

Can we finally get it right with cancer pain control?

The control of pain in cancer patients has been an international priority for nearly two decades, since the first publication and updating of the World Health Organization (WHO) cancer pain control programme (WHO, 1990). The modern hospice movement, which has its origins in the religious foundations at the turn of the 20th century but which really became a force in the 1970s, also made cancer pain its leading target.

More recently, there have been several advances in our understanding of basic mechanisms of how pain is generated and maintained, and much progress in the availability of new drugs and of new formulations, which should have made it easier to ensure that more patients can receive the most appropriate medication (Ahmedzai, 1997). However, we have entered the 21st century with cancer pain, shamefully, just as much a public health problem as it was in the last.

PATIENTS ARE STILL IN PAIN

The reality is that pain is a significant problem for between 40–80% of cancer patients at home, attending hospital services and even in hospices (Foley, 1998). Pain is therefore not surprisingly still the most feared aspect of cancer — apart from death itself — for both public and professionals. It may arise from the primary cancer, its metastatic spread, non-metastatic manifestations, and from the treatment modalities (Foley, 1998). Moreover, pain can cause, and be exacerbated by, psychological or spiritual distress in cancer patients.

An individual patient has around seven separate pains, in any combination, including pains from co-morbidity (e.g. arthritis or osteoporosis). It is reasonable to expect all doctors to be able to recognize the common cancer

pain syndromes, such as brachial or celiac plexus pains from lung, breast or pancreatic cancers; the pain of pelvic infiltration from a progressive rectal, bladder or prostate cancer; or postherpetic neuralgia after shingles in a debilitated patient. Yet these are frequently overlooked, or given scant attention and treated blindly with increasing doses of opioid and paracetamol. All these examples, however, include a significant neuropathic element which is only partially responsive to opioids and non-steroidal anti-inflammatory drugs (NSAIDs).

Unrelieved neuropathic pain is severe, unremitting and demoralizing and accounts for 34% of cancer-related pains: the rest consists of soft tissue myofascial (i.e. somatic) pain (45%), bone pain (35%), visceral pain (33%), and unknown causes account for 6%. Each of the discrete aetiological classes of pain are best approached with different management strategies. It is not difficult to learn these, but many studies have shown that doctors simply do not think analytically when dealing with pain, and apply either the same simplistic approach to all pains, or worse, approach pain management with no rational strategy at all.

Why should pain be regarded as needing a less rigorous approach than the assessment and management of, say, angina or asthma? While it is true that patients do not die directly of unrelieved pain, clinicians can surely take no pride in being implicated in the sheer scale of the suffering caused by a lack of care and failure to apply current knowledge.

PAIN TREATMENT GUIDELINES

The WHO cancer pain programme (1990) set out simple guidelines, primarily to aid developing countries to recognize the place of opioids along-

side simple analgesics such as paracetamol. The model proposed was the WHO 3-step analgesic ladder, which has been very widely adopted. Put simply, it encourages the use of paracetamol for 'mild' pain (\pm a NSAID), a 'weak' opioid such as codeine (again \pm a NSAID) for 'moderate' pain, and a 'strong' opioid such as morphine (\pm a NSAID) for 'severe' pain. The ladder also recommends the use of so-called adjuvants or co-analgesics, which are drugs that are not primarily analgesics but can relieve specific types of pain by other mechanisms, e.g. antiepileptic or tricyclic antidepressants for neuropathic pain, or corticosteroids for nerve compression pain.

The Royal College of Physicians (RCP) has recently published a pamphlet on cancer pain control (Ethical Issues of Medicine Committee, 2000; available at www.rcplondon.ac.uk), which reiterates the WHO principles and gives helpful guidance on how to proceed when increasing morphine doses do not work, or produce intolerable side-effects. Inexplicably written by an anonymous team from the Ethical Issues of Medicine Committee of the RCP, it unfortunately contains errors, such as a formula for morphine titration which could lead to overdose. The correct approach is to add up each day the total morphine taken the previous day (regular + as required doses) and to make that the new day's dose; only if there have been no as required doses taken, and the patient is still in pain, should the regular dose be increased by 30%, as stated in the RCP pamphlet. The most significant concern about the RCP document is that it ties up cancer pain control with issues of dying and palliative care, which could lead many doctors to ignore the pain of cancer patients who are not seen as terminally ill.

The WHO ladder is said to bring pain relief in up to 80% of cancer patients. This does admit to lack of benefit for 1 in 5 patients, and it does not reveal the scale of toxicity experienced if this limited range of drugs is used to the full.

A systematic review has found little research evidence to support the view that the WHO 3-step ladder per se leads to better pain control (Jadad and Browman, 1995). Its most helpful message is to first evaluate the pain, then prescribe accordingly. It is useful for teaching a logical approach to students, and it may still be relevant for countries with a limited supply of analgesics and other pain strategies.

However, specialists in pain and palliative medicine now recognize many deficiencies in this model. The division of opioids into 'weak' and 'strong' itself is arbitrary, as newer agents such as tramadol cross over this boundary, and the increasing availability of 'strong' opioids in formulations which allow very low dosing has led many experienced practitioners now to restrict or even omit the second step, by going straight to a low dose of a 'strong' opioid.

Another problem is the WHO emphasis on the oral route, which is not always possible. The new RCP document at least refers to the transdermal, rectal and subcutaneous routes, but does not mention the spinal (preferably intrathecal) approach which can be very useful for a small proportion of patients.

NEW DEVELOPMENTS

But the WHO ladder has several other deficiencies, which are leading specialists now to develop improved models. First, it does not recognize the major advances in recent years in the role of anticancer therapies to control symptoms, such as the role of radiotherapy for metastatic bone pain (McQuay et al, 1997), chemotherapy in lung, colorectal and other solid tumours, and hormone manipulation in breast and prostate cancers.

Second, internal fixation or hip joint replacement is very effective for relieving pain from long bone metastases.

Third, bisphosphonates are a new class of drugs, not mentioned in the WHO model, which are effective in controlling metastatic bone pain (Mannix et al, 2000) and may be further helpful in breast cancer by long-term prevention of bone fractures. Fourth, referring to the examples of neuropathic plexopathies above, the judicious use of local anaesthetic or neurolytic nerve blocks can give sufficient pain control to allow the reduction of oral medication. Fifth, we now understand the role of the N-methyl-D-aspartate (NMDA) receptor in the spinal cord, which is implicated in both neuropathic pain and in long-term opioid tolerance (Ahmedzai, 1997). Ketamine is a pure NMDA antagonist and is extremely powerful against refractory pain. Methadone is interesting by virtue of its dual action on opioid and also NMDA receptors. Thus both these older drugs are making a comeback, but they need to be used by experienced pain specialists.

All the treatments just mentioned require consultation with or referral to specialists — surgeons, oncologists, palliative medicine teams or pain clinics. What can the general physician or surgeon do for patients in their care? They should be aware of the benefits of modern NSAIDs and cyclo-oxygenase-2 (COX-2) inhibitors, given with appropriate gastric protection.

Clinicians should also be familiar with the opioids now available. In the UK these include, apart from morphine: fentanyl, hydromorphone, oxycodone, methadone and tramadol. They should know about the use of newer antiepileptics such as gabapentin for neuropathic pain, and when to use anticholinergics such as hyoscine butylbro-

midate for the control of visceral colicky pain. The relative merits of these are well documented in the Palliative Care Formulary (Twycross et al, 1998), which is readily accessible on the internet (www.palliativedrugs.com).

Patients are increasingly expecting more information about their illness and treatments. They should also be given more choice on how their pain is controlled. This can only happen if clinicians are up-to-date and honest with patients about the current options.

Most importantly, all doctors should know how and when to refer to a specialist for increasing pain, or when psychological or spiritual distress complicates the symptom.

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KEY POINTS

Doctors should know and practise four basic principles when caring for any patient with pain:

- Make a full assessment of the cause and precipitating events.
- Prescribe rational analgesia by the most appropriate route, keeping toxicity to a minimum.
- Think about non-drug approaches.
- Learn when to refer to a specialist in pain control or palliative medicine.