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

Ziyad Alrabiah *, Syed Wajid, Ibrahim Alsulaihim, Sultan Alghadeer, Abdulaziz Alhossan, Salmeen D. Babelghaith, Mohamed Al-Arifi

Clinical Pharmacy Department, College of Pharmacy King Saud University, Saudi Arabia

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.

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 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 twofold 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...
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:

\[ N = \frac{z^2 \times p \times q}{d^2} \]

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.

\[ N = \frac{(1.96)^2 \times 0.055 \times (1 - 0.055)}{(0.05)^2} \]

\[ N = 79.86 = 80 \text{ patients.} \]

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 Kruskall–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% of (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       |

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

| 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 you are 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). Educat-
ing 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
ing (Bavishi et al., 2017). It is well known fact that adherence to term use of DAPT up to 12 months reduced the risk of major bleed- up to 12 months (Collet et al., 2014; Yeh et al., 2015; Lee et al., in patients receiving an oral anticoagulant short term or long term intestinal hemorrhage, is the main risk factor associated with DAPT (p < 0.05).

were significantly associated with the medication adherence score 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.

Acknowledgements

The authors extend their appreciation to the Deanship of Scientific Research at King Saud University for funding this work through research group no. RG-1440-098.

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.

References

Amsterdam, E.A., Wenger, N.K., Brindis, R.G., Casey Jr., D.E., Ganiats, T.G., Holmes Jr., D.R., 2014. 2014 ACC/AHA guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 130, e344–e426.

Bradley, E.H., Herrin, J., Elbet, B., McNamara, R.L., Magid, D.J., Nallamothu, B.K., et al., 2006. Hospital quality for acute myocardial infarction: correlation among process measures and relationship with short-term mortality. JAMA 296, 72–78.

Bally, K., Buechel, R.R., Buser, P., Tschudia, P., Martina, B., Zeller, A., 2013. Discontinuation of secondary prevention medication after myocardial infarction – the role of general practitioners and patients. Swiss Med Wkly 4, 143–149.

Bavishi, C., Trivedi, V., Singh, M., Katz, E., Messerli, F.H., Bangalore, S., 2017. Duration of dual antiplatelet therapy in patients with an acute coronary syndrome undergoing percutaneous coronary intervention. Am. J. Med. 130 (11), 1325.e1–1325.e12.

Col, N., Fanale, J.E., Kronholm, P., 1990. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. Arch. Intern. Med. 150 (4), 841–845.

Collet, J.P., Silvain, J., Barthélémy, O., Rangé, G., Cayla, G., Van Belle, E., Cuisset, T., Elhadad, S., Schiele, F., Lhoest, N., Ohlmann, P., 2014. Dual-antiplatelet treatment beyond 1 year after drug-eluting stent implantation (ARTIC- Interruption): a randomised trial. The Lancet. 384 (9954), 1577–1585.

Czary, M.J., Nathan, A.S., Yeh, R.W., Mauri, L., 2014. Adherence to dual antiplatelet therapy after coronary stenting: a systematic review. Clin. Cardiol. 37 (8), 505–513.

De Servi, S., Roncella, A., Reimers, B., 2011. Causes and clinical implications of premature discontinuation of dual antiplatelet therapy. Curr. Opin. Cardiol. 26 (1), 515–521.

DiMatteo, M.R., 2004. Variations in patients’ adherence to medical recommendations: a quantitative review of 50 years of research. Med. Care 42, 200–209.

El-Toukhy, H., Omar, A., Abou, Samra M., 2017. Effect of acute coronary syndrome patients’ education on adherence to dual antiplatelet therapy. J. Saudi Heart Assoc. 29 (4), 252–258.

Husted, S., 2009. Evidence-based prescribing and adherence to antiplatelet therapy–how much difference do they make to patients with atherothrombosis?. Int. J. Cardiol. 134 (2), 150–159.
Han, Y., Xu, B., Xu, K., Guan, C., Jing, Q., Zheng, Q., Li, X., Zhao, X., Wang, H., Zhao, X., Li, X. 2016. Six versus 12 months of dual antiplatelet therapy after implantation of biodegradable polymer sirolimus-eluting stent: randomized subset study of the I-LOVE-IT 2 trial. Circulat.: Cardiovasc. Intervent. 9 (2), e003145.

Iakovou, I., Schmidt, T., Bonizzi, E., Ge, L., Sangiorgi, G.M., Stankovic, G., et al., 2005. Incidence, predictors, and outcome of thrombus after successful implantation of drug-eluting stents. JAMA 293 (17), 2126–2130.

Kerry, L., Albert, F., 2017. Antiplatelet therapy in acute coronary syndrome. Eur. Cardiol. Rev. 12 (1), 33.

Krumholz, H.M., Merrill, A.R., Schone, E.M., Schreiner, G.C., Chen, J., Bradley, E.H., et al., 2009. Patterns of hospital performance in acute myocardial infarction and heart failure 30-day mortality and readmission. Circ. Cardiovasc. Qual. Outcomes 2, 407–413.

Kosobucka, A., Michalski, P., Pietrzykowski, Ł., Kasprzak, M., Obonska, K., Fabiszak, T., Felsmann, M., Kubica, A., 2018. Adherence to treatment assessed with the Adherence in Chronic Diseases Scale in patients after myocardial infarction. Patient Prefer Adherence 5 (12), 333–340.

Layne, K., Ferro, A., 2017. Antiplatelet therapy in acute coronary syndrome. Eur. Cardiol. 12 (1), 33–37.

Lee, C.W., Ahn, J.M., Park, D.W., Kang, S.J., Lee, S.W., Kim, Y.H., Park, S.W., Han, S., Lee, S.G., Seong, I.W., Rha, S.W., 2014. Optimal duration of dual antiplatelet therapy after drug-eluting stent implantation: a randomized, controlled trial. Circulation 129 (3), 304–312.

Mozaffarian, D., Benjamin, E.J., Go, A.S., Arnett, D.K., Blaha, M.J., Cushman, M., De Ferranti, S., Després, J.P., Fullerton, H.J., Howard, V.J., Huffman, M.D., 2015. Executive summary: heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation 131 (4), 434–441.

Muntner, P., Mann, D.M., Woodward, M., Choi, J.W., Stoler, R.C., Shiffman, D.L., et al., 2011. Predictors of low clopidogrel adherence following percutaneous coronary intervention. Am. J. Cardiol. 108 (6), 822–827.

Organization WHO. 2014. Global Status Report on Non-Communicable Diseases, World Health, 176. (cited 2015). Available from: http://www.who.int/global-coordination-mechanism/publications/global-status-report-ncds-2014-eng.pdf.

Osman, A.M., Alsultan, M.S., Al-Mutairi, M.A., 2011. The burden of ischemic heart disease at a major cardiac center in Central Saudi Arabia. Saudi Med. J. 32 (12), 1279–1284.

Patti, G., Cavallari, L., Antonucci, E., Calabrò, P., Cirillo, P., Gresele, P., Palareti, G., Pengo, V., Pignatelli, P., Ricottini, E., Marcucci, R., 2017. Prevalence and predictors of dual antiplatelet therapy prolongation beyond one year in patients with acute coronary syndrome. PLoS One 12 (10), e0186961.

Petel, P., Zed, F.J., 2002. Drug-related visits to the emergency department: how big is the problem?. Pharmacotherapy 22 (7), 915–923.

Risser, J., Jacobson, T.A., Kripalani, S., 2007. Development and psychometric evaluation of the Self-efficacy for Appropriate Medication Use Scale (SEAMS) in low-literacy patients with chronic disease. J. Nurs. Meas. 15 (3), 203–218.

Sanchis-Gomar, F., Perez-Quilis, C., Lesichik, R., Lucia, A., 2016. Epidemiology of coronary heart disease and acute coronary syndrome. Ann. Translat. Med. 4 (13).

Sperutz, J.A., Kettelkamp, R., Vance, C., Decker, C., Jones, P.G., Rumsfeld, J.S., et al., 2006. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: results from the PREMIER registry. Circulation 113 (24), 2803–2809.

Sattler, E.L., Lee, J.S., Perri, M., 2013 Jun 1. Medication (re)fill adherence measures derived from pharmacy claims data in older Americans: a review of the literature. Drugs Aging 30 (6), 383–399.

Schulz, B., Wolff, J.K., Warner, L.M., Ziegelmann, J.P., Wurm, S., 2014. Multiple illness perceptions in older adults: effects on physical functioning and medication adherence. Psychol. Health. 29 (4), 442–457.

Sullivan, S., Kreling, D.H., Hazlet, T.K., 1990. Noncompliance with medication regimens and subsequent hospitalizations: a literature analysis and cost of hospitalization estimate. J. Res. Pharm. Econ. 2 (2), 19–33.

Wijns, W., Kolh, P., Danchin, N., Di Mario, C., Falk, V., Folliguet, T., et al., 2010. Guidelines on myocardial revascularization. Eur. Heart J. 31, 2501–2555.

Windecker, S., Kolh, P., Alfonso, F., Collet, J.P., Cremer, J., Falk, V., 2014. ESC/EACTS guidelines on myocardial revascularization: the task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J. 35, 2541–2619.

Yallapragada, S., Siddiqui, S., Gindi, R., Shroff, A., 2013. Adherence to dual antiplatelet therapy: can we do better?. Expert Rev. Cardiovasc. Ther. 11 (10), 1417–1424.