Cancer Chemotherapy in Older Adults
A Tolerability Perspective

Gretchen G. Kimmick,1 Ronald Fleming,¹ Hyman B. Muss¹ and Lodovico Balducci²

1 Comprehensive Cancer Center of Wake Forest University, Winston-Salem, North Carolina, USA
2 H. Lee Moffitt Cancer Center and Research Institute, University of South Florida, Tampa, Florida, USA

Contents

Summary .................................................................................................................. 34
1. Specific Issues in Treating the Older Cancer Patient ........................................... 35
   1.1 Comorbidity ................................................................................................. 35
   1.2 Drug Interactions ......................................................................................... 35
   1.3 Psychosocial Issues ...................................................................................... 36
   1.4 Age-Related Physiological Changes ............................................................ 36
2. Age and Pharmacodynamics of Anticancer Agents ........................................... 39
3. Common Antineoplastic-Related Toxicities and Possible Solutions ................. 40
   3.1 Myelotoxicity ............................................................................................... 40
   3.2 Gastrointestinal Toxicity ............................................................................ 40
   3.3 Cardiotoxicity ............................................................................................ 41
   3.4 Pulmonary Toxicity .................................................................................... 43
   3.5 Nephrotoxicity ........................................................................................... 44
   3.6 Neurotoxicity .............................................................................................. 45
4. Conclusions ....................................................................................................... 47

Summary

The incidence of cancer increases with age. Since the geriatric population is growing, we will be confronted with an increasing number of patients with cancer who are >65 years of age. The purpose of this review is to address the use of cancer chemotherapy in older persons with respect to its tolerability.

We performed a review of the literature using 'Medline' and the bibliographies of pertinent publications. Information about cancer treatment in older adults was extracted with particular attention to chemotherapy-related toxicity in patients aged >65 years. Comorbid disease, polypharmacy/drug interactions, psychosocial issues and age-related physiological changes are major issues in caring for older patients with cancer. Since older individuals may have a greater number of comorbid illnesses, treatment should be initiated on the basis of physiological rather than chronological age.

Comparative studies show that chemotherapy-related toxicity is similar in older and younger patients, with the exception of haematological toxicity, which may be more severe in older patients, and cardiotoxicity, which is more frequent in the elderly. Other evidence suggests that gastrointestinal and neurotoxicities may also be more severe in older individuals. The dosages of chemotherapeutic agents that are primarily renally excreted may require adjustment in older patients.
Haematological reserve is decreased in older individuals, and drugs that cause myelosuppression must be used with care. The use of haemopoietic growth factors in geriatric patients is currently being investigated.

Cancer and its treatment are major issues in the geriatric population, because the incidence of cancer increases with age and because the elderly population is growing. We need to familiarise ourselves with issues in geriatric medicine, such as normal age-related changes in human physiology, comorbidity, and psychosocial conditions that make medical care of the older individual unique.

Older adults, defined here as people aged >65 years, are traditionally treated with lower dosages of antineoplastic agents than younger patients for fear of causing excessive toxicity. However, studies have shown that generally healthy older patients, who may otherwise live 5 or more years, obtain similar benefits from standard antineoplastic regimens to their younger counterparts, with few exceptions. This article addresses the use of antineoplastic therapy in older adults with respect to its tolerability, based on a review of the literature. Where appropriate, preventive measures and methods of ameliorating toxicities are suggested.

1. Specific Issues in Treating the Older Cancer Patient

There are 4 major issues in caring for older patients with cancer: (i) comorbidity; (ii) drug interactions; (iii) psychosocial issues; and (iv) age-related physiological changes.

1.1 Comorbidity

The incidence of chronic disease increases with age. Almost 80% of people aged >65 years have at least 1 chronic disease, and approximately one-third will have 3 or more. Comorbid illnesses influence the choice of antineoplastic therapy and the risk of treatment-related toxicities. For instance, the incidence of heart disease and congestive heart failure (CHF) increases with age. Patients with severely limited cardiac function should not be treated with anthracyclines such as doxorubicin. This is true at any age, however, and age itself should not preclude the use of antineoplastic therapy.

Comorbidity may also influence choice of therapy, because coexisting diseases correlate with increased overall mortality rates. In the study by Satariano and Ragland, comorbidity was a strong predictor of 3-year survival in women with breast cancer (a greater number of comorbid conditions correlated with poorer 3-year survival). When comparing the overall survival of young versus old patients in trials of antineoplastic therapy, survival must be adjusted for comorbidity. Clearly, the overall benefits of life-prolonging antineoplastic therapy may be lessened in the presence of shortened life expectancy.

1.2 Drug Interactions

Older people are more likely to be receiving multiple medications. These include both over-the-counter and prescription medications, which can affect first-pass hepatic metabolism, renal blood flow and/or renal tubular properties, and may alter the pharmacology of antineoplastic agents. Specific examples of this are discussed in sections 1.4 and 3.

Corcoran et al. reported that >50% of cancer patients aged ≥65 years were taking more than 5 daily medications (for indications other than cancer), and 20% of these were taking 10 medications or more (M.B. Corcoran, personal communication). In addition, a direct correlation exists between age and untoward effects of medications. Adverse drug reactions occur in 10 to 25% of hospitalised geriatric patients, and are the sole cause of hospitalisation in 10% of geriatric hospital admissions. This includes adverse reactions to antineoplastic agents, antiemetics, narcotics and analgesics, medications that are all used in cancer patients. Alertness to drug interactions and adverse effects of medications in older patients should be heightened.