

Futile medication use in terminally ill cancer patients

Rachel P. Riechelmann · Monika K. Krzyzanowska ·
Camilla Zimmermann

Received: 2 September 2008 / Accepted: 7 November 2008 / Published online: 22 November 2008
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Abstract

Background Cancer patients usually take many medications. The proportion of patients with advanced cancer who are taking futile drugs is unknown.

Materials and methods We retrospectively reviewed the charts of all consecutive ambulatory patients with advanced cancer and who were receiving supportive care exclusively at palliative care clinics, Princess Margaret Hospital, to gather information on futile medications used by them. Futile medications were defined as unnecessary (when no short-term benefit to patients with respect to survival, quality of life, or symptom control was anticipated) or duplicate (two or more drugs from the same pharmacological class). Summary statistics were used to describe the results.

Results From November 2005 to July 2006, 82 (22%) of 372 patients were taking at least one futile medication

before consultation; after initial consultation, this proportion dropped to 20% (78): 70 patients were taking unnecessary medications, while eight were on duplicate medications. The most frequent unnecessary medications used by patients were statins (56%). The most common duplicate medication involved the use of two different benzodiazepines (seven patients).

Conclusion About one fifth of cancer outpatients at the end of life take futile medications, most commonly statins. Prospective and population-based studies are warranted to further evaluate the magnitude and consequences of futile medication use in oncology.

Keywords Cancer · Drug therapy · Medical futility

Introduction

Medical futility has been defined as “an intervention that no longer provides patient benefit, does not achieve a valuable goal, has a potential for harm and lacks benefits to justify resources” [1], but this definition remains conditional on treatment aims, patient and family desires, and ethical issues [2, 3]. Cardiopulmonary resuscitation and mechanical ventilation are examples of futile interventions that have been reported in terminally ill general medicine patients [4–6]. Studies of terminally ill patients with cancer have shown that end-of-life decision-making is ethically challenging [3, 7, 8], with patients commonly exposed to futile interventions [9–11]. A study of acutely ill cancer patients admitted to a palliative care unit found that 26 out of 106 consecutive patients were taking futile or inappropriate drugs, most commonly cardiovascular agents [12]. However, the proportion of ambulatory patients with advanced cancer (which comprise the majority of cancer

The authors have no financial conflicts to declare.

R. P. Riechelmann (✉)
Department of Internal Medicine,
Federal University of Sao Paulo,
R: Luisiania 255, Apt 11,
São Paulo, SP 04560-020, Brazil
e-mail: rachelri@terra.com.br

M. K. Krzyzanowska
Department of Medical Oncology, Princess Margaret Hospital,
610 University Avenue,
Toronto, ON, Canada
e-mail: monika.krzyzanowska@uhn.on.ca

C. Zimmermann
Psychosocial Oncology and Palliative Care,
Princess Margaret Hospital,
610 University Ave,
Toronto, ON, Canada
e-mail: Camilla.zimmermann@uhn.on.ca

patients) who take unnecessary medications is unknown and is the focus of this report.

Materials and methods

We conducted a retrospective analysis of medication profiles [13] and potential drug interactions [14] among 372 consecutive adult patients with advanced/incurable solid or hematological malignancies attending palliative clinics at the Princess Margaret Hospital (PMH) in Toronto between November 2005 and July 2006. Patients still receiving cancer-directed therapy were excluded. Data on patient demographics, cancer type, comorbidities, and medications were gathered from the chart, specifically from the first palliative care consultation. At PMH, patients are referred by medical and radiation oncologists to palliative care clinics for symptom management and/or for end-of-life planning [15]; the median survival of patients seen by our palliative care service is approximately 2 months (including those patients still receiving cancer-directed treatment; range 2 days to 3.5 years) [16]. Following the first consultation, the palliative care physician dictates a comprehensive medical history [13], including information on medications which is systematically collected by a specialized nurse.

For the purpose of this study, the medication profile of each patient was reviewed to determine whether any of the drugs being taken was futile. To classify a drug as futile, we considered the usefulness of each drug to treat a comorbid illness or a self-reported symptom and defined a futile medication as unnecessary or duplicate. An unnecessary medication was an agent that did not result in significant patient benefit in terms of symptom control or survival; had no scientific evidence for the purpose of its use (e.g., unproven alternative compounds); or had a goal of therapy that was expected to take place only with long-term chronic use (e.g., statins to treat hypercholesterolemia). We also took into account that the discontinuation of drugs classified as futile was not expected to cause adverse outcomes in the short-term (6 months). Drugs prescribed by physicians as well as those self-used by patients (over-the-counter drugs) were considered for this study; we did not gather information on herbal compounds or complementary therapies.

Antihypertensive and hypoglycemic agents were not considered unnecessary if they were continued by the palliative care physician, since we were not able to reliably determine retrospectively blood pressure and serum glucose level. We also did not consider medications added by the palliative care physicians to be futile because they were exclusively prescribed to treat cancer-related symptoms. Duplicate medication use was considered to be present

when two or more drugs from the same pharmacological class were being taken by a patient. The evaluation of appropriateness of drug dosage, frequency, schedule, and duration of therapy were beyond the scope of this study. Summary statistics were used to describe the results.

Results

Characteristics of the cohort have been described previously [13]: the median age was 66 years (range 22–94 years), 49% were female, and gastrointestinal tumors were most common. The most common pharmacological classes of medication used by patients were opioids (67% of patients), laxatives/stool softeners (54%), acetaminophen (40%), and corticosteroids (38%). More than half of the patients were taking at least six medications each (range 0–21). Cardiovascular diseases (36% of patients), diabetes (14%), musculoskeletal disorders (11%), respiratory diseases, and thromboembolism (10% each) were the most frequent comorbidities.

Among the 372 patients, 82 (22%) were using at least one futile medication; of these, 90% were unnecessary medications and 10% involved duplicate medications (Table 1). Among the futile medications ($N=85$), most involved the use of statins (56%) and multivitamins (30%). Four patients (5%) with hematological malignancy and no history of hyperuricemia, gout, or current leukocytosis were taking allopurinol; folic acid was used by two patients and ferrous gluconate by three patients without history of folic

Table 1 Futile medications used by patients

Characteristic	Number (percent)
Number of patients taking futile medications	82 (22)
Type of futile medication	
All	82 (100)
Unnecessary	74 (90)
Duplicate	8 (10)
Unnecessary medications taken by patients before palliative care consultation	
All ^a	85 (100)
Statins	48 (56)
Allopurinol	4 (5)
Multivitamins	25 (30)
Other	8 (9)
Duplicate medications	
All	8 (100)
Benzodiazepines	7 (88)
Nonsteroidal anti-inflammatory drugs	1 (12)

^a The total number of futile medications is 85 because, among the 82 patients taking futile medications, three patients were using two futile medications

acid or iron deficiency anemia, respectively; and fenofibrate in one patient with hypercholesterolemia. Multivitamins, folate, and iron likely reflect over-the-counter use. Eight patients were exposed to duplicate medications: seven patients were taking two different benzodiazepines and one patient was taking two different nonsteroidal anti-inflammatory drugs. After being assessed by the palliative care team, 78 (20%) of patients continued on at least one futile drug; statins were discontinued in four patients. None of the duplicate medications were discontinued.

Discussion

This retrospective analysis suggests that about one fifth of cancer outpatients at the end of life take futile medications, most commonly statins. Previous studies have shown that many cancer patients continue to receive aggressive interventions, including chemotherapy, sometimes days before their death [9, 10]. While physicians may consider many therapeutic interventions futile, it is not unusual for caregivers to request that “everything be done” [7]. A prospective study of severely ill cancer patients admitted to a palliative care unit showed that approximately one quarter were taking unnecessary or inappropriate drugs [12]. However, the authors did not specify which drugs were considered futile (unnecessary) or inappropriate (a drug used with a wrong purpose or schedule, or expected to cause adverse outcomes). Also, the population was composed of dying cancer inpatients, as opposed to ambulatory patients with advanced cancer and limited life expectancy who were the focus of our report.

Patients with terminal cancer often take numerous medications to treat comorbid illnesses and cancer-related symptoms [13]. A recent study showed that the number of medications prescribed to cancer patients increases as death approaches with the number of drugs to treat comorbid conditions decreasing and the number of supportive care agents increasing [17]. This is particularly important in view of the potential clinical consequences of polypharmacy, which has been associated with increased risk of adverse drug events [18], including drug interactions [14, 19]. We found that statins were commonly used by terminally ill cancer patients. However, it is unlikely that a decrease in serum cholesterol levels would impact on the survival of cancer patients with a limited life expectancy. Moreover, although statins usually have a good safety profile, they may interact with other drugs, are expensive, and can result in rare but serious side effects such as hepatitis and rhabdomyolysis [20]. A systematic review on the use of lipid-lowering drugs by noncancer patients at the end of life discussed the burden of long-term use of statins to patients and the complexities of discontinuing medica-

tions that do not necessarily impact on patient quality of life or survival [21]. Although multivitamins usually do not cause adverse clinical consequences, they may interact with other drugs [22] and can be costly; these likely reflect patient self-prescription.

It is not clear why one fifth of our patients were taking futile drugs nor why there was so little change in the use of futile and duplicate medications before and after the initial palliative care consultation. Studies have shown that physicians overestimate the survival of cancer patients by up to 40% [23]; therefore, it is possible that they continue to prescribe futile medications because of overestimation of prognosis. Also, physicians may hesitate to compromise patient hope by discontinuing a drug for which clinical benefits are expected only with long-term use. This may be the case for the continuation of these drugs by palliative care physicians after the initial consultation, as they might fear compromising the newly developing patient–physician relationship. Other potential reasons include lack of medication reconciliation, patient requests, lack of medical knowledge, the reasonably good safety profile of drugs such as statins [21], physician and patient belief in the potential benefits and lack of harm of the futile drugs, and recommendations from other medical specialists. With respect to multivitamins, doctors may feel that such compounds would neither help nor harm their patients; patients, in contrast, often have faith in the benefits of alternative medicines [24, 25]. These issues underline the need for improvement in communication both between physicians and patients [26] and among health care professionals.

This report was limited in that it was a single-institution study with retrospective data collection. Given that we did not assess patients prospectively, and thus could not evaluate the need for each drug based on patient clinical condition, we may have misclassified unnecessary medications as *not* futile, thereby underestimating the proportion of patients taking futile medications. Over-the-counter medications may not have been mentioned by the patient at the initial palliative care consultation, and our estimate of such medications, including multivitamins, may, therefore, be particularly underestimated. Also, we could not estimate the severity of patients’ comorbidity in order to evaluate the true need for pharmacological therapy, nor could we evaluate why physicians in this sample chose to continue or discontinue a given drug. Lastly, it was not possible to evaluate whether patients taking futile medications experienced adverse clinical outcomes. The inappropriate continuation of antihypertensives or hypoglycemic agents is particularly important in this regard and needs to be assessed in future prospective studies.

The use of medications which are futile in patients with terminal cancer can lead to adverse drug events, which may

compromise treatment efficacy and patient quality of life, or be misinterpreted as cancer progression. In addition, it is wasteful of resources for patients and/or third party payers. Continuous reassessment of patients' medication lists is a logical first step to prevent the continued use of medications that have become futile due to the patient's advanced illness. Improved communication among health professionals and between patients and their physicians could increase understanding of why patients are taking a given drug, how long it has been taken, who prescribed it, and for which purpose.

In summary, the present retrospective report showed that about one fifth of cancer patients at the end of life use medications that lack benefit in the short-term. Prospective studies in the community setting and population-based analyses are warranted to evaluate the clinical and economic impact of futile medication use in oncology practice.

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