The shift in cancer treatment from IV to oral formulations is occurring quickly, with many benefits for both the patient and provider. Although reduced administration costs and improved patient acceptability are promising, this shift has also introduced new challenges for medication adherence. As a nurse and the primary point of contact for patients and their families, you need specific strategies for your role—which is exactly what this session offers. You’ll start by reviewing the emerging literature on adherence in oncology, as well as findings from other disease sites such as HIV. You’ll end by picking up practical strategies that nurses can use to impact adherence to oral chemotherapy.

Content Area: Clinical Practice

Content Level: Intermediate

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Objectives:
At the end of this session, participants will be able to:
1. Define the scope of adherence problems in cancer treatment.
2. Describe the current oncologic literature on adherence to oral cancer treatments.
3. Identify innovative approaches that have been used in other disease sites (HIV) that address adherence issues.

Content Outline:
I. Define the scope of the problem of adherence issues in cancer treatment.
   A. Define non-adherence.
      1. Intentional
      2. Unintentional
   B. Discuss how to identify patient non-adherence.
   C. Discuss the impact of non-adherence.

II. Describe the current literature in oncology on adherence to oral cancer treatment.
   A. Research literature on risk factors for non-adherence.
   B. Research strategies to impact adherence in oncology.

III. Identify innovative approaches that have been used in other disease sites (i.e., HIV) that address adherence issues.
   A. Illustrate how patient education has impacted adherence.
   B. Examine specific strategies that have been used to improve adherence and how nurses have been able to incorporate these strategies into their practice.

IV. How can nurses encourage patients to be adherent?
   A. Synthesize what we have learned from oncology research and research on other disease sites.
   B. Review strategies supported by evidence to impact adherence.

Toolkits:
Tools for Oral Adherence Toolkit—available at www.ons.org

Bibliography:
Adherence to Oral Chemotherapy

Adherence to HIV Treatment


**Measurement of Adherence**


**Adherence to Oral Cancer Treatment (Review Articles)**


**Adherence to Oral Cancer Treatment (Strategies and Interventions)**


Objectives

• Define medication non-adherence and contrast with the term medication compliance
• Describe the impact of non-adherence in healthcare
• Identify contributing factors and predictors of poor adherence to medication that impact successful treatment for chronic illness
• Describe innovative strategies to promote medication adherence

State of the problem

For all medications:
— One third to one half of all patients do not take medications as prescribed
— Improving adherence to all medications can save as much as $300 billion in health care costs
For oral cancer treatment:
— Rates of adherence remain unknown but some studies in breast cancer have documented rates of 53-93% (Given, 2010)
— The number of agents and the number of patients taking these agents will only increase.
— 50% of therapies in development are oral. (Given, S., Spoelstra, J., & Grant, M., 2011)
— Due to the gravity of a cancer diagnosis our goal should be as close to 100% adherence as possible.

Shift to oral cancer treatments

Advantages
• Patient convenience
• No need for IV access
• Can achieve sustained drug levels
• Minimal disruption in daily life
• Patient preference

Disadvantages
• Distances patient from provider
• Changes the way patients are monitored
• Safeguards for prescription or administration may be lacking
• Patients have more responsibility for their own care

Definitions

Adherence/Compliance
— Adherence is preferred but both terms are imperfect, and unfortunately, can stigmatize patients
Definitions of adherence
— World Health Organization
  • “The extent to which a patient’s behavior coincides with medical advice”
— International Society for Pharmacoeconomics and Outcomes Research
  • “The degree or extent of conformity to the recommendation about day-to-day treatment by the provider with respect to the timing, dosage, frequency and duration of time from the initiation to discontinuation of therapy”
— Adherence is often defined to be taking 80% or more of a medication as prescribed
  • This is an arbitrary number
  • Adherence is impacted by multiple factors

How do we measure adherence?

• No gold standard
• Most studies have used direct and indirect methods to measure adherence
• All methods have advantages and disadvantages

Definitions

Persistence
— Duration of time a person takes medication, from initiation to discontinuation

Overadherence
— Defined as taking more than the prescribed amount of a medication
— Reasons can include taking longer than prescribed or taking extra doses on a single day
— One study found that overadherence was more likely than underadherence (20% compared to 13%)
— More complex regimens were more likely to have overadherence

[spoelstra et al. CION 2013]
Direct measurement

- Directly observed (in person or remotely)
- Level of medication or metabolite in blood
- Level of biomarker in blood

Advantages – most accurate and objective

Disadvantages – patients can hide pills, impractical, variations in metabolism, expensive

Indirect measurement

- Patient self-report, questionnaires
- Pill counts
- Electronic pill caps
- Prescription bottle refills
- Physiologic markers (heart rate, BP)

Advantages – simple, inexpensive, some are objective

Disadvantages – susceptible to error, easily altered by patient, other factors can affect response

Factors influencing adherence

- Patient factors
- Socioeconomic factors
- Therapy factors
- Clinician factors

Factors influencing adherence

**Patient and condition-related factors**

- Cognitive impairment
- Co-morbidities (depression)
- Gender
- Psychological stress, anxiety, anger
- Other medications
- Beliefs about treatment and outcome
- Health literacy
- Confidence in ability to follow treatment regimen
- Substance abuse

**Other Psychosocial Factors**

- Ability to follow a prescribed regimen
- Communication with provider
- Patient satisfaction
- Health beliefs
- Adherence history
- Family stability and social support

Factors influencing adherence

**Therapy-related factors**

- Adverse events
- Length/complexity of treatment
- Pattern of dosing
- Side effects (actual or perceived)
- Refills
- Polypharmacy/drug interactions
- Label warnings

Dosing

Simple dosing helps but 10-40% of patients on a simple regimen have imperfect dosing

Adherence is inversely proportional to frequency (QID dosing has average adherence rates of about 50%)

Factors influencing adherence

**Socioeconomic-related factors**

- Attitude towards treatment
- Cost of treatment
- Financial support
- Difficulty accessing pharmacy
- Distance to treatment center
- Social rank of illness
- Social support
- Cultural beliefs
Factors influencing adherence

Clinician-related factors
- After care management
- Communication skills
- Belief in treatment
- Provider/patient relationship
- Use of guidelines
- Provision of information

Predictors of poor adherence
- Presence of psychological problems, particularly depression
- Cognitive impairment
- Treatment of asymptomatic disease
- Inadequate follow up or discharge planning
- Side effects
- Patient lack of belief in treatment
- Poor provider-patient relationship
- Barriers to care or medications
- Missed appointments
- Complexity of treatment
- Cost of medication, copayments

Medication adherence across disease states
- It's important in every disease state....
- Remember previous medication adherence history impacts adherence to oral chemotherapy

Diabetes
Asthma
CAD / CHF
Hypertension
HIV / AIDS

HIV experience with adherence research

Why look at HIV adherence research?
A significant amount of research has been conducted
- Adherence is strongly related to the degree and durability of viral suppression
- Adherence is associated with decreased rates of progression, hospitalization, and mortality
- Poor adherence correlates with treatment failure and can limit options for future treatment due to cross-resistance
- Viral load can be assessed as a marker for adherence
Similar to oral cancer treatment in many ways
- Complex regimens
- Multiple side effects
- High degree of toxicity
- High pill burden

Barriers to adherence in patients with HIV

Sample: 110 men and women from 4 US cities
Results:
- Numerous factors and multiple types of factors that seemed to effect adherence
- Many issues affected their medication adherence
- Adherence was described as a dynamic phenomenon that changed over time, with changing beliefs, attitudes, emotions, and daily events as well as larger life experiences

Major themes identified
- Belief and trust in treatment and health care providers
- Experiences of side effects and concerns about toxicity
- Self monitoring and taking person control
- Regimen demands and planning
- Priorities, competing concerns and mood states
- Social support
- Future orientation
HIV Patient support & education interventions

Factors that were associated with improved adherence

- Individual interventions
- Interventions that were longer in length
- Interventions that targeted practical medication management skills compared to those that targeted cognitive behavioral or motivational approaches

(Rueda et al, 2010)

HIV Patient support & education interventions

Gross et al, 2013 studied Managed Problem Solving (MAPS) vs usual care

- MAPS – four in person and 12 weekly meetings over 3 months followed by monthly phone calls for 8 months
- The odds of being in a higher adherence category was 1.78 times greater for patients who received MAPS than usual care
- The odds of having an undetectable HIV RNA level were 1.48 times greater for patients who received MAPS than usual care
- These results were sustained throughout the intervention (12 months)
- Involved minimal interaction with health care professionals

Nurse counseling intervention

- Telephone counseling was given by a trained nurse to 98 participants
  - Patients received telephone counseling (median of 3 sessions)
  - Nurses assessed readiness for adherence, provided support to overcome barriers, and offered information based on participants questions
- Results
  - Counseling was associated with a high percentage of participants reaching target adherence levels

(Cook et al, 2010)

Mobile phone & text messaging interventions

2 studies from Kenya showed promise for text messaging interventions

- Lester, 2010 – patients were randomly assigned to receive a brief text message weekly vs standard care
  - Patients who received the text message had a lower risk of nonadherence and a lower risk of virologic failure
- Pop-Eleches, 2011 – patients were randomly assigned to short or long text messages either daily or weekly vs standard care
  - Patients who received any message had higher adherence although weekly messages were more effective

What can we learn from the HIV adherence work?

- Interventions providing education and support can be effective
- Technology can help to improve adherence and does not need to be frequent

We still need to know:

- Does the effects of the intervention remain after it is completed?
- Is support and education required continuously or are there time when support is more necessary?
Rethink our practice patterns

What are current practices in the US regarding care and safety of patients on oral cancer treatment?

— Survey of 577 oncology nurses

- 51% of nurses had specific policies, procedures and resources for patients on oral chemotherapy
- Barriers included cost (81%) and adverse effects (27%)
- Many practices had erratic procedures and inadequate communication

Implications

— Nurses should provide thorough education and repeated teaching to improve patient safety, adherence, and self-monitoring for adverse effects

Nursing role

Qualitative study of 18 oncology nurses

“The need for a nursing presence” during oral chemotherapy treatment

4 themes emerged

- Patient isolation in current practice
- Involvement in entry
- Proactive patient care
- Coordination

Proactive care leads to predictive care (prevention)

Involvement from the beginning....

- Nurses should be involved early

- Nurses are more likely to consider the family/living situation more than other healthcare professionals

Proactive patient care

- Need to connect with the patient and family

- Develop a trustful relationship

Coordination

- Nursing coordination during treatment

- Follow up

- Coordinate interpersonal communication among health care providers

Nursing process and adherence

Assessment

— Assess adherence at every visit

Planning

— Assessment challenges make planning difficult

Intervention

— Can be costly and time consuming

— Incorporate small changes into your practice

Evaluation

— Is the plan working for this patient?
**Education**

**Traditional counseling**
- Healthcare provider is the expert
- Assumes patient lacks knowledge
- Tells patient what to do
- Hopes patients follow directions
- Goal is to motivate the patient
- HCP persuades the patient to change behavior
- HCP expects respect from the patient

**Motivational interviewing**
- HCP develops a partnership with the patient
- Exchanges information to facilitate an informed decision
- Patient has the right to decide own care
- HCP and patient negotiate behavior and reach agreement
- Goal is to access motivation and elicit patients’ commitment to change behavior
- HCP understands and accepts patients’ action
- HCP must earn respect from patient

**Patient perceptions of education**
- Women with breast cancer on hormonal agents
- Reasons for nonadherence
  - Side effects (63.8%)
  - Cost (20.8%)
  - Forgets (7.5%)
- Factors that would improve adherence
  - Knowing it would improve outcome
  - Better management of side effects
  - Reminded of the reasons to take medications as directed
  - Asking at every visit

**Education**

S – simplify the regimen
I – impart knowledge
M – modify patient beliefs and behavior
P – provide communication and trust
L – leave the bias
E – evaluate adherence

**Education**

**Who and when?**
- All patients on oral agents should see a nurse at start of treatment and in follow-up
- MD and pharmacist should be involved
- Building trust helps patients to be honest about missed or late doses
- Caregiver should be included (for ALL patients)
- Education should be ongoing and in multiple forms

**Where?**
- On going – in person and over the phone

**What?**
- Patients should know name (generic and brand), dose and schedule, how it’s taken (food, time), safety, side effects/therapy management.

**Education**

**Sommers et al, 2012**
- Feasibility pilot of a face to face educational intervention, medication diary and nurse-initiated telephone call to support patients’ adherence and knowledge of oral chemotherapy
- 30 patients with gastrointestinal cancer
  - Patients demonstrated high adherence scores
  - The intervention was feasible and the scale used to measure adherence was easy to administer

**Interventions**

**Communication strategies**
- Ask the patient how they remember to take their medications
  - Avoid closed ended questions
  - “Do you have a way to remember to take your oral chemotherapy?”
  - “Everyone forgets to take their medication from time to time. When was the last time you forgot to take any of your medication?”
- If you know what the pill looks like, let them know
Interventions

- Reminder triggers
  - Pill diaries, pill boxes, calendar or spreadsheet, checklist
  - Postcard reminder for refills
  - Blister packs
  - Cell phones, alarms – message texting when doses are due
- Teach back
  - “I want to be sure that I explained your medication correctly. Can you tell me how you are going to take this medicine?”
  - “We covered a lot today about your treatment, and I want to make sure that I explained things clearly. So let’s review what we discussed. What are three strategies that will help you take your chemo correctly?”
  - “What are you going to do when you get home?”

Automated voice response system

- 30 patients with solid tumors
- Received a Symptom Management Toolkit and weekly automated voice response calls
- If patients reported adherence less than 100% or symptoms of 4 or greater (on 0-10 scale) received a call from a nurse

Outcomes:

- 23.3% nonadherence rate (most common reason – forgetfulness)
- An association between symptom management and adherence was found
- Nurses should ask patients how they are taking their medications at each visit
  - “Similar to smoking cessation, just asking will improve the outcome

(Decker et al, Cancer Nursing 2009)

Case study

Carla, a 67 year old woman, has been treated for colorectal cancer. She had a good response to first line therapy. After 5 years a routine CT found a local recurrence and liver metastasis. She was started on capecitabine, 2500mg/day (1500/1000). She also has diabetes, HTN, sleep problems and vision loss. She is on 5 other medications daily. She lives with her husband and grandchildren (6 and 8 years old).

- What should the nurse include in her teaching?
- What specific strategies would help Carla?

Karin is a 49 year old female who was diagnosed with HER-2 positive breast cancer 8 months ago. She had a lumpectomy followed by adjuvant chemotherapy followed by radiation. She is then started on Herceptin.

She is a lawyer and lives with her husband and teenage son. She has a busy work schedule and takes no other medications. She has never eaten breakfast and is often at work by 8am and not home until 6 or 7pm.

On follow up she is found to have liver metastasis and is started on capecitabine and lapatinib. Her capecitabine is 4 pills in the am and 3 in the pm for 14 days on/7 days off. She is to take 5 lapatinib pills daily for 21 days.

- What factors about Karin and her treatment stand out?
- What strategies should the nurse consider when educating Karin about her treatment?

Summary

- Educational interventions show promise to increase adherence
- Technological based interventions also show promise to increase adherence
- Additional research (high quality RCT) are needed
- Nurses, in collaboration with other health care professionals, play a vital role in developing and implementing studies aimed at improving adherence

- Oral therapy for cancer treatment is here to stay and only going to increase as additional agents are developed
- Our practice settings need to change to accommodate a new treatment paradigm
- Nurses are the best advocates for patients on oral treatment regimens
- They can educate, manage symptoms, improve patient quality of life and help patients to stay on treatment
- We should have a significant presence in planning for patient care, research and guidelines related to oral cancer treatment
Intervention tools for adherence to oral cancer treatment

ONS adherence toolkit (https://www.ons.org/sites/default/files/oral%20adherence%20toolkit.pdf)

- 12 tools for nurses
- Provides strategies and resources that nurses can use to facilitate adherence among patients with cancer related to:
  - Safety concerns: drug-drug and food-drug interactions, adverse effects
  - Pharmacy and reimbursement/financial resources
  - Monitoring of adherence
  - Motivational interviewing and counseling
  - Change theory and helping patients to change nonadherence into adherence.

MASCC teaching tool (www.mascc.org)

- Developed in response to a nurse from Turkey who completed a study that showed nurses were lacking teaching tools and guidelines for oral cancer treatment.
- This teaching tool has been prepared to assist health care providers in the assessment and education of patients receiving oral agents as treatment for their cancer.
- The goal is to ensure that patients know and understand their treatment and the importance of taking the pills/tablets are prescribed.

**Key Assessment Questions**

1) What have you been told about this treatment plan with oral medications? *Verify that the patient knows that these oral agents are for cancer and are taken by mouth for their cancer.*

2) What other medications or pills do you take by mouth? *If you have a list of medicines, go over the list with the patient.*

3) Are you able to swallow pills or tablets? If no, explain.

4) Are you able to read the drug label/information?

5) Are you able to open your other medicine bottles or packages?
6) Have you taken other pills for your cancer?  * Find out if there were any problems, for example, taking the medications or any adverse drug effects.

7) Are you experiencing any symptoms that would affect your ability to keep down the pills, for example nausea or vomiting?

8) How will you fill your prescription?  * Delays in obtaining the pills may affect when the oral drugs are started

9) Have you had any problems with your insurance that has interfered with obtaining your medications?

* Recommended information to assess is noted in italics

Special Considerations when assessing patients receiving oral agents for cancer:

When teaching the patient, you may need to adapt your teaching to accommodate special considerations such as, age, feeding tube, vision problems/color blindness, dietary issues, mental problems (dementia, depression, cognitive impairments).