

Feasibility Pilot on Medication Adherence and Knowledge in Ambulatory Patients With Gastrointestinal Cancer

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The increase in development and approval of new oral cancer therapies has changed chemotherapy administration. That shift in the treatment paradigm has led healthcare professionals to address the need for the development of new models of care in patients receiving oral chemotherapy agents. Patients must now assume responsibility and control for self-administration of those agents. Various factors that may be predictors of adherence to the prescribed regimen include patient perceptions; clinician beliefs; economic, disease, and sociodemographic factors; or knowledge deficits (D'Amato, 2008; Given, Spoelstra, & Grant, 2011; Partridge, Kato, & DeMichele, 2009). In addition, self-administration may lead to safety concerns because of errors in administration, exposures related to handling oral chemotherapy agents, drug interactions between chemotherapy agents and other medications, and failure to report side effects (Bartel, 2007; Winkeljohn, 2007). In a survey by Weingart et al. (2007) of 42 U.S. cancer centers, 10 centers reported no formal procedures in place for monitoring adherence. Medication nonadherence also may lead to unnecessary hospitalizations, poor clinical outcomes, and increased healthcare costs (McDonnell & Jacobs, 2002; Senst et al., 2001).

Adherence rates in patients receiving medications vary from lower than 20% to as high as 100% in patients receiving oral chemotherapy (Partridge, Avorn, Wang, & Winer, 2002; Ruddy, Mayer, & Partridge, 2009). Descriptive adherence studies on oral chemotherapy use have demonstrated the extent of the issue (Lebovits et al., 1990; Levine et al., 1987; Partridge, Wang, Winer, & Avorn, 2003). As reviewed by Schneider, Hess, and Gosselin (2011), few interventions have been evaluated

Purpose/Objectives: To evaluate the feasibility of face-to-face education, a nurse-initiated telephone call, and patient use of medication diaries to support patients' self-reported medication adherence and knowledge of oral chemotherapy.

Design: Descriptive, feasibility pilot study.

Setting: An outpatient oncology unit at a National Cancer Institute–designated comprehensive cancer center.

Sample: 30 patients with gastrointestinal cancer who were prescribed at least one oral chemotherapy agent.

Methods: Participants received verbal and written education and a nurse-initiated educational telephone call within 72 hours of receiving education. Each was asked to complete a medication diary at home during the first cycle and the eight-item Morisky Medication Adherence Scale (MMAS-8) at the end of the first cycle of oral chemotherapy.

Main Research Variables: Verbal and written education, telephone contacts, drug diary, self-reported medication adherence, and patient knowledge.

Findings: Most patients ($n = 29$) received both verbal and written education, participated by telephone ($n = 25$), and completed the medication diaries ($n = 21$) correctly. Seventeen participants documented side effects within the first 72 hours of treatment initiation, with eight participants needing additional assistance with management of side effects. At the end of the first cycle of therapy, MMAS-8 adherence scores were high ($\bar{X} = 7.89$, $SD = 0.55$).

Conclusions: This study demonstrated the feasibility of a nurse-initiated educational and monitoring protocol for patients with gastrointestinal cancer receiving oral chemotherapy. In addition, the adapted MMAS-8 was a feasible adherence measure.

Implications for Nursing: Pilot findings support targeted nurse interventions with face-to-face and telephone education to enhance self-monitoring and adherence for patients with gastrointestinal cancer receiving oral chemotherapy.

with patients in ambulatory oncology care, but several interventions that may promote oral medication adherence, primarily written and verbal education deployed at specific times, have been tested in samples of adults with chronic conditions.

Literature Review

A systematic search and critical appraisal of the literature was conducted to identify best evidence interventions that improved compliance or adherence. The databases PubMed, Cochrane Library, CINAHL®, DynaMed, PsycINFO, and Database of Abstracts of Reviews of Effects were searched from January 2003 to May 2010 for the following key terms: *medication adherence, cancer, antineoplastic, reminder systems, Cochrane Consumer and Communication Group, patient education, interventions, patient compliance, patient non-compliance, patient adherence, patient nonadherence, cancer therapy, chronic disease, HIV, and randomized clinical trials*. Reference lists of all relevant articles were manually searched to identify additional studies. Key oncology journals, including the *Journal of Clinical Oncology* and *Clinical Journal of Oncology Nursing*, published from January 2007 to May 2011, were hand-searched.

An additional search was conducted in PubMed and included medical subject heading terms such as *patient compliance/psychology* and *self administration/psychology*, limited to humans, meta-analysis, randomized clinical trials, and systematic reviews. Many intervention studies were directly related to long-term treatments for chronic medical conditions and, therefore, information was extrapolated given that patients with cancer may be seen routinely in outpatient clinics for a number of years. The systematic reviews were grouped according to types of interventions that were single, comparative, or complex with either technical, educational, behavioral, or family-social components.

Medication Adherence Interventions

Although many researchers have conducted studies of interventions to improve medication adherence in short-term and chronic medical conditions, limited studies have examined medication adherence, interventions, and safe practices surrounding oral chemotherapy self-administration. In a series of systematic reviews for adherence in chronic diseases (Bangalore, Kamalakkannan, Parker, & Messerli, 2007; Bennett & Glasziou, 2003; Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Mahtani, Heneghan, Glasziou, & Perera, 2011; Reuda et al., 2006; Schedlbauer, Davies, & Fahey, 2010; Schroeder, Fahey, & Ebrahim, 2008; Williams, Manias, & Walker, 2008), interventions to improve medication adherence differed substantially in terms of patient populations (those with chronic diseases

such as diabetes, hypertension, and HIV), measures of adherence (subjective and objective assessments), health outcomes (e.g., blood studies, reduction in blood pressure, hospitalizations, reduction in healthcare costs), and interventions (individual or complex).

Data were extracted for analysis specific to interventions that improved medication adherence. Categories or themes included technical interventions; comparisons of behavioral, educational, and social interventions; and complex or multifaceted interventions. Technical interventions, such as reminder packaging (Mahtani et al., 2011) and fixed-dose regimens (simplified dosing) (Bangalore et al., 2007; Haynes et al., 2008; Schroeder et al., 2008), were effective in improving adherence. Behavioral interventions, including computerized reminders and physician-patient feedback systems (Bennett & Glasziou, 2003), and combination regimens incorporating educational and behavioral interventions (Haynes et al., 2008; Reuda et al., 2006; Schedlbauer et al., 2010; Williams et al., 2008) provided a positive effect on medication adherence. Behavioral interventions included tailored counseling sessions with follow-up telephone calls led by pharmacists (Williams et al., 2008), patient support and education (Reuda et al., 2006), patient reminders (face to face, telephone call, and diaries) and reinforcement (Schedlbauer et al., 2010), reminder packaging (Mahtani et al., 2011), and computerized reminders (Bennett & Glasziou, 2003).

In an updated review by Haynes et al. (2008), three groups of investigators (Marquez Contreras et al., 2005; Rudd et al., 2004; Sadik, Yousif, & McElnay, 2005) reported that interventions (telephone calls and education) provided by nurses and allied health professionals demonstrated positive adherence and outcomes. Complex interventions for chronic conditions including “combinations of more convenient care, information, education, reminders, self-monitoring, reinforcement, counseling, family therapy, psychological therapy, crisis intervention, manual telephone follow-up, and supportive care” (Haynes et al., 2008, p. 21) may improve adherence and outcomes.

The increase in approved oral cancer therapies has introduced new challenges, including a shift in responsibility from clinicians to patients and families for self-administering and managing side effects. Studies exploring nursing support in delivering symptom management interventions to patients during the cancer treatment experience have had positive outcomes. For example, Given et al. (2004) examined the effects of a nurse-delivered intervention to reduce the severity of physical and psychological symptoms in patients with solid tumors receiving chemotherapy for the first time. The study found that patients in the experimental group who entered the trial with higher symptom severity had lower symptom severity postintervention.

That study later was modified to compare the use of an automated telephone response system and a nurse-assisted symptom management protocol using an evidence-based symptom management toolkit to reduce symptom severity in patients receiving chemotherapy (Sikorskii et al., 2007). The results suggested that both interventions produced a significant reduction in symptom severity over baseline.

McCorkle et al. (2009) tested the effects of a standard nursing intervention protocol delivered by an advance practiced nurse and a psychiatric consultation liaison nurse to women with gynecologic malignancies who received treatment with surgery and adjuvant therapy. Women who received the standard nursing intervention protocol had significantly reduced uncertainty and significant improvements in symptom distress, as well as mental and physical quality of life over time.

Evidence exists for nursing support using education and monitoring before and during home administration of oral therapy (Courtney, 2009; Cunningham, Henson, Sikma, Hammer, & Berry, 2008; Decker et al., 2009). Decker et al. (2009) explored the use of an automated voice response system to monitor adherence to oral chemotherapy and assess the severity of symptoms. In addition to weekly automated voice response calls, 30 participants in that pilot study received a symptom management tool kit, which provided evidence-based strategies for 15 symptoms. Patients who reported moderate to severe levels of any symptoms for three consecutive weeks were called by a nurse for assistance in symptom management or adherence to oral chemotherapy. The results indicated a 23% nonadherence rate to oral chemotherapy related to symptom severity and forgetting to take medications. In addition, Cunningham et al. (2008) reported significantly improved knowledge and self-reported use of oral discharge medications after deploying a nurse-initiated support telephone call made 72 hours after discharge in adults who received inpatient cancer chemotherapy.

In summary, components of behavioral, educational, social, or complex interventions may lead to improvement in medication adherence. Moderate evidence from a limited number of trials supports face-to-face patient education followed by telephone support by clinic nurses to promote safe adherence to oral chemotherapy agents. However, no published study has documented the feasibility of conducting such clinical practices in a busy ambulatory cancer center. The purpose of this feasibility study was to evaluate a collaborative multiprofessional approach to promoting oral chemotherapy adherence in patients with gastrointestinal (GI) cancers. In addition, the investigators aimed to describe patients' self-reported adherence, knowledge of oral chemotherapy, and reported side effects.

Theoretical Frameworks

The theoretical frameworks that guided this pilot study were the nursing practice model at the study site, Synergy Model of Patient Care (Curley, 2007), and Ottawa Model of Research Use (Graham & Logan, 2004). The Synergy Model of Patient Care (Curley, 2007) is based on the principle that patient needs and characteristics influence and drive increased competencies of nurses, thus improving outcomes. Through the use of that model, advance practice nurses and program nurses, as facilitators of learning, provide patients and families with knowledge and skills to allow them to understand and manage their medication side effects. As part of the multiprofessional team, experienced oncology nurses were able to articulate patients' needs, recognize potential problems, and meet the educational goals of patients and their families, with the main goal of optimizing outcomes.

The Ottawa Model of Research Use (Graham & Logan, 2004) guided the process of piloting the intervention with members of the multiprofessional team. Existing institutional data surrounding medication adherence, the practice environment, and potential adopters were assessed. The study site fosters an environment that promotes shared governance, as well as participation in quality improvement and evidence-based research endeavors.

Recognition of the role of patients, families, and healthcare providers (physicians and nurse practitioners [NPs]) as early adopters was paramount for the project to be successful. Meetings were conducted with executive leadership, the physician division director, and team members to examine barriers and facilitators to implementing and evaluating a new practice. With that information, strategies were tailored to address barriers and implement the intervention.

Methods

This feasibility study involved a convenience sample of 30 eligible, consecutive patients with GI cancer who were aged 18 years or older, able to read and understand English, and receiving a treatment regimen that included at least one oral chemotherapy agent, and also had access to a telephone. The study was conducted in a National Cancer Institute–designated comprehensive cancer center in an urban community in the northeastern United States.

Procedures

The principal investigator met with the study team, which included physicians, clinic nurses, research nurses, and NPs in the division, to provide onsite training on how to screen for eligible participants and how to proceed with the study. After institutional

review board approval was obtained, potential participants were identified by one of 13 attending physician or one of three NPs. The physician or NP then determined whether patients were interested, reviewed the details of the study, and obtained signed informed consent for those willing to participate. A flow diagram depicting the study schema and intervention is shown in Figure 1.

At the time of consent, patients and designated caregivers or family members were provided with scripted oral instructions and written education materials about the oral chemotherapy medication. That information included brand name of the drug, timing of drug administration in relation to meals, what to do with missed or vomited doses, handling and storage of the drug, side effects, self-care management of side effects, and information on when and how to contact their healthcare professionals about questions and concerns. The study team discussed completion of the medication diary with participants at their initial visit. Patients were instructed to bring the diary to their first clinic visit following completion of the first cycle of therapy. Additional information collected included the date when the participant needed to be contacted, the participant's telephone number, date of planned initiation of therapy, date of next scheduled clinic visit, and name of oral chemotherapy medication.

The program nurses contacted the patient's attending physician or nurse practitioner for any medical concerns that needed to be addressed before the following clinic visit (study visit 2). At the end of the first cycle of therapy, the principal investigator or study team member reviewed the medication diary with each participant in person and requested completion of the adapted eight-item Morisky Medication Adherence Scale (MMAS-8) questionnaire.

Intervention

The telephone education guide was developed by the study investigators as an intervention. Within 72 hours of initiating oral chemotherapy, patients were contacted and queried regarding their understanding of their oral medication. Topics included knowledge of medication (including drug name), schedule of administration, drug information, missed or skipped doses of oral chemotherapy pills, tracking of administration, side effects, symptom management, and storage of medication. Misconceptions were corrected at the time of the nurse-led telephone intervention call.

Instruments

The **MMAS-8** (end of cycle) and a **medication diary** (throughout the cycle) were used to measure adherence or knowledge during the first cycle of oral chemotherapy.

Medication adherence: The original four-item MMAS was developed as a self-reported adherence measure using a sample of patients being treated for hypertension (Morisky, Ang, Krousel-Wood, & Ward, 2008). The extended eight-item MMAS-8 demonstrated greater reliability and sensitivity than the four-item scale (Morisky, Green, & Levine, 1986). The questionnaire was adapted with permission to better fit the oral chemotherapy scenario. The reliability coefficient of the adapted MMAS in the current study was 0.75.

Medication diary: The diaries were clinic developed and similar to drug diaries used in previous trials in the GI oncology division to help improve adherence to oral chemotherapy.

Data Analysis

Descriptive statistics were calculated for demographic characteristics of the 30 participants and

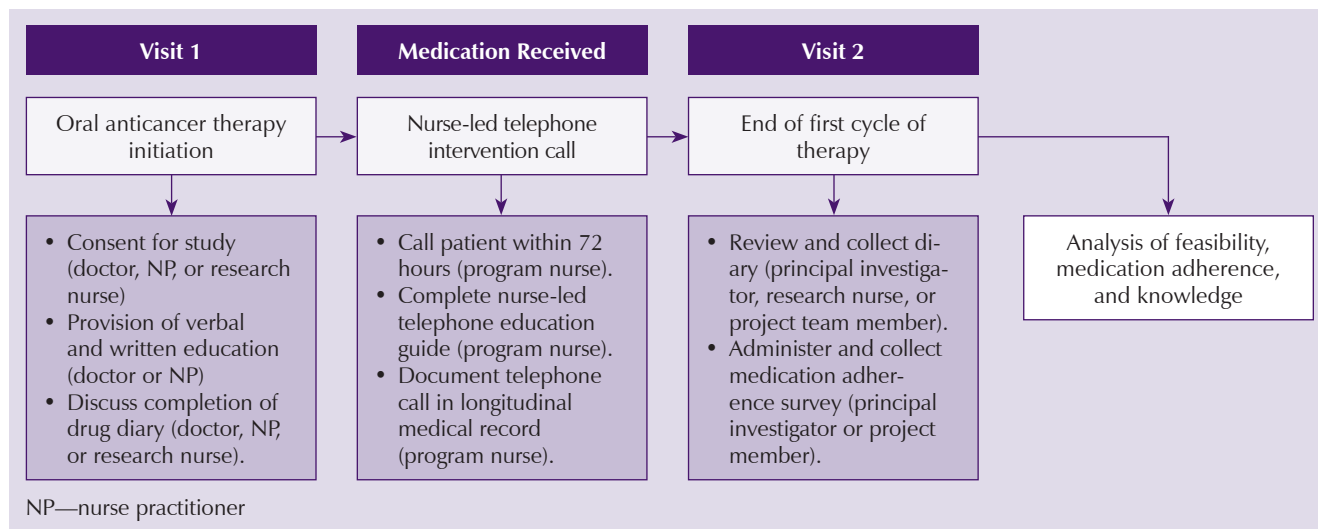


Figure 1. Study Intervention Procedure

the MMAS-8. Data from the medication diary were described using frequency distributions and content. Patient understanding of the oral medication regimen discussed during the nurse-led intervention telephone call were described. Adherence levels were scored according to instructions for low, medium, and high adherence (Morisky et al., 1986).

Results

Thirty eligible patients with GI cancer who initiated an oral chemotherapy regimen were approached, and all consented to enroll in this pilot study. Twenty-three were men and seven were women, with a mean age of 53 years (SD = 13.6, range = 28–79). During the nurse-led intervention phone call, the GI clinic nurses successfully reached 21 participants by telephone within 72 hours of treatment initiation, and another three within one week. The investigators were unable to reach six participants, despite several attempts.

Twenty-three of 24 contacted participants were able to verbalize knowledge of the drug name, purpose, administration schedule, and what to do in case of missed or skipped doses. All 24 participants reported using a method of tracking administration, including the medication diary, an alarm, and reminders from family. Follow-up telephone call information indicated that 17 participants experienced symptoms within 72 hours, with eight participants being unable to discuss how to manage symptoms. Most participants (n = 21) could identify one to three side effects of their medication, but could not always identify the most common side effect. For example, five participants receiving single-agent temozolomide did not identify hematologic toxicity as a potential side effect, whereas two of four participants receiving capecetabine did not identify hand-foot syndrome as a possible side effect. In addition, three of six participants did not identify high blood pressure as a potential side effect associated with sorafenib therapy, two of three participants did not identify mucositis symptoms associated with sunitinib therapy, and most participants receiving everolimus did not identify diarrhea (three of five) or rash (five of five) as potential side effects. Ten participants had medical issues that were referred to the NP or doctor. Finally, 23 participants verbalized satisfaction with the follow-up telephone call and teaching.

At visit 2, most participants (n = 29) reported receiving verbal and written information from their physician. Twenty-one of 30 participants completed the drug diary correctly. Six participants had evidence of missing dates and times or use of the wrong diary, two participants lost their drug diary, and one participant could not be reached and was lost to follow-up. Among the 27 participants who returned their drug diary at the completion of the first cycle,

seven had therapy held per recommendation of their medical provider because of medication-related toxicity. Finally, MMAS-8 scores collected from all 30 participants ranged from 5–8 ($\bar{X} = 7.89$, $SD = 0.55$), with higher scores indicating higher adherence.

Discussion

Findings of this project demonstrated feasibility of a collaborative multiprofessional partnership in an academic medical center to promote adherence to oral chemotherapies. The investigators encountered few challenges during this feasibility study. In most cases, the nurses were able to implement the verbal education by telephone within 72 hours; however, a small number of participants could not be reached during work hours. Through a follow-up telephone call, the nurses were able to assess the participant's knowledge and needs, tailor education, and refer medical issues that required a provider referral accordingly.

The findings indicated that most participants experienced symptoms within 72 hours of taking their medication, and some were not able to discuss how to manage their symptoms. Although a majority of patients were able to verbalize one to three side effects, most often fatigue and nausea, oral agent-specific side effects typically were not recalled by participants. That finding may suggest that potential barriers, such as patient-related factors (e.g., sociodemographic characteristics, social support, cognitive deficits, health literacy, psychological issues) or condition-related factors (e.g., disease, multiple comorbidities and polypharmacy, psychological issues), may pose particular challenges (Partridge et al., 2002; Schneider et al., 2011).

The deployment of a nurse-led telephone call was similar to procedures reported in other oncology trials. Courtney (2009) reported that patients' ability to manage symptoms improved from 80% preimplementation to 94% postimplementation. In addition, investigators using a pre-post design study in another comprehensive cancer center (Cunningham et al., 2008) demonstrated that knowledge and use of discharge medication in adult patients with cancer improved with the implementation of medication reconciliation procedures and a nurse postdischarge telephone call.

As shown in the literature, nurses may not always be available or involved in the process of patients receiving oral chemotherapy (Weingart et al., 2008; Winkeljohn, 2007). Those findings suggest that nurses play an important role in the education, monitoring, and follow-up of patients prescribed oral chemotherapy. Results of the current study highlight potential safety issues in the management and reporting of symptoms, thus indicating a continued need for reinforcement of

education and monitoring of symptoms in patients receiving oral chemotherapy using a multiprofessional team approach.

Although most participants reported adherence to the prescribed regimen using the medication diaries, seven participants filled out the diary incorrectly (e.g., missing dates or times) and two participants lost their diaries. The inconsistent use and completion of medication diaries for measuring self-reporting adherence was consistent with the literature regarding indirect methods of measuring patient adherence (Partridge et al., 2002; Ruddy et al., 2009). Use of measures such as self-reported diaries may lead to inadequate recall issues or patient reluctance to admit to nonadherence. However, the adapted MMAS-8 was a feasible measure of adherence with high self-reported rates that mainly were consistent with the completed medication diaries.

Limitations

Participants were enrolled only for the first cycle of therapy (three to four weeks); therefore, adherence may have been high given the short duration and possibly would decline in time. The principal investigator administered the medication adherence scale, and a response bias from the participants may have been present. Evidence exists that patients may be more motivated to adhere when facing an immediate life-threatening illness versus a chronic condition (DiMatteo, Haskard, & Williams, 2007). High self-reported adherence rates may have been influenced by the Hawthorne effect (Gehlbach, 2006), given that participants were aware of the investigator's interest in the rates. Without an objective measure of adherence (e.g., serum values), the investigators were unable to confirm self-reported adherence.

The convenience sample of patients with GI cancer may not be representative of a larger ambulatory patient population and has limited generalizability. Highly motivated patients that wished to improve self-care also may have agreed to participate. More importantly, given that participants exclusively were able to read and speak English, the study may not have captured high-risk patients, including those with language barriers or health literacy issues.

Conclusion

Physician- and nurse-delivered education in clinic followed by telephone support from clinic nurses was a feasible approach to promoting oral chemotherapy adherence. Daily self-monitoring was feasible and important, as side effects were documented and addressed when patients were unclear how to self-manage the side effects. In addition, the adapted MMAS-8 was a feasible adherence measure.

Implications for Nursing

The results of this project are an important first step in providing excellent care to all patients, notably those who are asked to self-administer oral chemotherapy. Early reporting of side effects and symptoms is critical to patient safety. As patients traditionally do not have consistent face-to-face access with a nurse in the clinic setting for oral medication counseling, the findings suggest that nurses have an important role in the education, monitoring, and follow-up of patients who are prescribed oral chemotherapy. In addition, future tailored intervention studies are warranted to address the needs of patients with cancer receiving oral chemotherapy.

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