The importance of supportive care for patients with cancer

Supportive care encompasses managing symptoms and side effects before, during and after cancer treatment

Supportive care involves the management of the symptoms of cancer and the side effects of treatment across the whole course of cancer, from diagnosis through treatment to survivorship and end-of-life care. Cancer requires multimodality treatment, including chemotherapy, immunotherapy, radiotherapy and surgery, each of which can be used to palliate symptoms but may also have adverse effects that need managing. Likewise, supportive care needs multidisciplinary team support, including cancer specialist clinicians, nurses, pharmacists and allied health practitioners in addition to palliative care practitioners.

Breakthroughs in cancer treatment are widely heralded but less prominence is given to the significant advances made in supportive care. With a strapline of "supportive care makes excellent cancer care possible", the Multinational Association of Supportive Care in Cancer (MASCC) will celebrate 25 years of promoting these advances at its scientific meeting in Adelaide in June 2016. Good supportive care enables the delivery of optimal therapy and improves a patient's quality of life. Where has the most progress been made?

Broadening the spectrum of treatable side effects

Febrile neutropenia can be a life-threatening side effect of chemotherapy if patients develop a bacterial infection when their neutrophil levels are low. This usually occurs at mid-cycle, 10–15 days after chemotherapy. On recovery, subsequent chemotherapy doses could be reduced; however, this would diminish their efficacy when given with curative intent. The advent of the use of granulocyte colony-stimulating factor, longer-acting formulations and recombinant stem cell factor, given with chemotherapy, has significantly decreased the severity and duration of neutropenia, thereby reducing the chance of infection or hastening recovery.[1] With this strategy, the dose intensity of chemotherapy can be maintained.

A side effect that may have a profound impact on the quality of life of a patient being treated for cancer is nausea and vomiting. The introduction of cisplatin was associated with severe nausea and vomiting which responds poorly to standard antiemetics such as metoclopramide. The vomiting was controlled by the discovery of new antiemetic drug classes. The 5-hydroxytryptamine 3 receptor antagonists (5-HT 3 RA) assist in alleviating vomiting in the first 24 hours after chemotherapy. The neurokinin 1 receptor antagonists (NK1 RA) are more effective in delayed emesis that occurs between 24 hours and 5 days following chemotherapy. When these antiemetics are combined with dexamethasone, vomiting can be controlled in up to 80% of patients.[2] Long-acting 5-HT 3 RAs are used and now long-acting NK1 RAs are being trialled, but they are yet to find their place in antiemetic combinations. The MASCC antiemetic guidelines are updated regularly to keep up with these advances.[3] A further challenge is that nausea is not as well controlled as vomiting with these newer agents. Phenothiazines (eg, chlorpromazine) and atypical antipsychotics (eg, olanzapine) that inhibit multiple receptors may be a more appropriate choice in the setting of nausea. Other investigations suggest that what is reported as nausea may be a symptom cluster where multiple symptoms may need to be treated.[4]

Pain control is one of the largest supportive care examples of disparities in cancer treatment. It is highlighted by the restricted availability of morphine in many low income countries. There are international programs such as the Global Access to Pain Relief Initiative to address this problem, but much more needs to be done. A recent finding that low dose morphine was superior to other weak opioids for moderate cancer-related pain will be helpful, given the relatively low cost of morphine.[5]

Therapy-induced mucosal injury to the gastrointestinal tract remains a problem, particularly from new targeted cancer therapies such as tyrosine kinase inhibitors and vascular endothelial growth factor receptor inhibitors. However, the lack of effective treatment has stimulated many studies of the mechanisms of mucositis and the inflammatory response to an injury and of the cytokines that mediate the response. This will direct future treatments. Guidelines for the management of oral and gastrointestinal mucosal injury help standardise practice and keep clinicians current on new initiatives.[6] Advances in enteral nutrition are also relevant to this area. The study

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of nutrition and the alleviation of cancer cachexia is a continuing field for supportive care research.

A largely non-pharmacological approach is being advocated for cancer-related fatigue, which is a lack of energy to carry out routine daily activities and is very commonly associated with both cancer and its treatment. There are many possible causes which need to be identified and corrected. Some patients may be anaemic or have hypothyroidism. Some may have nutrition issues leading to anorexia and weight loss. Others may be depressed or have difficulty sleeping. In addition, a lack of exercise has been found to contribute to this symptom, and there is increasing evidence of the impact of exercise for alleviating fatigue.

For some side effects, there is conflicting evidence over optimal management. An example is the role of morphine in dyspnoea associated with cancer. It is now apparent that the most appropriate routes of administration of morphine are oral and intravenous rather than nebulised.[7] Broader medical research is required for other toxicities. For example, the prevention and treatment of skeletal complications coincidentally paralleled research on osteoporosis and the development of bisphosphonates and a monoclonal antibody that binds to the receptor activator of nuclear factor KappaB ligand.[8] These treatments can be effectively used for patients with metastatic bone disease to decrease pain and reduce fractures. There are other side effects that emerge as prime targets for further research. A good example is the need to control the impact of treatment on the neurological system, where there is little progress in prevention and limited management options.

Psychosocial and spiritual wellbeing

In terms of the impact on patients' quality of life, the management of the psychosocial sequelae of cancer is at least as important as dealing with the physical symptoms. Moreover, these symptoms extend from diagnosis through to the survivorship phase. The issue here is not so much the treatment of symptoms such as anxiety and depression, but whether the symptoms are recognised. The challenge is to predict patients at risk and employ preventive strategies.

Aside from psychosocial distress, spiritual wellbeing has been found to have an independent impact on quality of life.[9] Spirituality is about patients seeking meaning in their experiences and trying to achieve a sense of peace; it is not just a matter of faith. However, as a MASCC survey found, even among clinicians who focus on supportive care, this area presents a challenge. It is important to patients that their treatment team recognises their existential distress.[10]

New challenges

The largest of the new challenges in supportive care comes from the transition from conventional chemotherapy, with its well known side effects, to the newer targeted therapies and a range of different toxicities. Taking the example of new immune checkpoint inhibitors, such as anti-cytotoxic T lymphocyte-associated protein and programmed death 1 (PD1) antibodies, there are a range of adverse effects including skin toxicities, gastrointestinal side effects and oral complications, as well as immune-related infections. Their mechanisms require definition and preventive or management strategies need to be developed and implemented.

"Good supportive care enables the delivery of optimal therapy and improves a patient's quality of life"

Skin toxicities associated with cytotoxic chemotherapy include extravasation injury, alopecia, photosensitivity, graft-versus-host reactions, and rarer rashes and syndromes such as hand–foot syndrome. Toxicity to nails and hair may also occur. There are more severe toxicities with targeted therapies. For example, the papulopustular reaction requires treatment in a third of patients who received epidermal growth factor receptor inhibitors (EGFRi). Guidelines were produced for the prevention and management of this type of severe skin reactions and a tool, the MASCC EGFR Inhibitor Skin Toxicity Tool (MESTT), has been developed to help record the skin adverse events associated with EGFRi therapy.[11]

Proto-oncogene *BRAF* inhibitors are associated with a spectrum of skin eruptions, including seborrhoeic dermatitis, keratosis pilaris eruptions, hyperkeratotic plantar papules similar to those seen with sorafenib (a protein tyrosine kinase inhibitor) and, perhaps strange for a drug used to treat melanoma, squamous cell skin cancers. The newer PD1 inhibitors have been associated with a maculopapular rash in up to 40% of patients and often require treatment with steroids.[12]

A new "toxicity" that has emerged with the advent of personalised medicine — the use of the molecular profile of a patient's cancer to make treatment decisions — has been called financial toxicity. The high prices of the targeted therapies and the tests to identify targets are often an unintended economic harm of therapy, and a cause of financial distress to patients and their relatives. It is important to ascertain which patients are at risk and scales have been published to assess the financial burden of cancer care based on the ability to pay, as determined by income stream and liquid assets.[13] There are other scoring systems, such as the Comprehensive Score for Financial Toxicity, that can be used to measure this toxicity of treatment to identify which patients most need support.[14] The problem that needs resolution here is determining the value of a drug, based on patient outcome, and then better aligning the cost of the drug to that value.

There are many aspects of supportive care that make a good quality of life in patients with cancer possible.

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