E5. Symptomatic and supportive care in metastatic disease

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The incidence of breast cancer is increasing annually with a mean rate of 1–2% and it is estimated that nearly one million women will develop this disease in every year of the coming decade. Despite the effectiveness of screening programmes and the widespread use of adjuvant therapies, approximately 10% of newly diagnosed patients will present with metastatic disease, and 50–70% of the remaining women are designated to develop metastatic disease in which cure is not a realistic option and palliation of symptoms with possible prolongation of life is the goal of treatment.

Early in the course of the disease, palliative chemotherapy and radiotherapy may ameliorate tumour-related symptoms at the expense of treatment-related toxicity. The supportive care in the narrow sense (the management of the toxic effects of antineoplastic drugs) which is extremely important during this phase has developed vastly in the past 15 years. The introduction of 5-HT3 antagonists and steroids into anti-emetic therapy resulted in much better control of vomiting in patients receiving highly emetogenic, platinum or anthracycline-based therapy. Complete control of vomiting could be achieved in up to 90% of these patients [1]. Despite the efficacy of 5-HT3 antagonists, nausea and delayed emesis still remains a clinical problem. The introduction of corticosteroids in the treatment of delayed emesis seems promising. In addition, a new generation of anti-emetics, neurokinin1 (NK1) antagonists, are expected to further improve the control of acute and delayed emesis [1]. Unfortunately, anti-emetic therapy is far from optimal in clinical practice and the use of precise clinical guidelines should be enforced widely [2]. The rate of significant complications related to neutropenias is low in breast cancer patients treated with cyclophosphamide, methotrexate, 5-fluorouracil (CMF) and/or anthracycline-based therapy, but much higher rates can be expected in patients treated with taxanes and in pre-treated patients. In these special circumstances, selected use of granulocyte colony-stimulating factors could protect patients from serious infections and unnecessary hospitalisation [3]. The optimal use of another growth factor, erythropoetin which was found to improve both the quality of life and energy level in chemotherapy patients, still needs to be defined. The new, risk-based approach, allows an outpatient oral-based antimicrobial therapy in the majority of breast cancer patients with febrile neutropenia [4], which may have a positive impact on the quality of life.

Later in the course of disease, the number, variety and severity of symptoms related to widespread disease increases and symptom control becomes extremely important. The proper symptom management should be seen as a continuous process, from diagnosis to death, helping patients and their families to cope with the disease and treatment. The emphasis on curing cancer instead of patients resulted in the major clinical problems experienced by many patients being ignored for many years. According to the results of two studies, performed in the early 1990s, the most frequently observed symptoms in patients with advanced cancer are pain, easy fatigue, weakness, anorexia, weight loss, lack of energy, dry mouth, constipation, dyspnoea and early satiety [5,6]. The prevalence of these symptoms ranged from 50% to 84%, every patient experiencing 11 symptoms on average. Most symptoms were moderate or severe in intensity and varied with age, sex, primary tumour and extent of disease.

The main symptoms experienced by advanced breast cancer patients are pain, fatigue, anorexia and weight loss, nausea, early satiety, dyspnoea and delirium. New long-acting opioids together with transdermal and transbuccal formulation of these drugs provide the possibility of an adequate pain relief for the majority of patients, at their home. Due to the fear of addiction, tolerance and side-effects of these drugs, many patients do not use them as prescribed. These effects can be countered by improving the control of side-effects, opioid rotation and patient awareness. In addition to analgesics, bisphosphonates were found to reduce significantly the pain and skeletal complications in metastatic breast cancer [7]. The anorexia, cachexia syndrome has undergone some investigation in recent years. There is good evidence that megestrol acetate is an effective agent for reversing this symptom [8], alternatives being corticosteroids and tetrahydrocannabinol. Metoclopramide should always be used as a first-line drug for patients with early satiety, which is a common symptom in advanced breast cancer. Fatigue occurs in more than half of cancer patients who are not receiving antineoplastic therapy and is severe in almost 20% of breast cancer patients [9]. Any underlying causes should be identified and corrected, if possible. In addition, non-pharmacological measures such as structured aerobic exercise and energy conservation activities should be encouraged.

Dyspnoea is a common symptom, especially for patients with lung metastases. However, it can also be seen in a substantial proportion of patients without lung involvement thus pointing to the multidimensional nature of this symptom. Management should be directed at both the possible underlying cause and the symptom. Corticosteroids may be useful for managing dyspnoea related to lymphangiocarcinomatosis. Systemic opioids are undoubtely beneficial for these patients, but the role of oxygen is less clear [10]. Cold air directed across the cheek and positive communication with the patient and relatives also go a long way. A highly prevalent symptom is delirium. Attempts to identify and reverse possible underlying causes like drugs, brain metastases, hypoxia, metabolic disturbances and infection should be made. However, in the terminal phase of the disease, the underlying aetiologies of delirium are diverse and may not be easily identifiable. The proper symptomatic therapy with neuroleptics offers patients and their families substantial relief from suffering.

There are some principles of symptom control that should be followed. Treating all symptoms rather than just focusing on one is important. Polypharmacy should be avoided and the skilled use of a small number of drugs, rather then randomly prescribing different agents, can help control many symptoms and prevent much unnecessary suffering. Whenever possible, drugs should be given by mouth. The drugs should be given regularly, the concept of titrated dosing and rescue dose, learned from analgesics, is essential. For proper palliation of symptoms, their regular assessment is necessary. The use of different assessment tools in routine clinical practice should be facilitated by the development of more comprehensive and practical instruments. Symptom assessment should be done by the patient regardless of the high prevalence of cognitive impairment and fatigue. The best tool is still dialogue with the patient.

It is important to realise that the treatment of metastatic disease should always be patient- and not tumour-oriented. The proper supportive and symptomatic care, encompassing disease-modifying therapies, surgical and physical procedures, pharmacological palliation and psychological and nursing interventions, helps the patients to gain not only quantity, but also quality of life.

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