



Review Article

Interventions for adherence with oral chemotherapy in hematological malignancies: A systematic review

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Abstract

Background: Poor adherence to treatment for chronic diseases including some hematological malignancies impedes health outcomes and increases costs. Oral chemotherapy is an emerging trend that raises concern about nonadherence problems in these targeted patients.

Objectives: This systematic literature review explores evidence and gaps in the literature regarding interventions to enhance adherence with prescribed oral chemotherapy in patients with hematological malignancies.

Methods: Searches of databases and abstracts from conferences were performed for 1987 to January 2013 using a modified Cochrane method. Studies measuring interventions to improve adherence alone or together with clinical, humanistic, and economic outcomes were included. Assessment of methodological quality was performed for each retained study.

Results: The literature search generated 6 studies that met inclusion criteria. Four of these reported a statistically significant increase in the adherence outcome, compared with baseline. Tailored and educational interventions were widely used among the retained studies. Post-intervention adherence rates were 41–96.1%; intervention groups yielded higher rates than comparison groups. Two studies reported statistically significant improvement in clinical outcomes (cytogenetic response and survival time). One study reported that severity of illness was associated with survival time but not with adherence. Studies that used both tailored and educational interventions showed significant relationship between adherence and clinical outcomes; however, the study that used dosage simplification did not. None of the studies explored humanistic or economic outcomes.

Conclusions: Interventions to improve adherence with oral chemotherapies in hematological malignancies remain limited. Though they were heterogeneous in nature, interventions tested in the retained studies suggested a positive impact on the adherence outcome; some established a significant relationship between adherence and clinical outcomes. The results yielded limited evidences regarding characteristics of a specific intervention, but supported a general structure for methods to improve adherence and other outcomes in real-life settings. Further rigorous methodological studies are needed to fully examine impact on adherence and clinical outcomes.

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Keywords: Oral chemotherapy; Hematological malignancies; Adherence; Intervention(s); Outcome(s)

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Introduction

An estimated incidence of 140,310 new cases of hematological malignancies, including leukemia, lymphoma, or myeloma were diagnosed in the United States in 2011.¹ Moreover, approximately 1,012,533 Americans are living with leukemia, Hodgkin's and non-Hodgkin's lymphoma, and myeloma.² According to the American Cancer Society, for 2012, non-Hodgkin's lymphoma and leukemia are among the 10 leading causes of cancer death in both men and women.³

Treatment decisions for these conditions include a choice between oral and intravenous administration and rely upon several factors such as the oncologist's decision, patient preference, and/or insurance eligibility, a paradigm shift in oncology considers some cancers as chronic diseases requiring chronic therapy; this has resulted in greater use of oral agents.^{4–7} It is estimated that more than 100 of the 400 anti-cancer drugs now in the development pipeline are planned as oral agents⁷; the nature of these cancers is such that chemotherapy is a primary treatment option and there are no surgical options as with solid tumor cancers, making adherence even more important. This emerging trend of targeted therapy administered orally is considered to have less myelosuppressive toxicity than classic chemotherapy. As a consequence, the perceived advantage and convenience of oral chemotherapy encourages oncologists to use this option as a monotherapy or in combination with other classic chemotherapy regimens for treatment, or for maintenance therapy after organ transplantation or cancer remission. It is unclear whether patients maintain the desired adherence level with oral agents when taking them on their own at home.^{7–11}

The World Health Organization has defined adherence with long-term therapy as “the extent to which a person's behavior -taking medication, following a diet, and or executing lifestyle changes, corresponds with agreed recommendations” and suggests that the health outcomes and economics may be more influenced by enhancing adherence than advancing medical therapies.^{12,13} Unfortunately, adherence to chronic medication therapy in ambulatory care is typically not as high as in the clinical setting.^{6–9,12–14} This is because an oral mode requires patients and caregivers to be more responsible for self-management, including adherence to complicated dosage administration and monitoring of side effects instead of the handling of intravenous

regimens by a health care provider in the hospital. It is suggested that an oral formulation might be successful in well-motivated and high literacy patients.^{6,7,15–17}

Nonadherence or poor adherence with oral therapies results in unsatisfactory consequences. It is an important factor that compromises treatment outcomes that are typically monitored in patients with hematological malignancies, including clinical outcomes like cytogenetic response, pharmacologic response, and pharmacokinetic response, adverse physical effects, and survival time. Nonadherence is also associated with lower rates of disease-free survival and can result in biased assessment of the efficacy of treatment because practitioners might not be able to determine whether the patient actually relapsed or if refractory disease resulted from chemotherapy resistance or from nonadherence. In 2010, Marin and colleagues revealed that adherence was the only independent predictor for achieving complete and major molecular response in patients with chronic myeloid leukemia with stable cytogenetic response. Additionally, poor adherence appears to be the only independent predictor for inability to achieve sustained molecular response.¹⁸ In particular, the degree of achieved complete molecular response is associated with improved duration of complete cytogenetic response which eventually leads to favorable prognosis and prolonged survival. Furthermore, nonadherence can prolong the duration and complexity of treatment regimens, can result in the development of drug resistance or toxicities, and can be costly from an economic sense.^{6,7,13,19} Typically, rates of adherence to and persistence with oral antineoplastic drugs are estimated to range from 16% to 100%.⁶ Interestingly, research has shown that full 100% adherence is rare in patients with chronic myeloid leukemia (CML) and more than one-third of patients are nonadherent.²⁰ However, little is known about the effect of nonadherence with oral antineoplastic agents in hematological malignancies; most studies of adherence in this field have been conducted with oral anti-cancer regimens for solid tumors.^{6–8,21,22} Additionally, there has been no gold standard measure of adherence, self-report or otherwise.

Aim of the review

The aim of this review is to summarize the existing research literature and to identify

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