

5-2011

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ScholarWorks Citation

Spoelstra, Sandra L.; Given, Barbara A.; Given, Charles W.; and Grant, Marcia, "Policy Implications of Oral Agents" (2011). *Peer Reviewed Articles*. 23.
https://scholarworks.gvsu.edu/kcon_articles/23

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Policy Implications of Oral Agents

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KEY WORDS: Cancer, Oral Antineoplastic, Adherence, Policy Implications

Abstract

OBJECTIVE: With the increasing use of oral antineoplastic agents in cancer management, patients and family members need to understand of how to obtain, safely handle, and store the medication, how and when the medications should be taken, and when to report toxic side effects to accomplish efficacious treatment.

DATA SOURCES: Research based articles and conference presentations.

CONCLUSION: Cancer centers to modify policies, protocols, or practices to assure safe and proper administration of oral antineoplastic agents.

IMPLICATIONS FOR NURSING PRACTICE: Clinicians need to monitor and facilitate administration of oral antineoplastic agents, and ultimately improve clinical outcomes.

KEY WORDS: Cancer, Oral Agents, Antineoplastic, Adherence, Scope of problems

Policy Implications

Oncology remains one of the few medical specialties where most patients are treated with intravenous (IV) rather than oral medication. However, this is beginning to change with the rapid increase in the number of oral therapeutic agents. This new paradigm in care requires that oncologists, primary care physicians, nurses, and pharmacists collaborate on the delivery of care that is patient-centered and includes family caregivers. There are very specific sets of protections and safety policies and procedures for other routes of cancer therapy.¹ However, cancer centers have failed to modify policies, protocols, or practices to integrate the use of oral therapeutics into practice. Use of oral agents requires an in-depth understanding of how to obtain the medications, how to safely handle and store the pills, of how and when the medications should be taken, and when to report toxic side effects. Patients and family members must have the knowledge and support to carry out administration of oral therapeutics in their home in order to accomplish efficacious treatment of their disease. The following sections discuss the cost of oral agents, how economics influence adherence, models of care, and how policies, procedures, and protocol may be modified to assure safe and efficacious use of oral therapeutics.

The Cost of Oral Therapeutic Prescription Drugs

Patients may be faced with financial challenges while taking oral therapeutics as the cost of oral chemotherapy can be expensive, ranging from \$5,000 to \$80,000. Further complicating the cost issue is the complexity of the reimbursement system for oral agents. Medicare Part D, Medicaid, and several private insurers cover some types of oral chemotherapy. However, the deductibles and co-pays are often burdensome to patients and their families. Consequently, this financial burden may interfere with access to the prescribed medication, impeding adherence.

Specialty pharmacies. Historically, oncologist offices and retail pharmacies managed the distribution of chemotherapy.² However, challenges with inventory, product knowledge, and management have led to more than three-fourths of healthcare providers using specialty pharmacies to dispense oral antineoplastics. The role of a specialty pharmacy is to 1) streamline the drug distribution, delivery, and management processes in ways that engage patients in their care; 2) help payers to understand the return

on investment in specialty drugs; and 3) assist manufacturers with inventory challenges and relationships with managed care organizations.² Many challenges still exist in relation to managing financial concerns, effective distribution, data collection and outcome measurement to assure efficacious cancer treatment. Electronic systems for giving oncologists access to information on current prescription processing status, reimbursement information, and adherence for complex regimens are in development at most specialty pharmacies, but remain in their infancy. Specialty pharmacies are on the edge of becoming a major force in delivery of oral therapeutics.

Access to payment for oral therapeutic prescription drugs. Many pharmaceutical companies sponsor drug assistance programs. However, busy clinicians do not have the time to understand the complexity of the drug assistance programs. In addition, many clinicians do not have access to the information to assist patients. Conversely, specialty pharmacies routinely assist patients and their families, as well as oncologist, with managing these financial challenges. Yet, little is known about how widely assistance information has been disseminated, patients' responses to the assistance programs, or if assistance extends over the entire course of treatment. Access to oral agents may also be a problem for those who are low income, as most do not receive their care from comprehensive cancer centers and are rarely prescribed oral agents.

Economic Factors Influencing Oral Therapeutics Adherence

The correct use of medications is the most cost-effective way to manage disease and reduce healthcare cost.³ In general, economic factors are known to directly influence medication adherence. For example, difficulty with affording medications⁴ and the amount of the co-payment are directly associated with medication adherence.⁵ In some diseases, such as diabetes and hypercholesterolemia, a high level of medication adherence is directly associated with lower disease-related healthcare costs.⁶ However, a gap exists in the literature, with little known about the influence of economic factors, such as prescription benefits, co-payments or out-of-pocket cost, and adherence to oral antineoplastic agents. Understanding the cost of oral antineoplastics, how patients obtain these medication and payment assistance through specialty pharmacies, and how this affects healthcare costs is necessary for all clinicians.

It has already been established that oral agents have the potential to save medical resources and reduce costs. For example, in one of the phase III trials of capecitabine versus 5-FU/LV, patients receiving oral capecitabine made 72% fewer hospital visits for drug administration and spent 23% fewer days in the hospital for treatment related to adverse events, compared to those treated with IV 5-FU/LV.⁷ The need for expensive drugs for managing adverse events was also substantially reduced with capecitabine.⁷ This may be true for all oral agents, creating significant savings in healthcare costs overall.

There may be situations when patients are not adherent to oral therapeutics, but do not disclose that fact to the healthcare provider. As a result, therapy may be stepped up to a more intensive and expensive medication because it was determined that the patient was not responsive to the lower dosing. Or failed treatment can lead to drugs that are more expensive. In addition, diagnostic tests may be ordered to try to identify reasons for the patient's poor response, adding further to the costs of therapy.⁸ Finally, when drugs are discontinued or changed, patients could find themselves with thousands of dollars of leftover medications. If non-adherence can be quickly identified, then it can be addressed and lower the economic burden of these expensive oral anti-cancer agents.

Models of Care for Oral Therapeutic Usage

Two models of care for promoting adherence to oral agents were found in the literature. One is a nursing-and pharmacy-led clinic and the other is an electronic monitoring system for adherence and symptom management. The following explains each.

A nursing-and pharmacy-led clinic to promote adherence to capecitabine in metastatic colorectal cancer patients was tested as a model of care.⁹ An agreed upon treatment protocol that included criteria for referral to the clinics, authorization of the oral therapeutics, toxicity assessment, dose modification, and medication referrals, CT scans, and administration of adjunctive therapy. The main function of the clinic was to provide education and counseling for early detection and management of treatment side effects and for the clinicians to oversee management of any treatment related events. Emphasis was placed on the patient's ability to recognize grade 2 toxicities during therapy so that subsequent interruption of therapy could reduce the occurrence of serious toxicities. Patients were provided diary

cards and a 24-hour telephone contact number for ongoing support. No costs of providing this clinic were reported. This model provides guidance for comprehensive cancer centers in how to restructure care for patients on oral agents.

A recent pilot three-arm trial of 119 patients with solid tumors from four cancer centers used an educational approach to symptom management coupled with electronic reminders to take oral therapeutic agents.¹⁰ Participants first received a Symptom Management Toolkit® and then participated in an interview to determine the severity of 15 symptoms, satisfaction, and belief about oral agents. This was followed by weekly Automated Voice Response calls (and some had 1-2 nurse calls) for nonadherence or behavioral self-management, if symptoms were severe. The study demonstrated effective strategies for reducing symptom severity and sustaining adherence to oral chemotherapy.¹⁰ Further refinement of systems to manage oral agents need to occur prior to use in clinical practice.

Policies, Procedures, and Processes of Care

Administrators of cancer centers and clinicians can modify policies, procedures and processes of care integrating what is known about oral therapeutic agent use. This includes educating clinicians, patients and family members, monitoring adherence, addressing safe handling and administering of the pills, and addressing effective coordination of care.

Education. Clinicians need to understand their role in providing education and counseling to patients on how to obtain the medications, how to safely handle and store the pills, and how and when the medications should be taken. They must also include instruction on when to report toxic side effects and how to oversee and manage any treatment related events. Emphasis should be placed on increasing the patient and caregiver's ability to recognize grade 2 toxicities to allow for early interruption of therapy, which could reduce the occurrence of serious toxicities. Clinicians need to provide tips to promote adherence, such as pill boxes or setting alarms on cell phone. Patients and caregivers need to understand their role in obtaining the medications, safely handling and storing the pills, adherence to the regimen, and when and how to report toxic side effects. Monitoring adherence can be provided by clinicians, such as drug diary cards, which can then be brought to each subsequent office visit.

Coordination of care. An ongoing flow of communication between the patient, caregiver and provider is necessary. In addition, coordination with the specialty pharmacy helps assure the right drug, in the right amount, is provided at the right time, and allows for immediate attention to any changes in prescribed dosage, so that too much or too little will not be dispensed. Providing contact information for the pharmacist is helpful to the patient and caregiver, who may want to call the pharmacist with specific questions. A 24-hour telephone contact number for ongoing support with symptom management and toxicities is also helpful. This is a common practice in comprehensive cancer centers, however, this approach is not always discussed with patients and caregivers within the context of this type of treatment.

Safety. There are multiple safety issues when taking oral therapeutics. First, over adherence (taking more than the prescribed dosage, either at the wrong time or day, or to make up for a missed dose) has been identified as a problem in numerous clinical trials.¹¹ Clinicians need to discuss timing of medication administration, not making up missed doses (for agents that must be taken on a time schedule), and when to report over adherence to the clinician. Adverse events may occur, and patients and caregivers need to be prepared to recognize and then report the event to clinicians. Biohazardous residue may occur when handling the oral agent pills and patients and caregivers need to know when gloves are required for handling the pills, and how to store the pill containers in a safe environment where children do not have access to the pills. Finally, some pills may be leftover when the treatment is stopped, the disease progresses, or a new drug is started, and proper dispensing of these pills by taking them back to the pharmacy is often necessary.

Payment and access to care. Developing a working relationship with a specialty pharmacy may be necessary for those clinicians who do not have the time or ability to assist patients with the complex reimbursement and access to care issues surrounding oral agents. Specialty pharmacies are becoming experts at solving payment problems by accessing pharmaceutical companies' drug assistance programs.

In summary, establishing policies, procedures and processes of care that address each of these issues will support patients and their caregivers in the use of oral therapeutic agent use at home. These are the initial steps and will evolve as more is known about oral agents as therapeutics.

Conclusion

The rise in use of targeted anti-cancer therapies, most of which are prescribed in oral form, raises a number of interesting policy issues. First, these agents are very expensive, their dosing is complex and the course of treatment is lengthy. Adherence is a crucial issue to the successful treatment and thus to the efficacy of these medications. All participants have a stake in examining how to modify the practice patterns in order to assure that these medications achieve their intended outcomes. Oncologists need to consider how to emphasize the importance of adherence and early reporting of side effects, and how to develop mechanisms for effective communication with their patients. Given the nature and complexity of oral agents, oncologists need to assume that mechanisms to prompt and manage adherence need to be put in place. The articles in this issue have reviewed alternatives for promoting and attaining sustained high rates of adherence. These efforts must be supported by payers. Oncologists need not bear the burden of adherence measurement and improvement alone. Payers can put into place standard, evidence-based quality indicators that provide reimbursement for high rates of patient adherence. With the advent of electronic medical records (EMRs) and electronic forms of monitoring, these evidence-based systems could be put into place quickly.

Second, specialty pharmacies that package and deliver oral antineoplastic agents can participate in these emerging systems. Improved coordination of care between oncologists and the pharmacies that deliver medications to patients can lead to adjustment in deliveries reflecting changes in dosages or patients' adherence rates. Furthermore, they can become an important vehicle for improving adherence, in assisting patients to obtain industry-supported financial assistance and to broker this information with oncologists.

Third, patients and their family members need to understand clearly the importance of adherence to these agents. They need to understand that some side effects are indicators that the drug is working, but at the same time, strategies exist to minimize the side effects on their daily lives.

In this issue, a broad range of issues have been addressed regarding oral anti-cancer agents. This work begins to frame some examples of health care policies that might influence these new approaches to cancer therapy.

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