



Original article

Adherence to prophylactic dual antiplatelet therapy in patients with acute coronary syndrome – A study conducted at a Saudi university hospital

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ABSTRACT

Objectives: The aim of this study was to evaluate patients' self-reported adherence to dual antiplatelet therapy (DAPT) and determine the factors associated with premature discontinuation of DAPT.

Methods: The cross-sectional interview-based study was conducted among adult outpatients who visited the outpatient department of King Khalid University Hospital, Cardiac Center in Riyadh, Saudi Arabia, over a period of 3 months from May to July of 2016. Medication adherence was assessed using the Self-efficacy for Appropriate Medication Use Scale (SEAMS), which is composed of 13 items with a 3-point Likert scale.

Results: A total of 192 patients participated in the study. The majority of the participants were male (82.1%), and the mean age was 55.66 ± 10.80 years. More than 84% (84.4%) of the patients reported that they were "confident" in taking several medications each day. The minimum and maximum SEAMS scores were 22 and 39, respectively, with the mean score being 30.8 ± 3.5 . Almost all patients had moderate scores and adherence; only one patient got a score of 39. Among sociodemographic characteristics, only health insurance and income were significantly associated with the medication adherence score ($p < 0.05$).

Conclusions: Study results concluded that patients had a moderate level of adherence towards DAPT in Saudi Arabia, however Patient education on DAPT is essential to improve adherence to medication treatment. More effective intentions and education methods should be developed to improve long-term DAPT adherence.

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1. Introduction

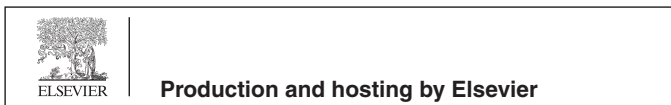
In the last four decades, one-third of the mortality was due to coronary heart disease (CHD) (Sanchis-Gomar et al., 2016). According to a World Health Organization report published in 2012, around 7.4 million deaths occurred from CHD globally, accounting for 42% of cardiovascular-related deaths and 13% of worldwide deaths (Organization WHO, 2014). Based on the latest Heart

Disease and Stroke Statistics update of the American Heart Association, approximately 15.5 million people in the United States were diagnosed with CHD in 2016 and the cost associated was 207 (Mozaffarian et al., 2015) billion dollars in 2011–2012. This cost is expected to increase by 43% between 2013 and 2030.3 In Saudi Arabia, CHD is associated with a high economic impact (10,710 dollars per patient), and has consistently been the leading cause of death from 2000 to 2012, accounting for a mortality rate of 21.7% mortality in 2012 (WHO statistical profile; Osman et al., 2011). In addition to the negative clinical and economic impact of CHD, hospital readmission remains one of the biggest challenges for healthcare authorities currently (Krumholz et al., 2009). Hospital readmission secondary to CHD increased by two-fold from 2005 to 2008 in the United States owing to several factors. One of these factors was a lack of medication adherence. Adherence to medication can play an important role in reducing

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hospital readmission and mortality associated with CHD (Bradley et al., 2006).

Nonadherence to medication regimens is a common cause of a suboptimal response to therapy in many diseases, such as hypertension, cardioembolic stroke, psychiatric illnesses, and pediatric diseases (Husted, 2009; DiMatteo, 2004). Dual antiplatelet therapy (DAPT) with aspirin and an oral P2Y12 receptor blocker is considered to be the standard therapy for preventing atherothrombotic events after percutaneous coronary stent implantation (Wijns et al., 2010). Nonadherence to DAPT as a secondary prevention strategy, particularly in patients with CHD, after percutaneous coronary intervention (PCI) was found to be the strongest independent predictor for stent thrombosis, and associated with a significantly high mortality rate (Iakovou et al., 2005; Spertus et al., 2006). Various factors and reasons for premature DAPT discontinuation have been reported, with psychological factors such as depression, psychiatric disorders, and anxiety being the most common reasons (Bally et al., 2013; Muntner et al., 2011; De Servi et al., 2011).

Despite the negative clinical outcomes and financial burden of CHD in Saudi population, neither the level of adherence of the patients to secondary prevention therapies, particularly DAPT, nor the causes of and factors associated with premature discontinuation have been investigated locally. Therefore, this study was aimed at evaluating patients' self-reported adherence to DAPT and determining the factors associated with premature discontinuation of DAPT.

2. Methods

2.1. Study design

In this cross-sectional study, structured interviews were conducted among 192 adults who visited the outpatient department at King Khalid University Hospital, Cardiac Center in Riyadh, Saudi Arabia, over a period of 3 months from May to July 2016. All patients who attended the outpatient clinic at the cardiac center during the study period were asked to participate in the study if they met the inclusion criteria. The following patients were included: patients aged 18 years or more who were discharged with a diagnosis of unstable angina, ST-segment elevation myocardial infarction (STEMI), or non-STEMI (NSTEMI) within the previous 12 months and whose hospital discharge documents were available. Patients who had received their diagnosis more than 1 year ago and whose discharge documents were unavailable were excluded. All study processes were approved by the institutional review boards of King Khalid University Hospital.

2.2. Sample calculation

The sample size was calculated using the following formula:

$$N = z^2 \times p \times q / d^2$$

where N is the minimum sample size, z is the constant (1.96), p is the prevalence of cardiovascular disease risk factors (5.5%), q is (1-p), Z is the standard normal deviation of 1.96 corresponding to the 95% confidence interval, and d is the desired degree of accuracy.

$$N = (1.96)^2 \times 0.055 \times (1 - 0.055) / (0.05)^2$$

$$N = 79.86 = 80 \text{ patients.}$$

2.3. Evaluation of medication adherence

Medication adherence was assessed using Self-efficacy for Appropriate Medication Use Scale (SEAMS) (Risser et al., 2007).

SEAMS was developed by researchers for patients with chronic illnesses but low literacy levels. It was developed by multidisciplinary groups with expertise in medication adherence and low literacy. SEAMS is composed of 13 items with a 3-point Likert scale (unconfident = 1, fairly confident = 2, and extremely confident = 3). The possible score for the 13-item scale ranged from 13 to 39. A score of 13 indicated low adherence while a score of 39 indicated that the participants were highly confident about receiving their medication. The questionnaire was translated into Arabic language using standard forward and backward method strategy.

2.4. Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 24 (SPSS Inc., Chicago, IL, USA). Non-normal distribution in addition to homogeneity of variances was determined using the Kolmogorov–Smirnov test. Comparisons of means SEAMS scores for adherence with sociodemographic features were performed using the nonparametric Mann–Whitney test and Kruskal–Wallis test.

2.5. Ethical considerations

Our study was conducted in full respect of local ethical considerations, namely obtaining authorization (E-16-2023) from the King Saud University College of medicine research ethics committee. After informing patients about the aim of our research, we asked for their consent and their agreement to participate in the study. All participants provided informed consent and all data were collected under anonymity.

3. Results

A total of 192 patients participated in this study. The majority of the subjects were male (82.1%). The mean age of the subjects was 55.66 ± 10.80 years. More details on the sociodemographic characteristics of the subjects are presented in Table 1.

More than 84% (84.4%) of the patients reported that they were “confident” in taking several medications each day. Most of patients stated that they were confident in taking their medication even when busy. In general, most participants reported being very confident except in response to three questions, for which the majority reported as being not confident as shown in Table 2. Most patients (76%) stated that they were “not confident” about taking their medications when they were unsure about the appropriate time for taking the medication. Furthermore, about 70% of patients reported that they are not confident about taking their medication when their doctor changes their medicines. More responses on self-medication adherence are listed in Table 3.

The minimum SEAMS score was 22 and the maximum was 39; the mean SEAMS score was 30.8 ± 3.5 . As mentioned in method section and passed on validation of SEAMS tool and reported scores less than 13 indicated non-adherence, score in the range of 14 to 38 indicated intermediate level of adherence, and a score of 39 indicated high adherence. Almost all patients had moderate to medium level of adherent, while only one patient got high score of 39. Therefore, we did not use univariate logistic regression. Among sociodemographic features, only health insurance and income were significantly associated with the medication adherence score ($p < 0.05$) (Table 4).

4. Discussion

There are a limited number of studies evaluating the adherence to prophylactic DAPT in patients with acute coronary syndrome

Table 1
Demographic characteristics of the study subjects.

Characters	Number	Percentage
Age (Means) years	55.66 ± 10.80	
Sex		
Male	157	81.8
Female	35	18.2
Nationality		
Saudi	107	55.7
Non-Saudi	85	44.3
Living in Riyadh		
Yes	162	84.4
No	30	15.6
Marital status		
Single	5	2.6
Married	172	89.6
Divorced	4	2.1
Widowed	11	5.7
Residence area		
Urban	142	74.0
Suburban	36	18.8
Rural	14	7.3
Native language		
Arabic	164	85.4
Non-Arabic	28	14.6
Educational level		
Illiterate	56	29.2
Primary, intermediate school	62	32.3
Secondary (high) school	24	12.5
High degree	37	19.3
Other	12	6.3
Place of living		
In an owned house/condominium	94	49.0
In an apartment	46	24.0
In a rented house/condominium	25	13.0
With family, friends	15	7.8
Other	12	6.3
Monthly income		
Less than 5000 SAR	111	57.8
SAR 5000–10,000	69	35.9
SAR 11,000–15,000	7	3.6
More than 15,000 SAR	5	2.6
Job		
Employed	79	52.2
Self-employed, business owner, manager	11	5.7
Retired	55	28.6
Unemployed	47	24.5
Health Insurance		
Governmental	181	94.3
Private	11	5.7
Smoking		
Yes	60	31.3
No	132	68.8

(ACS) in Saudi Arabia. Therefore, this study was conducted to assess and measure adherence to DAPT among adult outpatients who visited the Cardiac Center at King Khalid University Hospital, Riyadh, Saudi Arabia. Although we identified a number of relevant international studies, we could not find many local studies (Czarny et al., 2014; Bavishi et al., 2017; Yallapragada et al., 2013; Patti et al., 2017). Thus our study would be a significant contribution toward elucidating the adherence of platelet therapy in Saudi Arabia and would serve as a main resource for future research.

Several studies reported that older age and female gender (Sattler et al., 2013; Kosobucka et al., 2018) as the major determinants of low adherence in patients with chronic health complications. However studies also found that nonadherence to treatment results in therapeutic failures, increased complications rate, and rising costs of treatment (Sattler et al., 2013; Kosobucka et al., 2018). Antiplatelet therapy with one or more drugs has been considered as essential treatment for ACS for several decades and progress has been made in the class of the drug for its essential therapeutic activity in interfering with the platelet activation

Table 2
Responses to the Self-efficacy for Appropriate Medication Use Scale (SEAMS).

How confident are you that you can take your (antiplatelet) medicines correctly?			
Statement	Not confident N (%)	Somewhat confident N (%)	Very confident N (%)
1. When you take several different medicines each day	21 (10.9)	9 (4.7)	162 (84.4)
2. When you have a busy day planned	6 (3.1)	46 (24)	140 (72.9)
3. When are you away from home	11 (5.7)	37 (19.3)	144 (75)
4. When no one reminds you to take the medicine?	10 (5.2)	97 (50.5)	85 (44.3)
5. When you take medicines more than once a day	26 (13.5)	6 (3.1)	160 (83.3)
6. When the schedule to take the medicine is not convenient	18 (9.4)	28 (14.6)	146 (76)
7. When your normal routine gets disrupted	18 (9.4)	28 (14.6)	146 (76)
8. When you get a refill of your old medicines and some of the pills look different from how they usually do	17 (8.9)	25 (13)	150 (78.1)
9. When you are not sure how to take the medicine	146 (76)	2 (1)	44 (22.9)
10. When you are not sure what time of the day to take your medicine	147 (76.6)	21 (10.9)	24 (12.5)
11. When a doctor changes your medicines	133 (69.3)	24 (12.5)	36 (18.2)
12. When they cause some side effects	20 (10.4)	3 (1.6)	169 (88)
13. When you are feeling sick (like when you have a cold or the flu)	12 (6.3)	1 (0.5)	179 (93.2)

Table 3
Assessment of adherence by using SEAMS score.

Domain	Score interpretation	Frequency (%)
SEAMS score	39: high	1 (0.05)
	14–38: medium	194 (99.5)
	13: low	0 (0.5)

process in primary hemostasis (Yallapragada et al., 2013; Layne and Ferro, 2017) However, this could be the main reason for optimal adherence to DAPT in many studies around the world (Sattler et al., 2013; Kosobucka et al., 2018). Additionally recent reports revealed that DAPT is vital for the treatment of ACS. Additionally, the therapy offers the advantage of preventing ACS recurrence (Amsterdam et al., 2014 ; Windecker et al., 2014; Kerry and albert, 2017).

In our study, the mean SEAMS score was 30.8 ± 3.5, which means that approximately all patients who participated in the study had moderate to medium level of adherence to DAPT, while most patients (84.4%) reported as being “confident” about taking several medications each day. This percentage was lower than that reported in a previously published intervention-based study conducted among Saudi patients (94.4%) (El-Toukhy et al., 2017), Educating patients about DAPT and the importance of receiving medication at the right time for the management of the disease has proven to have a short-term benefit in terms of patients' adherence to treatment (El-Toukhy et al., 2017).

Previous data showed that prolonged use of DAPT in patients was attributable to a number of factors including recurrent ischemic events, the absence of anemia or bleeding during follow-up, and concomitant renal failure or peripheral artery disease (Patti et al., 2017). Furthermore, no relation was found between age, diabetes mellitus, or drug-eluting stent implantation and DAPT continuation (Patti et al., 2017). Additionally, our study

Table 4
Sociodemographic factors correlated with the SEAMS score.

	Mean	Median	P value
Sex			0.657
Male	30.9	31	
Female	30.4	31	
Nationality			0.564
Saudi	30.6 (3.7)	31	
Non-Saudi	31 (3.3)	31	
Marital status			0.768
Single	32 (3.6)	31	
Married	30.8 (3.5)	31	
Divorced	29.5 (2.9)	29.5	
Widowed	31 (2.9)	31	
Health insurance			0.012
Governmental	30.6 (3.4)	31	
Private	33 (4.5)	34	
Residence area			0.141
Urban	31 (3.7)	31	
Suburban	30 (2.9)	30	
Rural	30.2 (2.4)	30.5	
Native language			0.696
Arabic	30 (3.8)	31	
Non-Arabic	31 (3.1)	31	
Educational level			0.094
Illiterate	30.2 (3.4)	31	
Primary, intermediate school	30.7 (3.8)	31	
Secondary (high) school	30 (2.4)	30	
University	31.7 (3.7)	32	
Other	32 (2.8)	32	
Place of living			0.823
In an owned house/condominium	30 (3.8)	31	
In an apartment	31 (2.5)	31	
In a rented house/condominium	30 (4.08)	31	
With family, friends	30 (2.6)	31	
Other	32 (3.3)	33	
Monthly income			0.017
Less than 5000 SAR	30.2 (3.3)	31	
SAR 5000–10,000	31.5 (3.6)	32	
SAR 11,000–15,000	32 (4.6)	34	
More than 15,000 SAR	32 (3.2)	32	
Job			0.306
Employed	31.3 (3.1)	31	
Unemployed	30 (3.3)	31	
Self-employed	31 (3.8)	33	
Retired	30 (3.9)	31	
Smoking status			0.119
Yes	31 (3.9)	32	
No	30 (3.3)	31	

results showed that only health insurance and financial status were significantly associated with the medication adherence score ($p < 0.05$).

Several studies reported that bleeding, particularly gastrointestinal hemorrhage, is the main risk factor associated with DAPT in patients receiving an oral anticoagulant short term or long term up to 12 months (Collet et al., 2014; Yeh et al., 2015; Lee et al., 2014; Han et al., 2016). While another study reported that long term use of DAPT up to 12 months reduced the risk of major bleeding (Bavishi et al., 2017). It is well known fact that adherence to medication is crucial in achieving adequate health care. However nonadherence to medication is challenging, as it can result in numerous negative consequences for patients and considered as a burden to the health care system (Col et al., 1990; Schüz et al., 2014; Sullivan et al., 1990; Patel and zed, 2002). Increasing the frequency and availability of patient visits with healthcare providers is one simplest way through which adherence can be improved. Therefore an education Programme should be implemented to improve patients adherence to DAPT, through healthcare professionals such as pharmacist and family physician, are helpful in providing information about safety and effectiveness of drugs along with possible adverse effects in therapy, motivation

the patients and individuals for continues follow up for their treatment is vital in achieving quality of adherence in DAPT.

5. Conclusion

Educating patients about antiplatelet therapy and the importance of aspirin and dual therapy in the management of their disease are needed for more improvement on patients' adherence to DAPT and its management. Improvements should be made by health-care professionals and comprehensive efforts should be drawn by health authorities to provide more effective education programs for patients to improve DAPT adherence. Finally, more studies with longer duration as well as with large patients focusing on DAPT and its adherence, in Saudi Arabia are needed.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical considerations

Our study was conducted in full respect of local ethical considerations, namely obtaining authorization (E-16-2023) from the king Saud University College of medicine research ethics committee.

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