

Why are cancer patients still suffering unnecessary pain?

→ Marc Beishon

More than 20 years since the WHO published its three-step guideline for controlling cancer pain, European patients are still complaining of pain that is long lasting, interferes with their daily activities and can even be 'intolerable'. Better basic medical training in how to assess and control cancer pain is urgently required, say the experts.

From the sheer volume of information and guidance published on the topic, one might conclude that cancer pain is no longer a major issue. Cancer pain was specifically addressed by the World Health Organization back in the 1980s with a set of guidelines; the European Association of Palliative Care (EAPC) and other agencies have issued several updated recommendations; and many major cancer centres in Europe and the US have cancer pain experts and copious online resources and research in train. The website of the WHO Pain and Palliative Care Communications Program details no fewer than two decades of clinical practice guidelines concerning the management of cancer pain.

Yet evidence from a variety of sources indicates that many patients are still being left to suffer unnecessarily, and the International Association for the Study of Pain (IASP) has designated this year – October 2008 to October 2009 – the Global Year Against Cancer Pain, to try to galvanise healthcare providers to take action.

The IASP estimates that pain control is achieved in only 50% of cancer patients, despite evidence that as much as 90% of pain can be controlled if the

WHO guidelines are followed. Evidence from the European Pain in Cancer (EPIC) survey, released in 2007, also paints a very sorry picture of pain control. The survey of some 4,000 patients in 12 countries – the only large-scale study of its type – revealed that 73% of patients experienced pain that they attributed to their cancer. For those who experienced pain in the last month, their pain “was frequent and long lasting, with almost one in three having endured pain for more than a year.” Further, one-third of those who experienced frequent moderate-to-severe pain described their pain as ‘intolerable’ and two-thirds said daily activities were difficult to carry out.

The findings came as no surprise to Franco De Conno, director of the rehabilitation and palliative care unit at the National Cancer Institute in Milan. De Conno, who co-founded the EAPC and was an organiser of the first world conference on cancer pain, says EPIC confirmed the view of cancer specialists that a majority of patients suffer pain. But the present situation, he says, has seen marked improvement in Western Europe – if not elsewhere. “We now see cancer pain much better treated in countries such as the UK, Italy, Spain and especially Germany, which has the



highest use of opioids per head in the world,” he comments. “But we still have many problems in developing countries and also Eastern Europe.”

The Soros Foundation has been helping to target shortcomings outside the more well-off countries, offering grants for international pain policy fellowships, funding courses on increasing access to pain control drugs, and paying for palliative care special-

ists in hospitals. Yet evidence remains of a huge burden of uncontrolled cancer pain, which is still far from being eliminated even in the nations with the best policies and greatest professional awareness of the issues.

The 1986 WHO guidelines, *Cancer Pain Relief*, include the ‘analgesic pain ladder’, a simple three-step process that is said to be inexpensive and 80%–90% effective. The steps are: ‘non-opioids (aspirin and paracetamol); then, as necessary, mild opioids (codeine); then strong opioids such as morphine, until the patient is free of pain.’ As Marie Fallon, professor of palliative medicine at the University of Edinburgh, Scotland, comments, the WHO method has been validated mostly in specialist units and she feels a standardised approach is necessary for it to be more effective.

ASSESSING PAIN

“The guidelines assume a certain amount of knowledge of cancer pain and its assessment,” she says, “and assessment, in particular, is a key issue. Because there are a variety of physical and non-physical issues, pain control is not as good as the WHO guidelines claim it could be.”

Assessing pain can be hard as there is often a lack of communication between patients and doctors and nurses, she adds. “People often don’t want to bother professionals, and they can be frightened of being started on morphine. They may also feel that treating pain will

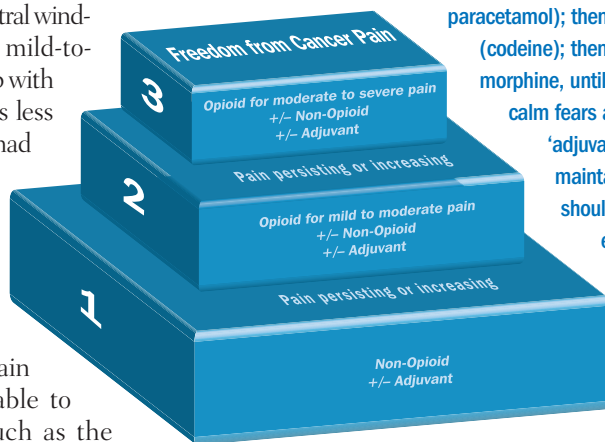
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mask the underlying problems, and they want to stay in control. But uncontrolled cancer pain can escalate, not because of tumour progression but because of a phenomenon called ‘central wind-up’, and someone with mild-to-moderate pain can end up with severe pain that responds less well to drugs than if it had been treated earlier on. So early identification of pain is key – it can be controlled and does not compromise tumour treatment.”

There are several pain assessment tools available to doctors and nurses, such as the Brief Pain Inventory, developed by Charles Cleeland and colleagues at the MD Anderson in the US, and the Edinburgh Pain Assessment Tool, produced by Fallon’s group, which aims to be a simple, bedside aid that can help to ‘institutionalise’ pain management in the same way that other vital signs of patients are measured and monitored. A psycho-oncologist in Edinburgh has also developed a touch-screen programme for patients to use, which can give a pain ‘readout’.

Other concerns of patients, identified by the IASP, include fear that early use of opioid medication may result in tolerance for drugs when pain becomes worse, as well as fear of addiction and unmanageable side-effects. Healthcare professionals need to address these concerns. As Rae Bell, director of the multi-disciplinary pain clinic and palliative care team at Haukeland University Hospital, Bergen, Norway, points out, most cancer pain can be well handled if it is identified and treated according to basic principles. “After a detailed evaluation, oral opioid analgesics, appropriate adjuvant drugs and psychosocial support will in the majority of cases provide good pain relief, but you need to follow up carefully, as pain can change with disease progression and you must tailor the treatment to the individual patient. The key is to



THE WHO'S PAIN RELIEF LADDER

If pain occurs, there should be prompt oral administration of drugs in the following order: non-opioids (aspirin and paracetamol); then, as necessary, mild opioids (codeine); then strong opioids such as morphine, until the patient is free of pain. To calm fears and anxiety, additional drugs – ‘adjuvants’ – should be used. To maintain freedom from pain, drugs should be given ‘by the clock’, every 3–6 hours, rather than ‘on demand’

be systematic in evaluation, treatment and follow up.”

As she says, there is no substitute for careful pain diagnosis, assessment of exacerbating factors such as anxiety, and good understanding of effects and adverse effects of pain control drugs. “But one problem is that there is often very little focus on pain treatment training in medical education. I cannot emphasise too much how important it is for primary care and hospital doctors to have basic pain training.”

Performing clinical trials in this patient population is a considerable challenge and, as yet, there are only limited clinical trial data on drug treatment of cancer pain, says Bell. “We were very surprised to find out that morphine itself has not been rigorously tested against a placebo. Some say it’s ridiculous to do this in a controlled trial, but we need to know more about opioid effectiveness.” The assumption that morphine – the gold standard drug for cancer pain – has been fully tested is probably shared by many.

As Fallon adds, “What needs to happen is that cancer pain is assessed, documented and treated in the same standardised way as a breast tumour, for example. Palliative care guidelines and pain assessment approaches are currently very broad and outcome measures are very diverse. We need to treat cancer pain as seriously as we treat the tumour.”

There are several types of cancer pain that are

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more challenging to treat, Fallon explains, notably neuropathic pain and cancer-related bone pain – about 20% of pain generally falls into the more difficult category, she estimates. Both types of pain are under investigation at Edinburgh, including translational studies for metastatic bone pain using an animal model. Pain researchers have also identified concepts such as ‘breakthrough pain’, defined as “transitory exacerbation of pain experienced by the patient who has relatively stable and adequately controlled baseline pain”, which is usually related to background pain and is severe and typically has rapid onset of within around five minutes (see www.breakthroughpain.eu). Generally there is a very wide range of research about cancer pain (and pain at large), from assessment to translational models, now underway. Indeed, some researchers feel that, in years to come, cancer pain treatment will be as individually tailored as targeted tumour therapies.

WHICH SPECIALIST?

A key issue, as with so many oncology topics, is that most research and optimal treatment for the spectrum of pain is found at multidisciplinary cancer centres where there are palliative care doctors, pain specialists, psycho-oncologists, nurse specialists and so on, although the pain and palliative care disciplines may not always be well integrated. Bell, who says her clinic is unusual in having both fields under one pain clinic director, comments that the two are largely separate at present. “But to be good in pain, you need to cover all areas, especially to distinguish and treat pain that responds well to basic treatment guidelines and more difficult pain,” she says.

A lack of cross-over between ‘pain’ specialists – i.e. members of IASP and various national pain

societies – and palliative care oncologists is also noted by Fallon. General pain professionals tend to take a very scientific, interventionist approach to their work (such as using nerve blocks), she says, and De Conno adds that pain generalists are not yet very interested in opioid use. But both he and Fallon are concerned that palliative care is relatively young, and there is patchy coverage of specialists around Europe and elsewhere, with not enough medical oncologists adequately trained or interested in pain to plug the gaps. “The EAPC has not yet had the time or resources to establish a unified front,” says Fallon.

Palliative care organisation is further advanced in some countries than others – De Conno identifies Germany as a good example, where at least four professorships in the speciality have now been established (the current president of the EAPC, Lukas Rudbruch, occupies one of them). German agencies acted 10 years ago to examine the need for cancer pain guidelines for the country; the UK has taken similar steps with palliative care organisation and research.

As well as bringing palliative care more into the research community, there does need to be more joint work between pain generalists and palliative care, says Fallon, rather than simply referrals from one to the other. “For example, I work with an anaesthetist to plan a nerve block rather than waiting for a crisis.” She notes that much more information about cancer is going up on the IASP’s website, in line with the focus on cancer pain this year, and there is an upcoming IASP research meeting on cancer pain in Chicago (see box, page 58).

Terminology is also problematic. “Professionals and patients do not always understand that palliative care does not just mean end-of-life care,” says



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Fallon. “Some units have tried changing the name to ‘supportive care’. When I see a patient, I say I’m an expert in pain control, and they don’t then feel they are being referred to hospice-type palliative care.”

Apart from the growing body of clinical and scientific research into cancer pain, there are also new guidelines in the pipeline and another survey, on opioid use in Europe, jointly carried out by the EAPC and ESMO (the European Society for Medical Oncology). This survey has gathered data on what opioids are available in each country and what

they cost patients, as well as barriers to access, such as the need for special permits and limits to where opioids can be dispensed. Results are to be presented by De Conno at the EAPC biannual conference this May in Vienna.

Certainly, a major barrier to effective pain control is a country’s regulatory regime concerning drugs from the standpoint of both limits on opioid availability and the pressures doctors may feel under from regulatory scrutiny (illegal dealing in oxycodone, for example, could mean life imprisonment in some countries). In March, ahead of the UN General Assembly Special Session on Drugs, Human Rights Watch issued a report, *Please, don’t make us suffer anymore... access to pain treatment as a human right*, which noted that, while international law requires states to make narcotic drugs available for the treatment of pain while preventing misuse, the strong international focus on the prevention of misuse has led many countries to neglect the obligation to those suffering pain.

De Conno says that, while the WHO guidelines are being updated, they cover forms of pain that are not related to cancer. His colleagues in the EAPC, however, are now updating guidelines specifically for the treatment of cancer-related pain to take into account new approaches, such as safe nasal drug delivery. Fallon points to a current European research network project focusing on pain, depression and fatigue in cancer, with the pain element including work on the all-important assessment side (see the European Palliative Care Research Collaborative at www.epcrc.org).

But as she concludes, “More guidelines won’t change practice. The cancer community has to take on board that uncontrolled pain can lead to pain that’s sometimes impossible to manage, deteriorating quality of life, depression, anxiety and huge distress. We need to institutionalise pain as a vital sign – and if you’re not controlling pain properly you may well not be managing other less common symptoms too.”

PAIN: SOURCES AND SITES

- The Eighth IASP Research Symposium, to be held 4–5 June this year in Chicago, is billed as a forum for in-depth discussion and analysis of basic and clinical research surrounding the problem of cancer pain. Objectives include analysing current basic science research and examining mechanisms of cancer pain; reviewing new findings on the role of anxiety and other mediators of pain, as well as the role of psychological interventions; and evaluating the reasons for ongoing pain and suffering in the developing world. See also www.iasp-pain.org
- A good source of information is the Shaare Zedek Cancer Pain and Palliative Medicine Reference Database, a free database of more than 30,000 references run by Nathan Cherny, director of the Cancer Pain and Palliative Care Service at the Shaare Zedek Medical Center in Jerusalem. As Cherny notes: “The literature regarding cancer pain and palliative care is characterised by its phenomenal diversity” – and he was inspired by a mentor in 1989 to begin the work. See www.chernydatabase.org
- The WHO’s pain publication, *Cancer Pain Release*, can be accessed at <http://whocancerpain.bcg.wisc.edu>. Among the articles of interest is an interview with Kathleen Foley, a cancer pain pioneer based at Sloane-Kettering, appraising the WHO analgesic ladder on its 20th anniversary (vol 19, no 1). That site also links to many country pain websites. The pain and policy studies group at the University of Wisconsin’s cancer centre also has a very useful site (www.painpolicy.wisc.edu), which majors, as expected, on public policy issues such as opioid availability.