Clopidogrel-taking behavior by drug-eluting stent patients: Discontinuers versus continuers

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Background: Each day, patients make choices whether or not to take their prescribed medications. Previous research has shown that 1 in 7 myocardial infarction (MI) patients discontinued thienopyridines within 1 month of receiving a drug-eluting stent (DES) with serious consequences. This qualitative research study explored in depth the clopidogrel-taking behavior among DES-treated patients who quit taking clopidogrel 1 month after treatment and those who continued therapy.

Methods: Sequential patients from a prospective MI registry who reported discontinuing clopidogrel within 30 days of DES treatment (N = 11) were matched with continuers (N = 11). Both groups underwent detailed qualitative phone interviews. Coding and thematic representation using directed qualitative content analysis by 3 PhD researchers was done.

Results: Patients were 41–77 years old and the majority was Caucasian and male. Multiple barriers were described by discontinuers that were not reported by continuers. The most frequently cited barrier was misunderstanding the intended duration of treatment. Discontinuers also described system weaknesses that contributed to early discontinuance such as gaps in the transition to primary care.

Conclusions: While premature discontinuation of a prescribed therapy is viewed by clinicians as a willful disregard for medical advice, early stopping of clopidogrel is influenced greatly by processes of care and system issues.

Keywords: medication discontinuance, drug-eluting stent post-care, myocardial infarction

Patients must make choices each day regarding their medications, such as obtaining the medication in a timely manner and following dosing instructions (Russell et al 2006). Consequences of medication nonadherence vary in severity depending upon the medication. The American Heart Association (AHA) and American College of Cardiology (ACC) have recently recommended continuing thienopyridines (ticlopidine and clopidogrel) for a minimum of 12 months after implantation of a drug-eluting stent (DES) (Grines et al 2007). These recommendations extend therapy beyond that recommended by the FDA-approved package insert and stem from data demonstrating that stopping antiplatelet therapy prematurely has been associated with subacute thrombosis, a frequently fatal complication (Iakovou et al 2005; Eisenstein et al 2007). Earlier research indicates that 14% of myocardial infarction (MI) patients in a national registry who received a DES after an acute myocardial infarction (AMI) stopped thienopyridines within one month of treatment, far short of the FDA-recommended 6 months and the AHA/ACC-recommended 12 months (Spertus et al 2006). The report also demonstrated that these patients were twice as likely to be rehospitalized and nine times more likely to die within one year of their DES implantation.

Extensive prior research describes the prevalence and nature of medication nonadherence (also known as noncompliance, nonconcordance) (DiMatteo et al 2002).
An extreme form of nonadherence is discontinuance, where the medication is stopped altogether. Ho and colleagues (2006) recently found that 34% of AMI patients discontinued at least one prescribed medication within one month of discharge. In another study of acute coronary syndrome (ACS) patients, 13%–34% discontinued at least one essential heart medication within one year of hospital discharge (Sud et al 2005). Common reasons cited for stopping medication(s) in that study were physician discontinuation and adverse effects. However, all previous studies examining reasons for medication discontinuation after an ACS have used close-ended surveys, which have several important limitations. Preconceived questions and answers restrain response options and, therefore, may not capture patients’ primary reasons for prematurely stopping medications. In addition, data were often collected from a single site, thereby limiting the diversity of reasons why patients may stop their medications. Last, noncompliance is frequently conceptualized as a problem in decision making, which ignores the role of patients’ values and beliefs (Morris and Schulz 1992). To overcome these limitations, we conducted a multicenter, qualitative research study in which we interviewed two groups of patients: discontinuers and continuers of clopidogrel at 1 month. We investigated why patients prematurely stop a life-sustaining medication that doctors feel should be continued by comparing the two groups’ perceived barriers to medication adherence along with patients’ responses to those barriers.

Methods

Participants

Patients for this study were recruited from a large prospective cohort study, the Translational Research Investigating Underlying disparities in acute Myocardial infarction Patients’ Health status (TRIUMPH) study. At the time of this study, approximately 1000 patients were enrolled in TRIUMPH and, approximately half of these had received a DES. In the one-month TRIUMPH interview, patients were asked if they had stopped taking any prescribed medications since they left the hospital for their heart attack. The 1-month follow-up was the first opportunity to assess discontinuance. With regard to clopidogrel, professional guidelines indicated a minimal duration of 6 months; therefore, no patient receiving a DES should have stopped clopidogrel at that early time point.

For the present study, only non-ST elevation myocardial infarction (NSTEMI) patients discharged on clopidogrel who indicated stopping their clopidogrel within 1 month were identified. Other medications were not studied. The cohort was further restricted to those receiving a DES as part of their AMI care to insure that the indications for continued thienopyridines use were strong. Approval for this study was granted from the Saint Luke’s Hospital Institutional Review Board prior to contacting any patients.

Between April 2006 and August 2006, 11 patients who reported discontinuing clopidogrel were matched by sex and education with 11 patients who continued their medication within one month of receiving a DES. Continuers and discontinuers were also similar on clinical characteristics. Initially, 17 patients were identified as discontinuers and were sent letters describing the study. Of those, the interviewer was able to contact 13 and 11 consented to be interviewed. A goal of qualitative data collection is to reach a level of saturation with the topic under study such that the information gained from participants becomes redundant, providing no new insights into the phenomenon (Marshall 1996). Saturation was achieved within the first 9 interviews and 2 additional interviews were conducted to confirm that no new concepts were being introduced. Two continuers per discontinuer were contacted for an interview. Eleven matched continuers were ultimately interviewed.

Procedures for collecting interview data

The research team mailed an individualized introductory recruitment letter to patients meeting the inclusion criteria (NSTEMI DES patients discontinuing or continuing clopidogrel at 1 month). The interviewer then called patients, with an average of 1.5 phone call attempts per patient. Telephone interviews were recorded, transcribed, and analyzed qualitatively. The average interview was 32 minutes in length.

Study materials

Study materials included a recruitment letter for patients, an interviewer biography and photo for the patient recruitment letter, and a patient interview guide. The letter explained the purpose of the study, asked for participation, and provided information about the interviewer to increase the likelihood that participants would be willing to be interviewed.

To develop the interview guide, we reviewed the existing literature on thienopyridines as well as relevant medical and health psychology literature (Rosenstock 1966; Becker 1974; Stimson 1974; Janz and Becker 1984; Conrad 1985; Morris and Schulz 1992; Bebbington 1995; Bhatt and Topol 2004; George et al 2005; Iakovou et al 2005; Lewis et al 2005; Spertus et al 2006). We adapted the Health Belief Model (HBM) (Janz and Becker 1984) as a paradigm for understanding why and how people make health decisions.
An application of this model articulates the decision to take a prescribed medicine as a conscious choice driven by patients’ beliefs that they can improve their outcomes by taking a medication or, conversely, that not doing so will result in adverse outcomes. Thus the decision to comply with therapeutic recommendations stems from a perception that the benefits of doing so outweigh the harms of not doing so. This decision to continue taking medications is also facilitated by reminders and cues to persist with recommended therapies. Previous studies have conceptualized noncompliance as a problem in medical decision making, but this limited approach can ignore the patients’ beliefs and values and the opportunity to identify actionable opportunities to improve compliance (Morris and Schulz 1992). Therefore, the HBM was used as a theoretical framework in developing questions for the patient interview guide, though the research team remained open to all content from the interviewees (Rosenstock 1966; Becker 1974; Janz and Becker 1984). A review of 17 studies using the HBM found that ‘perceived barriers’ was the most powerful dimension of the model (Janz and Becker 1984; Vermeire et al 2001). Thus, we oversampled this domain in the interview guide (see Appendix).

Data analysis procedures
The digitally-recorded interview files were transcribed by two research assistants. Following transcription, each interview was distributed to three Ph.D. researchers who coded the interviews. The three researchers reviewed the transcribed documents independently to develop a familiarity with the text and to search for patterns and themes that occurred frequently in a single interview or across interviews. Using this form of directed qualitative content analysis, the goal was to extend conceptually the HBM when applied to cardiac patients and the persistence of clopidogrel (Hsieh and Shannon 2005). The data were then manually coded by identifying passages that exemplified key concepts or ideas related to the major patterns and themes. Throughout the coding process, the researchers employed the HBM as the theoretical framework with which to understand patients’ perspectives.

The use of multiple coders is important for credible and trustworthy data reduction. Preliminary codes were identified and a visual display (affinity diagram) of key nodes and attributes was used to organize the reduced narrative data. The transcribed interview text was then entered into an electronic data analysis program, NVivo (NVivo 2, QSR International, Victoria Australia). Use of the computer program provided a check of the rigor of the manual coding of the data and assisted in organizing the large volume of narrative data.

Assuring rigor during analysis
First, any conclusions that were drawn from the qualitative data were reviewed in the context of the entire data set with the goal of finding discrepant information. If such information was discovered in the review of the data, the conclusions were modified. Second, the investigators worked closely with a physician consultant throughout the study to obtain feedback on transcript content and consistency with the investigators’ conclusions. This reduced the possibility of researcher bias or faulty clinical logic. Thirdly, data from multiple interviews was collected until data saturation had occurred. Lastly, once saturation had occurred, an additional two continuers and two additional discontinuers were interviewed to confirm saturation. These patients also served as a form of member-checking, a process to validate the conclusions drawn by the researchers by discussing conclusions drawn from earlier interviews with these patients. Although participants in qualitative research are fewer in number, the process results in much richer, narrative data.

Results
The final study cohort included 22 AMI patients who had similar sociodemographic characteristics (education, sex, age, and health insurance coverage) and comorbidities, including hypertension, prior heart disease, dyslipidemia, and diabetes. Eleven patients were “discontinuers” aged 45–77; nine (82%) were Caucasian; four (36%) were female; and 50% had less than a high school education. Eleven patients were “continuers,” matched on sex and education. Interviewed continuers were 41–63 years, five (45%) were female, nine (82%) were Caucasian, and five (45%) had a high school education or less. The HBM is comprised of four factors: disease severity, susceptibility/threat, barriers, and cues to action. These factors emerged clearly as important constructs in our analyses. However, discontinuers repeatedly described barriers to action and the severity of disease while continuers stressed their susceptibility and cues to action. The noticeable presence or absence of these themes by discontinuers is presented in Figure 1 (attributes are rank ordered with regard to prevalence). The four factors of the HBM provide an organizational framework for our analyses.

Severity of disease
This category contains the patient’s perception of the consequences of the condition as serious or not. Whether the patient viewed their MI or its subsequent treatment as a significant event and began to internalize the vital changes necessary carried over into how they addressed medication taking.
A discontinuer patient who reported “Well, I thought it was just indigestion,” and thus delayed his treatment, and then later determined that he “didn’t need to be taking all this medicine”, is very different from a continuer. An example of a continuer’s description of their condition: “Yes, I consider it serious, yes… I think it is going to limit my life from here.” The importance placed on either the signs or symptoms for the disease or receiving a diagnosis of myocardial infarction was interpreted and internalized differently for the two groups of patients.

Susceptibility/threat
Susceptibility or threat is reflected in a patient’s perception of their vulnerability to the condition and implies a defensive or alert strategy. Some discontinuer patients expressed a fatalistic approach to their MI believing that no matter what they did, they were going to have more heart attacks or die from their coronary artery disease. An example of such beliefs include the following patient quotes: “Everybody in my family has died from a heart attack or cancer. My parents both died within the last 4 or 5 years so I was taking care of both of them… I’m pretty familiar with it… We’re walking dead men.” Denial of their condition is another example of this helplessness that is a precursor to patients discontinuing their medication. In contrast, continuers routinely described how they took their condition seriously and that they didn’t want to have another heart attack.

Barriers to action
Discontinuers reported many barriers, whereas continuers may have reported a barrier, but then countered with their actions to overcome that obstacle. One of the most frequently reported barriers was a breakdown in communication which in turn lead to poor transitions in care (hospital to outpatient or specialist to primary care provider [PCP]). An important system-level issue identified by discontinuers was the lack of continuity between inpatient and outpatient care. One patient reported “Now when I first got out, the doctor, I think it was clopidogrel, he said I would have to be on it for the rest of my life. And when I went to the [PCP] doctor, you know, on my return visit, he just said it would be 30 days, and at the end of 30 days that was it.”
Correspondingly, an obvious distinction between discontinuers and continuers was that continuers did not report extensive gaps in their care. One continuer said he sees his heart doctor only once a year but “he still sends me letters like, you know it’s time for your cholesterol, it’s time for your sugar diabetes check, you know. He updates me on everything that I need to do. Then I got to go to my primary care and take it to him and he does all the tests and that stuff and sends the results back to my heart doctor.” This type of communication that provides a connection between specialists and primary care physicians was not described in discontinuer patient interviews.

Another difficult transition in care occurred when patients were geographically distant from the treatment center. The breakdown in communication and the distance with which a patient would need to travel sometimes precluded specialized follow-up. The discontinuer patients frequently reported struggling with relaying specific information to their primary care providers such as treatments received and new medications added. Discontinuers also stated that their local primary care physicians were not always familiar with the distant specialists and the specialist’s intended treatment plan. From comments made by discontinuers, if information regarding medication and recovery instructions was conveyed to the patient, he or she frequently interpreted it incorrectly or did not recall having received the information.

Poor communication beyond the transition of care was also an independent barrier for some patients. Several discontinuers reported feeling limited by the time available for seeking information from caregivers during hospital discharge and later during follow-up visits. A few continuers reported similar experiences, but then identified other sources that they used for gaining more information. Another difficulty reported by discontinuers and identified by the researchers was fragmentation in care created by multiple clinicians attending to a patient. For example, patients reported receiving contradictory information from clinicians; however, continuers reported seeking clarification, whereas discontinuers did not. A priori, cost was expected to be a frequently reported reason for discontinuing clopidogrel early. Surprisingly, difficulty affording the medication, or economic burden, was not a commonly described barrier by patients. Though one female discontinuer stated “The first time around, I got Medicaid from the social services here because I had an un-raised child in the house with me. Well he’s 20 years old now. And that cut it off. That cut the Medicaid off. That’s why I quit taking it.” Not surprisingly, when continuers reported cost as a potential barrier to clopidogrel continuance, they also described strategies to overcome it. For example, one patient remembered “the doctor told me if I can’t afford it, you know, because it is expensive, to let them know, and they would do what they can to get it for me for free.”

As anticipated, some discontinuer patients reported self-medicating by simply deciding to stop taking clopidogrel because they felt they no longer needed the medication (felt better or worse or that it resulted in no effect) or they perceived they were having unpleasant side effects (fatigue, rash, bleeding, bruising). They also reported stopping clopidogrel because they believed it was similar to other blood thinners, such as coumadin® and aspirin, and didn’t see the value in being on duplicate medications. Such barriers were not reported by patients who continued taking their clopidogrel.

Cues to action
The largest single difference between the discontinuers and the continuers was that the majority of continuers could recall having received education or information specifically on clopidogrel. One patient described the hospital discharge process as a cue to action: “Yeah. And they explained to me what they [medications] were and what they were for. Like on the clopidogrel they stressed the importance of taking [it].” The most frequent message among discontinuers, however, was that they were unaware they should be taking clopidogrel.

Discontinuers frequently were unable to recall receiving education about the medicine or clopidogrel’s specific purpose. Another important cue to action is whether the post-DES patient was aware of the intended duration for clopidogrel. Continuers reported knowing the duration for clopidogrel in contrast to discontinuers who did not know or were uncertain about duration. Several continuer patients reported that they would be taking the drug for a year, while one patient said “Well yeah I ask them and they said I may be taking it for the rest of my life.”

Continuers could easily recall having heard about their clopidogrel medication, including the purpose and specifically the duration. In addition, several described communications between their hospital physicians or cardiologists and their regular primary care physician. The consistency between interview findings for continuers pointed to knowledge received about the medication, its purpose and duration, which led the patient to assign value to continuing medications, and in this case, clopidogrel.
Discussion

Interventional cardiologists who implant DES uniformly believe that it is imperative that the patients continue thienopyridines after discharge, due to the potential fatal consequences from premature discontinuation (Iakovou et al 2005; Eisenstein et al 2007; Grines et al 2007). After interviewing both discontinuers and continuers, we identified a number of themes that distinguished discontinuers and continuers. These included multiple barriers that were reported by discontinuers, but not continuers; clarity of knowledge about clopidogrel purpose and duration; and system-level issues that were obstacles for discontinuers such as transition of care from in-patient to out-patient.

Review of prior studies examining medication noncompliance identified weaknesses in the nature or design of these studies. First, an implicit assumption is often made that the patient is a passive, obedient, and unquestioning recipient of medical instructions (Stimson 1974; Conrad 1985). Second, many studies focus upon what was wrong with the patient that led to their noncompliance (Bebbington 1995). Third, previous researchers have noted that “very little attention has been paid to the patient’s perspectives of adherence” (George et al 2005, p 3199). The findings of our study support the HBM, in which the patient first perceives a health threat that may then cue the patient to take action. The impact of patients’ perception of barriers on discontinuing clopidogrel is consistent with the finding of Janz and Becker (1984) that “perceived barriers’ is the most powerful dimension of the HBM. Some patients reported discontinuing medications for a variety of barrier-type reasons, such as not believing in taking medications, not recalling education on clopidogrel purpose or duration, perceiving unlikely side effects (eg, fatigue) or experiencing real side effects, and maintaining generally unhealthy lifestyles. Economic burden, while an obstacle for some patients, was not a commonly described barrier. Conversely, continuers could describe barriers, but identified more benefits and cues to action, thus, overcoming most barriers.

A recent article reported an observational study of physician and patient surveys surrounding new medication prescription communication and found that while 74% of the new prescriptions were identified by name to the patient, only 34% of the time was the intended duration of the medication communicated (Tarn et al 2006). This is consistent with our findings in that several patients who discontinued clopidogrel responded that they were not supposed to be taking the medicine when asked why they had stopped taking it. This gap in communication highlights a need for clearer patient education at discharge and during early follow-up regarding clopidogrel treatment duration.

Gaps in transitions of care were identified as a major obstacle and breakdown in processes that could sustain medication-taking behavior. Kripalani and colleagues (2007) recently published a review of studies on communication between hospital-based and primary care physicians. They identified 73 studies on information deficits or interventions designed to improve the information hand-off. The conclusion was that deficits adversely affected patient care, especially the transition from hospital discharge to outpatient follow-up care. Our findings, on an individual patient level, confirm the difficulty of this transitional time. Additionally, medication reconciliation problems were evident in patients’ portrayals of their experience with their MI and medication continuance. The healthcare system seems to fail in sufficiently educating many patients who are discharged on clopidogrel following DES and thus the need for customized or more patient-friendly material is necessary, especially stressing duration of clopidogrel.

This study has some limitations. The sample size is small; however, the richness of the data and the attainment of saturation in the present study indicate a sufficient number of patients to make the results credible, trustworthy, and meaningful. Furthermore, as with any study using a patient registry, the patients drawn from this national AMI registry may not be representative of all AMI patients or even of typical AMI patients. In addition, qualitative data analysis relies on researcher interpretations with the potential for bias. In the present study, multiple reviewers from different disciplines (nursing, psychology, and anthropology) analyzed the data and discussed the findings with clinicians from other disciplines (medical doctors and patient interviewers). Lastly, a technique called member checking, which takes preliminary findings back to similar subjects for accuracy of conclusions drawn, was used to assure the trustworthiness of the researchers’ interpretations.

In conclusion, rather than representing a negative patient behavior, our study suggests that early stopping of clopidogrel is influenced greatly by healthcare processes. Second only to education, system-level issues such as lack of continuity between inpatient and outpatient care were identified as common problems among discontinuers, but not among continuers of clopidogrel therapy. Continuers consistently described having received information and knowledge about clopidogrel’s purpose, benefits, and duration. Future research should explore the efficacy of interventions to improve continuance, such as efforts that increase patients’ awareness.
of medication indication and duration, clinician short and longer-term telephonic follow-up, providing the patient with the recommended number of pills in the same packaging as the DES, and changes in hospital discharge medication forms to include a duration column. These qualitative findings should be considered exploratory in nature and could be well utilized as the foundation for future quantitative work seeking to develop a tool to identify patients at risk for premature medication discontinuance. Thus, identifying barriers and factors that promote better transitions of care can be the first step towards aligning clinician and patient beliefs for post-MI and post-DES care to avert potentially fatal consequences.

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Appendix
Interview guide: Core questions and probe items for patients

Background information
1. Would you please tell me a little bit about your experience with your heart attack?
   a. What was it like?
   b. How did it happen and what prompted you to go to the hospital?
   c. What were the events involved?
2. Please tell me about your experience when you were discharged from the hospital.
   a. What was good and bad about the experience?
   b. When you were discharged from the hospital, who gave you instructions for taking your medications – the doctor, the nurse, or some other hospital staff person?
   c. Who provided information about your medications and other healthcare matters?
   d. In what ways were you involved in the discharge process? How did you participate or what did you do?
3. When you were discharged from the hospital could you identify the medications you were prescribed?
   a. If not at the time, do you now know what each medication does for you?
   b. Who or what materials provided the best information for you to understand your medications?
4. Since experiencing your heart condition, and returning home from the hospital, how have you been feeling? How are you feeling today?

Reasons for discontinuing
1. In your 1-month TRIUMPH interview, you indicated that you stopped taking certain medications. We are particularly interested in why people might stop taking Plavix. Would you talk about your reasons for discontinuing use of that medicine?
   a. Can you tell me why Plavix was prescribed to you? Why is it supposed to be beneficial to you?
   b. What other medications have you stopped taking and why have you stopped taking them?
   c. What person(s), procedures, processes, or materials would better help you understand the purpose of your medications?
   d. From your unique perspective, what would make it easier for you to continue taking the medications, particularly Plavix?

Economic Burden and Insurance (depending on patient financial/insurance data points from TRIUMPH, certain questions may not be necessary)
2. How much of a financial burden is it to you with or without your insurance?
3. Do you have insurance that helps pay for the medications – I am thinking specifically of Plavix?
   a. Please tell me about your experiences when working with your insurance company? In what ways is it easy or difficult?
   b. (DEPENDING ON THE ABOVE RESPONSE) From your perspective, what would make it easier to work with the insurance company to ensure your healthcare needs are met?

Healthcare system
4. Given your current experiences with the healthcare industry, please tell me why you think they are doing the best that they can or not doing the best that they can for you and others like you.
   a. Why do you feel as though you can or cannot openly share your medical problems and concerns with your doctor about your medical treatment and progress?
   b. Why do you feel as though you can or cannot openly share your medical problems and concerns with your pharmacist about your medical treatment and progress?

Threat/susceptibility
1. Why would you say that your heart condition is a serious matter or not?
2. In what ways do you believe that your heart condition affects your day-to-day life now?
   a. In what ways do you think it will affect you in the future?
3. What do you think caused your heart attack?
   a. Do you know why a heart attack happens?
   b. What are the conditions that exist within you – your arteries and heart that cause a heart attack?

Cues
1. Who or what provided the best information for you to understand your heart condition and the reasons for your heart attack?
   a. What person(s), procedures, processes, or materials would better help you understand the causes of your heart condition?
2. DEPENDING ON THE PATIENT TRIUMPH DATA POINT REGARDING SOCIAL SUPPORT:
   Do you have family, friends, neighbors, or anyone else who stops by regularly (eg, daily, weekly) to check up on you and to ensure that you are taking your medications and simply just doing well?

Note: Patients will be prompted to expand on responses with questions like “Could you tell me more about that?” or “How so?”
