three months, with no such significant changes observed in control group (Table 5). Similar pattern of findings was reported by a randomized controlled trial done in United Arab Emirates where pharmacist interventional program consisting of patient education about diabetes, hypertension, and hyperlipidemia as well as their medications resulted in marked improvement in lipid profile among the intervention group [39]. Also, a study verified that pharmaceutical care resulted in improved serum cholesterol and triglycerides among the intervention group [37]. Furthermore, Lee *et al* reported reduction in LDL cholesterol following pharmacist intervention [38]. Moreover, in United States, a controlled trial showed that pharmacist educational intervention resulted in obvious achievement in LDL cholesterol among the intervention group [40]. This finding could be attributed to the high level of medication adherence among the intervention group which caused improvement in lipid profile. Despite a big proportion of cardiovascular events might be due to poor medication adherence [8], the present study showed that there was no considerable difference in hospital readmission between the intervention and control group. This finding was in line with Nguyen *et al* (2018) who stated that pharmacist educational intervention increased patients' medication adherence without effect on hospital readmission rate [26]. Another randomized controlled trial carried out in United Stated verified that pharmacist delivered intervention resulted in no significant improvement in hospital readmission [41]. This might be explained by existence of factors other than medication adherence that affect readmission such as complications following primary PCI, and quality of medications used. Limitations of the present study could be related to the small sample size and being conducted in a single cardiac center so the results cannot be generalized.

Conclusion

The present study showed that pharmacist mediated intervention through patient education and follow up had notable impact on optimizing patient' medication adherence with subsequent improvement of heart rate, blood pressure, and lipid profile, but with no improvement in hospital readmission.

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Study approval

This study was approved by the Scientific Committee of Researches of AnNajaf Health Directorate (Ref# 2018-684), as well as by the Ethics and Scientific Committee of Faculty of Pharmacy/ University of Kufa (Ref# 2018-199).

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