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Cancer pain and the importance of its control

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In 1985 there were almost 5 million deaths from cancer, and it is estimated that in 2015 there will be over 9 million, of which almost three-quarters will be in developing countries. Seventy to eighty per cent of these patients will experience moderate or severe pain at some stage of their illness and at present most of these will die in pain. This is true in spite of the fact that there is substantial evidence which shows that in as many as 80% of patients with cancer pain it is possible to obtain complete relief with orally administered analgesics, either alone or supplemented with co-analgesic (adjuvant) drugs. Management is based on the three-step analgesic ladder whereby the choice of analgesic (non-opioid, weak opioid, or strong opioid) is determined by the severity of pain. The main reasons for failure to achieve control of pain are inexperience and lack of knowledge of the simple principles of effective analgesic use, and in many countries the non-availability of strong opioid analgesics. The most important advances in management have been the simplification and refinement of analgesic treatment which have made relief of cancer pain more widely accessible to patients. The introduction of controlled-release oral formulations of morphine has had a considerable impact because they are convenient and simple to use. The recent development of a long-acting non-invasive transdermal delivery system for strong opioid administration promises a further step forward in terms of flexibility and convenience for cancer patients.

Introduction

"For many people, the fear of cancer is the fear of pain"[1]

The incidence of cancer is increasing and this increase is greatest in the developing world. In 1985 there were almost 5 million deaths from cancer, and it is estimated that in 2015 there will be over 9 million, of which almost three-quarters will be in developing countries.[2] The majority of patients with cancer will experience chronic pain at some stage of their illness. It is estimated that some 30% of patients undergoing curative anticancer treatment have pain, and this figure increases to 70%–90% in patients with advanced or terminal disease.[3] In developing countries, the great majority of cancer patients present with advanced disease. For such patients curative treatment is inappropriate and the priority is to offer them effective cancer pain relief and palliative care.

Pain in cancer is therefore a common problem affecting many hundreds of thousands of patients all over the world. As is evident from the quotation at the beginning of this paper, the diagnosis of cancer often provokes fear of pain. It is commonly believed that cancer invariably causes pain, that because the cancer is incurable the pain also may not be relieved, and thus the outcome of the disease is likely to be a painful death. In spite of the great developments in cancer pain relief and palliative care in recent years, such misconceptions are still prevalent. In a recent survey of 757 adults in the UK, cancer was top of the list of frightening diseases[4] because it was perceived as an incurable disorder causing much pain.

Cancer pain relief

Most cancer pain can be controlled by pharmacological treatment with orally administered analgesics, either alone or supplemented with co-analgesic (adjuvant) drugs. Only a small proportion of patients, around 10%–20%, have pain which does not respond well to conventional analgesic management. Of these, patients with neuropathic pain are the most difficult to treat.

These figures reflect the considerable advances that have been made in the management of cancer pain over the last two decades. The World Health Organization (WHO) Cancer and Palliative Care Unit has played a pivotal role in defining and promulgating the principles of treatment. A simple stepwise approach to the use of analgesics is effective, and the concept of the three-step analgesic ladder – moving from non-opioid, to weak opioid, to strong opioid – is the central idea of the so-called WHO method of cancer pain relief.[5]

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The WHO analgesic ladder

Non-opioid analgesics

Non-opioid analgesics represent the first step on the WHO analgesic ladder (Figure 1), where paracetamol (acetaminophen) or aspirin are used for the treatment of mild pain. In general, paracetamol is preferable because it lacks the gastroduodenal mucosal toxicity and platelet effects of aspirin. The usual dose is 1 g every 4–6 h.

Weak opioid analgesics

Pain which is not controlled adequately with a non-opioid analgesic requires the addition of or substitution by a weak opioid such as codeine or dextropropoxyphene. The combination of a weak opioid with a non-opioid produces enhanced analgesia without the side effects associated with increasing the dose of the opioid.[6] An adequate dose (for example two tablets of dextropropoxyphene 32.5 mg and paracetamol 325 mg) should be given every 4–6 h. Used in this way there appear to be no significant differences between codeine and dextropropoxyphene, the most widely available weak opioid analgesics.

Strong opioid analgesics

Morphine is the standard strong opioid analgesic for cancer pain and its use is governed by well proven principles.[7]

- It is given by mouth.
- It is given regularly to prevent the recurrence of pain, and may have to be maintained for long periods.
- The dose must be titrated against effect, and there is no arbitrary upper limit.
- Dose requirements may vary from 2.5 mg 4-hourly to 2,500 mg 4-hourly (or the equivalent in controlled-release formulations) and occasionally the dose may be even higher.
- An immediate-release formulation of morphine is required for dose titration but a controlled-release morphine preparation is usually used for maintenance treatment.

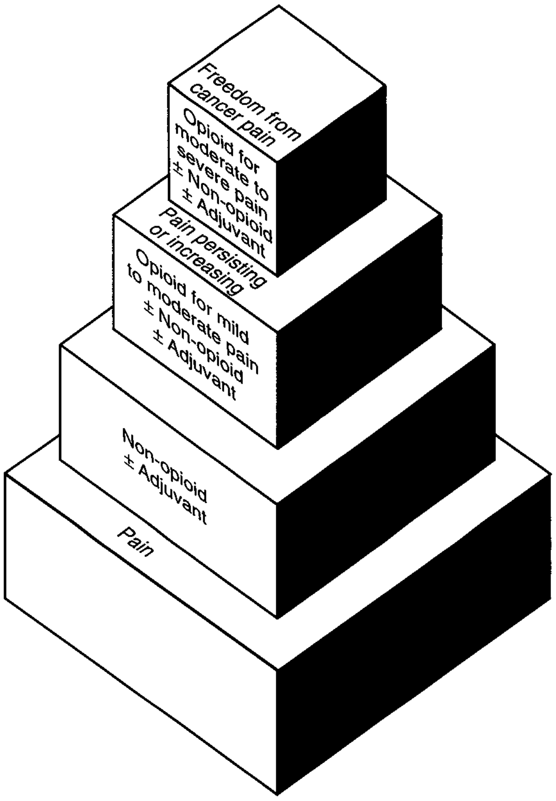

Figure 1. The WHO analgesic ladder approach to cancer pain control. Reproduced with permission from *Cancer Pain Relief and Palliative Care.* Technical Report Series 804. Geneva: WHO 1990, 9.

Dose-limiting side effects with morphine are generally neither dangerous nor disturbing. Constipation is the main persistent problem. Drowsiness is common at the start of treatment but usually resolves after a few days. Nausea and vomiting occur in one-half to two-thirds of patients but also frequently improve. In practice, respiratory depression and 'addiction' are not construed as problems. Adjuvant analgesics (psychotrophic drugs, corticosteroids, anticonvulsants, anti-arrhythmic agents, muscle relaxants) may all have an important role to play in individual patients.

The WHO method has been evaluated extensively in studies involving several thousand patients [8–12] which have demonstrated that relief of cancer pain can be obtained in around 80% of patients using this approach.

Such high response rates, however, are by no means generally achieved outside of specialist units. It has been estimated by the WHO that actual rates of cancer pain relief are around 50% in developed countries and 10% in developing countries. The main reasons for failure are inexperience and lack of knowledge of the simple principles of effective analgesic use, and also, in many parts of the world, non-availability of appropriate strong opioid analgesics. This situation is improving slowly, though in many countries there have been few changes over the past 15–20 years and treatment of cancer pain, particularly in the terminal phase, remains quite inadequate.[13–16]

Educational initiatives are crucial and cancer pain management is now increasingly incorporated into the core curricula for medical and nursing students. Postgraduate education is more difficult to achieve in a comprehensive manner, but there are now many publications, courses and meetings devoted to the subject. The WHO booklet *Cancer Pain Relief* has been the most influential publication in the field.[5] Since 1986, over a quarter of a million copies have been distributed in 20 different languages.

The WHO, in collaboration with the International Narcotics Control Board, have also embarked on a programme in which they have jointly called on governments to re-evaluate their needs for opioids in the treatment of pain, particularly cancer pain. In the period between 1972 and 1989, there has been a more than three-fold increase in global morphine consumption, though this increase has not been evenly distributed. The 10 countries that have the highest morphine consumption per million population per day have shown the greatest increase.[2]

Prescribing regulations and restrictions

A major constraint to the use of strong opioid analgesics in many countries is the oppressive prescribing regulations which surround the use of these drugs.[17] Special prescription forms are required in many countries, and total daily doses of drugs such as morphine may be severely limited, as may the duration of the prescription. All of these factors deter doctors from giving appropriate prescriptions.[18–20] Again, an important part of the WHO strategy is to press governments to rationalise their prescription regulations.

Palliative care

The developments described above relating to cancer pain relief have been closely associated with the growth and recognition of the new discipline of palliative care. 'Palliative care is the active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms and of psychological, social and spiritual problems is paramount. The goal of palliative care is achievement of the best possible quality of life for patients and their families.'[21]

Modern palliative care has its origins in the opening of St. Christopher's Hospice in London in 1967. Since that time, palliative care has developed around the world and has 'irreversibly improved the standards of care for the dying'.[22] The WHO strategy for the future development of palliative care is illustrated in Figure 2, which shows how resources for cancer treatment and care are currently allocated and how they should be allocated in the future. The emphasis is on integration of palliative care into comprehensive cancer care programmes so that patients have access to palliative care services from the time of diagnosis if appropriate. This strategy is to a large extent encapsulated in the WHO definition of palliative care, which does not include the words 'dying' or 'cancer' and gives emphasis to the fact that palliative care has broadened its scope since the early days of the hospice movement. Palliative care is more than terminal care, and its principles and philosophy may also be applicable to non-cancer patients with incurable disease.

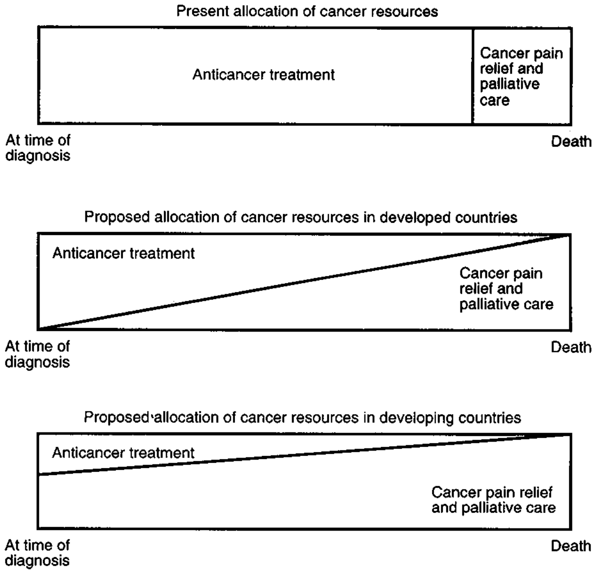

Figure 2. Proposed allocation of resources for cancer treatment and care from the WHO Cancer and Palliative Care Unit. Reproduced with permission from *Cancer Pain Relief and Palliative Care.* Technical Report Series 804. Geneva: WHO 1990, 16 (Figures 2, 3, 4).

Palliative medicine is recognised in Britain and Australia as a medical subspecialty – there are diploma and degree courses for doctors, nurses and other professionals involved in its practice, and undergraduate curricula have been developed. There are textbooks, journals and conferences devoted to various aspects of palliative care. These are all reflections of the fact that there is a defined body of knowledge and special skills required by those working in this area, but also that a basic level of knowledge of its principles is necessary for all doctors and nurses.

The goal of cancer pain relief and palliative care is to improve the quality of life of cancer patients, whatever the stage or severity of their disease. Much has been achieved over the past quarter of a century, but much is still to be done.

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