

What do we know about the long term medication adherence in patients following percutaneous coronary intervention?

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KEY WORDS

medications, percutaneous coronary intervention, adherence

ABSTRACT

Background

Percutaneous coronary intervention (PCI) is a revascularisation intervention for patients with acute coronary syndrome. It is a common procedure, increasingly used over the past decade. Along with PCI, patients are also prescribed a number of medications and adherence to the pharmacological therapies is vital to improved morbidity and mortality.

Objective

This cross-sectional study sought to evaluate the long term adherence to medications in patients following PCI.

Subjects

270 participants who underwent PCI between April 2003 and March 2004 and who met the inclusion criteria were followed up 12-24 months following the PCI.

Methods

Following obtaining informed consent, a self administered questionnaire was mailed to participants. Information was collected relating to the types of medications taken, medication taking behaviours and storage of medications.

Results

Overall high rates of self-reported medication adherence were reported. In spite of this, patients continued to miss medications or reported stopping medications if they felt better or worse. Knowledge of storage of medication in particular nitro-glycerine medications was poor.

Conclusions

Findings suggested that following PCI medication adherence is high, however knowledge about medication storage is limited and patients report cessation of medications which they consider to be deleterious or unnecessary. These findings are useful for informing development of nursing interventions.

BACKGROUND

Percutaneous coronary intervention (PCI) is a widely used revascularisation strategy for patients with acute coronary syndrome (ACS). Over the past decade, refinement in the technology has seen an increased use of this method for revascularization (Davies 2003). Although PCI is effective in treating the culprit lesion, modification of the physiologic risk factors is essential to prevent progress of coronary artery disease (Lisspers et al 2005; Yusuf et al 2004; Haddock et al 2003; Johansen et al 2001).

Following PCI the majority of the patients receive several pharmacological therapies that have been demonstrated in randomised controlled trials to be effective in the secondary prevention of coronary artery disease (Fonarow et al 2001; Rogers et al 2000; Alexander et al 1998; Krumholz et al 1998; Krumholz et al 1997) as well as to prevent restenosis of the treated vessel (Spertus et al 2005; Rana et al 2005).

Adherence to medication regimes, described as the extent to which patients take medications as prescribed (Mihalko et al 2004), is imperative to prevent coronary artery disease progression. For example, adherence to lipid lowering treatment is associated with lower risk of recurrent coronary events (Wei et al 2002), while poor compliance with hypertension medications is associated with adverse health outcomes such as stroke and left ventricular hypertrophy (Schroeder et al 2006).

Despite compelling evidence about the effectiveness of medications, adherence to treatment has been recognised to be a major problem in patients with chronic illness (Osterberg et al 2005; Vermeire et al 2001) and a large proportion of patients become non-adherent at six months (Osterberg et al 2005; Chapman et al 2005). Rates of non-adherence with any long term medication treatment vary from 17% to 60%, depending on the characteristics of the condition, the treatment, the patient, and the setting (Sud et al 2005; Gottlieb 2000). Of significance, non-adherence is the highest when the patients are symptom-free (Gottlieb 2000). This observation is of particular significance in implementation of secondary prevention interventions.

Long term adherence has been estimated to be between 40% (Esposti et al 2004) to 70% (Gislason et al 2006; Halpern et al 2006) for hypertensive medications and 37-80% for lipid lowering medications (Gislason et al 2006; Kulkarni et al 2006; Newby et al 2006; Tsuyuki et al 2001). Among elderly patients with ACS adherence to long term lipid therapy was significantly higher (40.1%) compared to patients with chronic coronary artery disease (36.1%) (Jackevicius et al 2002). Adherence rates at 1-2 year follow up for aspirin was 83-88% (Newby et al 2006; Kulkarni et al 2006; Sud et al 2005), betablockers 61-78% (Newby et al 2006; Kulkarni et al 2006) and 66-72% for ACE inhibitors (Sud et al 2005; Kulkarni et al 2006).

Lack of adherence to medication results in suboptimal control of risk factors leading to risk for further cardiovascular events and increased hospital admissions (Sokol et al 2005; Aday et al 2004; Kennedy et al 2002), consequently resulting in increased financial burden on the health care system (Vermeire et al 2005; Aday et al 2004).

Numerous studies have identified factors associated with poor adherence. These factors include lack of knowledge, denial, adverse effects, poor memory (Moser et al 1999) and adverse attitudes to treatment (Vermeire et al 2005). Other factors influencing patients' adherence to medications include patients characteristics such as: the cost of medications, the number of medications taken by the patient, the type of medical intervention and the nature of the medical condition (Krueger et al 2005). In addition the longer the duration of therapy, the complexity of the regimen, and a low perception of need such as in asymptomatic conditions influence adherence to medications. Further the occurrence of side effects and low tolerance to effects impact upon adherence (Krueger et al 2005; Gregoire et al 2001).

Strategies to improve medication adherence include multidisciplinary educational and behavioural interventions (World Health Organization 2003) such as reminders and reinforcement of the importance of medication adherence. Three systematic reviews published in the Cochrane library have investigated

the effectiveness of various interventions to promote adherence to medications. The interventions demonstrated to be effective were multifaceted and included: education, reminders, counselling, self monitoring, reinforcement, simplifying dosing regimens, and using adherence aids (Haynes et al 2000; World Health Organization 2003).

A recent systematic review of the effects of interventions for adherence to antihypertensive medications reported that reducing the number of daily doses, motivational strategies and other complex strategies were effective in maintaining adherence and improving patient outcomes (Schroeder et al 2006; Fahey et al 2005b). Interventions used to increase medication adherence include: educational interventions, patient behavioral interventions, and provider interventions (Krousel-Wood et al 2005; Fahey et al 2005a; Fahey et al 2005b; Schedlbauer et al 2004).

Patients who have had PCI generally underestimate the severity of their cardiovascular disease and have a misconception they are cured due to the short hospital stay, rapid procedural technique, and immediate potential success of PCI without requiring open-heart surgery (Higgins et al 2001), reducing the amount of pain experienced, and facilitating an early return to work (Gulanick et al 1998). Given that the perception of risk may be lower it is important to investigate the medication adherence behaviour in people following PCI.

This study aimed to assess long term medication adherence in patients following PCI.

METHODS

Recruitment

All patients who underwent elective, primary or rescue PCI, between April 1st 2003 and March 31st 2004 at a major metropolitan teaching hospital in NSW Australia were identified from the cardiology database and a list was compiled. Attempts were made to identify deceased patients. A total of 541 participants underwent PCI during the study period of whom 518 were considered to be potentially eligible and who were sent an invitation to participate in

the study along with a subject information sheet. A detailed description of the recruitment method has been presented elsewhere (Fernandez et al 2006). In brief, participants who had undergone elective, primary or rescue PCI, were eligible for the study if they were aged between 18-80 years, had no cognitive impairment (telephone mini mental score of more than 30) and had a reliable and verifiable telephone contact number. Participants were excluded from the study if they had: a failed PCI procedure requiring surgical intervention; significant co-morbidities such as cerebrovascular accident with significant neurological deficit; malignant disease and were undergoing active therapy; any condition of sufficient severity to impair co-operation in the study eg chronic alcoholism; a length of hospital stay of more than 30 days following the PCI; been transferred to a nursing home following the procedure; or unable to be contacted. Data were collected from December 2004 to March 2005. Approval to undertake the project was obtained from the facility and university ethics committee. Numerical unique identifiers and password-protected files were used to maintain patient privacy and confidentiality.

Data collection

A 20 item investigator developed questionnaire consisting of items relating to demographic details (age, gender, level of education, marital status), past medical history, medications currently taken and a test battery using validated medication adherence questionnaires was administered. Participants meeting eligibility criteria were mailed a questionnaire, consent form and a reply paid envelope. Methods to increase response to postal questionnaires, such as telephone reminders were used (Edwards et al 2002). In order to obtain a representative sample, participants from non-English speaking background were encouraged to complete the questionnaire with assistance.

OUTCOMES ASSESSMENT

Cognitive status

As impaired cognitive status was an exclusion criterion, potential participants completed a telephone interview to assess their cognitive status to

determine their eligibility for the study. The Telephone Interview of Cognitive Status (TICS) which is a 11-item screening test modelled on the Mini Mental State Examination (MMSE) questionnaire was adapted for this purpose (Brandt et al 1988). The maximum score obtainable is 41 points and participants with a score of less than 30 are considered to be cognitively impaired. The TICS correlates very highly (0.94) with the MMSE. Test-retest reliability of the TICS has also been estimated to be high ($r = 0.97$) (Brandt et al 1988). A score of 30 was identified as the minimum for inclusion in the study, however all patients assessed had a TICS score more than 30 and were eligible for inclusion.

Current medications

Participants were asked if they were taking medications for control of high blood pressure, cholesterol, depression, diabetes, body weight, breathing difficulties, depression or pain. A chart audit was undertaken, to confirm participant's responses. In addition participants were also asked if they were receiving medications for quitting smoking and preventing blood clots and if they found it bothersome to take their medications.

Adherence to medications

Adherence to medication was assessed by self report using the Haynes validated questions (Haynes et al 1980) and the Morisky Medication Adherence Scale (MAS) (Morisky et al 1986). Pooled data from methodologically strong studies demonstrates that when compared to pill counts, self reports have a sensitivity of 55%, specificity averaging 87% and a likelihood ratio for a positive test of 4.4 (Stephenson et al 1993).

The Haynes Questions

This instrument consists of two items. The first item was a previously validated question: "Do you regularly miss taking any of your medications" (Haynes et al 1980). As the method of questioning has been reported to affect the accuracy of responses (Stephenson et al 1993) non threatening, non judgemental approaches as described in the literature were used (Haynes et al 1980). The question

was therefore prefaced with the following statement: "People often have difficulty taking their pills for one reason or another". We are trying to learn more about that experience. If the response was affirmative, participants were asked to report the numbers of pills missed in the previous day and week (Haynes et al 1980). When compared to pill counts, these questions have been reported to have a correlation coefficient of 0.74 ($p < 0.0001$), sensitivity of 96%, specificity 50% and a positive predictive value of 70 % (Haynes et al 1980).

Morisky Medication Adherence Scale (MAS)

The Morisky Medication Adherence Scale (MAS) (Morisky et al 1986) comprises of three questions which include:

- Do you ever forget to take your medicine?
- When you feel better do you sometimes stop taking your medicine?
- Sometimes if you feel worse when you take the medicine do you stop taking it?

Reliability of these items (item to total correlation coefficients of 0.48 to 0.56) and the total scale has been reported and is modest ($\alpha = 0.64$) (Morisky et al 1986).

Storage of medications was assessed using questions adapted from Gray's recommended items (Gray 1990). Medication management systems, such as any unit dose system (Dosett® systems, blister packs), were referred to as compliance aids in the Medication Management Ability section of the questionnaire. Patients were asked particularly about the storage of sublingual nitro-glycerine medications.

Statistical analysis

All analyses were undertaken using SPSS Version 13. Categorical data have been presented as percentages and continuous data are presented as means (SD). Differences between continuous variables were assessed using t-tests and the Chi-square test was used for categorical variables. Comparisons were considered to significant at $p < 0.05$.

RESULTS

Questionnaires were sent to 270 participants of which 202 (males n=148, females n= 54) were returned demonstrating a response rate of 75%. The age of the participants ranged from 35-87 years with a mean age of 64 years (SD 11.7). Overall female participants were significantly older than males ($p < 0.0001$). More than half the patients (60%) were retired and nearly three quarters of the participants were married or living with a partner.

Table 1: Demographics

	Frequency (%)
Marital status	
Married/de-facto	146 (72.3)
Single/divorced	25 (12.4)
Widowed	31 (15.3)
Educational level	
< 10 years	78 (38.6%)
≥ 10 years	123(60.8%)
Occupation (n=193)	
Retired	115 (59.5)
Unemployed	17 (8.8)
Working	60 (31)
Student	1 (0.5)

Use of Medications

All except three patients reported taking medications, most commonly to control high cholesterol, high blood pressure and to prevent blood clots. Approximately 50% of the patients were taking 3-4 types of medications each day. The use of nitro-glycerine medications for the relief of angina was minimal, with the majority (84%) reporting not taking the medication in the previous four weeks. The remaining patients indicated they used nitro-glycerine medications less than once a week (9%), 1-2 times each week (3.7%), 3 or more times each week (2.7%) and 1-3 times each day (0.5%).

Medication adherence

A large proportion of the participants (94.6%) reported they did not regularly miss taking their

medications, however approximately 11% indicated they had missed some of their medications in the previous week. Of those participants who reported they missed taking some of their medication four had missed more than three tablets. A small proportion of the participants reported they intentionally missed tablets if they felt better, worse or were going out.

Figure 1: Medications taken by participants

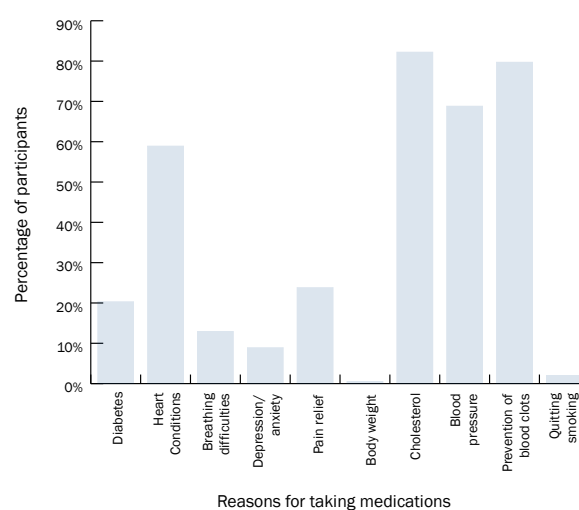


Table 2: Medication adherence rates of participants

	Frequency (%)
Regularly miss taking medications	7/198 (3.5%)*
Missed tablets in the last week	22/198 (10.9%)*
Number of tablets usually missed in a week	
None	183/202 (90.6%)
1-3 tablets	15/202 (7.5%)
4 or more	4/202 (2%)
Could not remember	8/202 (4%)
Stops taking medications if feeling better	4/196 (2%)*
Stops taking medications if feeling worse	9/195 (4.5%)*
Stops taking medications if going out	10/197 (5%)*

*Missing data

Medication Storage

One hundred and sixty eight participants (83%) indicated they stored their medications in their original containers and a third used some form of compliance aids to organise their medications, while

35% kept all their medications in one container. Of those who used compliance aids, more than half (59.6%) indicated they used an approved compliance aid which included Webster packs, weekly dosette boxes, and daily pill boxes to organise their medications. The remaining used plastic cups, containers or bags, checklists, palm cards, aluminium foil and boxes to organise their medications. Some participants indicated they relied on their partner to organise the medications.

A fifth of the participants reported using special systems to remind them to take their medications. These methods included use of an approved system, reminder by spouse, keeping the medications in a prominent location in the house and according to the meal or sleep schedule. Approximately half the patients stated it was not bothersome to take medications. Participants had excellent knowledge of recommended actions when they felt side effects of medications, with the majority (87.8%) reporting they would notify their doctor before making any changes to their medications. The remaining participants indicated they would stop taking their medications until the next time they visited their doctor (10.2%) or did not know what to do (2%).

Table 3: Storage of medications

	Frequency (%)
Keeps medications in original containers	168/199 (83.2%)
Keeps medications in one container	75/192 (35.1%)
Currently using a compliance aid to organise medications	60/195 (29.7%)
Using an approved compliance system	34/57 (16.8%)
Currently using a system as a reminder to take medications	41/200 (20.3%)
Using an approved reminder system (n=44)	15/44 (34.1%)

Specific questions were asked relating to the incidence of chest pain, the use and storage of medications for the relief of chest pain. Nearly a third (29%) of the participants indicated they were not

prescribed any medications for relief of chest pain. The majority of the patients (84%) did not have any chest pain in the four weeks prior to the survey and therefore did not require any nitro-glycerine tablets or sprays.

Less than three quarters (68.1%) of the participants reported the correct method for storage of nitroglycerine medications and 25% indicated they were not aware of the correct method for storage. The remaining 6% stated these medications could be stored in tissues, refrigerator or along with other medications.

DISCUSSION

There is overwhelming clinical evidence that supports the use of medications for patients following acute coronary syndrome to prevent morbidity and mortality. Therefore adherence to medication recommendations is crucial for the reduction of risk factors and the prevention of the progress of coronary artery disease. The evidence also indicates that a substantial proportion of people have diminished adherence to long term therapy. Pharmacological management is most likely to be effective when people adhere to their prescribed medication regimes on an ongoing basis. Non-adherence has important economic implications, because patients who fail to adhere to medication regimens cannot realise the cardio protective benefits that are associated with continuous treatment.

A large proportion of the participants reported taking medications for lowering cholesterol, blood pressure and prevention of blood clots which is consistent with the general literature (Newby et al 2006; Kulkarni et al 2006). However due to the method of data collection it is difficult to differentiate between patient non-adherence and physician non-prescription for the remaining patients.

In spite of the lower perception of risk attributed to people undergoing PCI, very few patients in this study reported they missed taking their medications. However the study highlights the fact that a limited number of participants reported the correct method for the storage of nitro-glycerine medications, which is

of concern as improper storage of these medications can render them ineffective leading to increased morbidity and hospitalisations.

Implications for nursing practice

In light of the importance of medication adherence in modulating patient outcomes, nurses need to recommend strategies to integrate medication adherence. The findings from this study confirm that patients need the knowledge, attitude, and skills to follow an appropriately prescribed regimen. In addition, patients also require knowledge for the proper storage of medication which is vital as improper storage can render the medication ineffective and thus all attempts made to enhance adherence are futile. Multidisciplinary efforts to enhance adherence to medication may improve adherence to medications. Many patients are unaware of the importance of adhering to the medication regime which is reflected in their reports of not taking medication when they feel better, their condition worsened, or if they were going out. Another reason for non-adherence could be the fact that the majority of these patients had multiple co-morbidities and the evidence supports poor adherence among persons with three or more co-morbid conditions. This finding is important for nursing practice as nurses can play an important role in raising their awareness of non-adherent behaviours.

Once adherence problems have been identified, effective communication between patients and nurses or other health care providers is essential and forms the basis for actions and strategies. In addition, nurses can provide detailed and specific information in a manner that is easy to understand to increase knowledge and thereby increase adherence to medications. Nurses can also assist patients to identify mechanisms that promote adherence to a prescribed regimen.

Providing patients with skills such as problem solving, self-monitoring, and developing self-prompting and reminder systems, can also empower patients and increase adherence. Nurses are in a unique position to educate patients about the importance of medication adherence in reducing overall health

care costs and improving health outcomes. Thus, a multidisciplinary approach led by nurses could be an effective strategy to improve medication adherence rates in patients with chronic disease.

Strengths and Limitations

The major strength of this cross-sectional study was the high response rate obtained from a well defined cohort, free of cognitive impairment, as judged by TICS criteria. In addition, this study provides data relating to medication adherent behaviours of patients following PCI in a usual care setting.

A limitation of the self report method used to measure adherence in this study is that it can overestimate adherence when compared to chemical markers and electronic monitoring of pill use, and its accuracy depends on the patient's cognitive abilities and the honesty of replies (Fisher 1993). Currently various methods are used to measure medication adherence and until a gold standard that is cost effective is available, measurement of medication adherence will continue to have limitations. The high adherence rates could be due to a Hawthorne effect. Another limitation was that adherence to blood pressure or cholesterol lowering medications could not be compared against actual blood pressure and cholesterol values to assist with examining the effect of adherence and blood pressure or cholesterol control. The findings should be considered in light of the fact that this study was undertaken in patients who had PCI at a single centre and the socio demographic patterns of the participants could influence their adherence to medications. In addition, despite extensive efforts to increase response rates, patients who were non-adherent to medications would be less likely to respond to questionnaires resulting in a significant participant bias.

Further studies need to be undertaken to accurately measure adherence and the factors that influence adherence in this group of patients. To improve the medication taking behaviour in this cohort of patients it is vital to explore the characteristics of patients who do not adhere to long term treatment; the results can then be used to develop new strategies to improve medication adherence in this cohort. In addition

studies linking medication compliance with improved patient risk factors need to be undertaken.

In spite of these limitations, through the exploration of medication adherence behaviours, interventions to increase the effectiveness of medication adherence may extend the benefits of PCI and reduce the need for subsequent revascularisation.

CONCLUSION

Adherence to medications remains imperative to prevent the progress of coronary artery disease and restenosis of the revascularised artery. Multidisciplinary efforts with increased patient-centeredness, emphasis on the patient's perspective and shared-decision-making might lead to improved adherence to medications.

Summary of key points

Non-adherence to medications can result in progress of coronary artery disease, further need for revascularisation and poor outcomes.

The majority of the participants were receiving pharmacological therapy according to guidelines.

Adherence to medications in these participants was similar to those with chronic illness.

Participants had a decreased knowledge of the storage of nitro-glycerine medications.

Strategies to enhance medication adherence need to be incorporated into patient care.

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