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Pain services and palliative medicine – an integrated approach to pain management in the cancer patient

Tony O'Brien[1,2,3] and Christopher M Kane[4]

Abstract

The vast majority of cancer patients will experience pain during the course of their illness. Thankfully, in most instances, the consistent application of analgesic guidelines, tailored to the unique needs of each individual patient, will deliver a satisfactory outcome. These guidelines recommend the skilled use of analgesic medications, often in conjunction with a range of adjuvant therapies as may be required. Despite the consistent and rational application of such strategies, it is recognised that a small but significant proportion of cancer patients continue to experience more refractory pain. In addition, these patients may experience a plethora of unwanted dose-limiting side effects associated with their analgesic medication, sometimes even at low dose. All such patients with more complex and refractory pain syndromes require a more comprehensive review and many will require interventional therapy and/or adjuvant approaches. Unfortunately, the availability and accessibility of such services are variable. Even in circumstances in which palliative medicine and pain services co-exist in the same region, there may be poor integration between the two services. Each specialty area holds a unique set of skills and competencies, yet there is considerable overlap. Patient care and outcomes will be enhanced by establishing more formal relationships between these two specialty areas.

Keywords

Pain management, chronic pain, neuralgia, nociceptive pain, pain, intractable

> *It is far more important to know the person who has the disease, than what the disease the person has.*
>
> Hippocrates

Introduction

It is estimated that up to 80–90% of patients with advanced cancer experience pain.[1,2] Fortunately, the majority of these patients will have their pain managed satisfactorily by using simple guidelines as articulated in the World Health Organization (WHO) analgesic ladder. Approximately 90% of patients with cancer pain will have their symptoms controlled using this approach.[3,4] In studies of self-reported poor pain control, this may fall to 70%.[5] Based on the number of cancer deaths in the United Kingdom in 2011, up to 48,000 patients suffer uncontrolled cancer pain per year.[6] If the number of cancer survivors with chronic pain is taken into consideration, this number climbs further still.

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[1] Marymount University Hospital & Hospice, Cork, Ireland
[2] Cork University Hospital, University College Cork, Cork, Ireland
[3] College of Medicine & Health, University College Cork, Cork, Ireland
[4] Academic Unit of Palliative Care, Leeds Institute of Health Sciences, School of Medicine, University of Leeds, Leeds, UK

Corresponding author:
Tony O'Brien, Marymount University Hospital & Hospice, Cork, Ireland.
Email: tony.obrien1@hse.ie

Philosophy of palliative care

The importance of achieving and maintaining an optimal level of pain and symptom control throughout the course of any progressive illness is highlighted in the WHO definition of palliative care.[7] This quite proper focus on pain and symptom management may cause confusion in the minds of some observers. Good pain control is not the sole or even primary objective of palliative care per se; it is merely a means to an end. Good pain control is not the end-point in itself; it is the starting point. Improving individual quality of life is at the heart of palliative care philosophy and practice. Individual quality of life is a complex phenomenon that is not always easy to measure. However, we do know that it is always individual, multi-dimensional and dynamic.

Good pain and symptom management are one of the means by which patients are enabled and encouraged to live the life they choose to live, in the manner and setting of their choice, for the natural duration of their life. Good pain control, combined with skilled psychosocial and spiritual support, provides the foundation on which individual patients may build their life in the manner of their choice. Patients define their own quality determinants, and it is the function of palliative care and indeed of healthcare, in general, to support and enable them in this regard to the greatest possible extent.

Palliative medicine physicians have significant expertise in the management of pain in advanced cancer patient tailoring and adapting their approach to fit in with the patient's biomedical and psychosocial framework. There is potential for growth, development and enhanced synergies between palliative medicine and specialist pain services. Whilst the majority of patients will respond well to standard palliative medicine approaches to analgesia, a significant minority will benefit from the unique skills and expertise of a specialist pain service. Close integration between the two specialist services will result in appropriate interventions being undertaken in a timely fashion, to the benefit of patients and their families. The primary focus of this paper is to explore the interface between palliative medicine and specialist pain services. It is not intended to provide a detailed review of advanced cancer pain management.It is not intended as a review of advanced cancer pain management, but seeks to highlight this area.

Evolving profile of palliative care

Over the past decade or more, the focus of palliative care has changed to include involvement at a much earlier stage of disease. In many instances, patients are referred from the moment of first diagnosis. Thus, palliative care services are involved with patient care throughout all stages of the cancer journey, including multi-modality neo-adjuvant treatments and all manner of disease-modifying interventions. So, while palliative care continues to incorporate end-of-life care, palliative care is not defined by end-of-life care.

Another change that has occurred in recent years is the integration of specialist palliative care services across a range of care domains, including acute hospitals, community settings and free-standing hospice units. In essence, the service follows the patient's journey at each and every stage.

Nature of pain

Pain in a cancer patient is a subjective, multi-dimensional human experience, with complex interactions between sensory and emotional components.[8] In the clinical context, one never sees pain. The clinician observes an individual patient's emotional responses to his or her pain, which typically manifests as distress and suffering. The extent of the manifest distress is in part related to the severity of the pain. However, a variety of other factors, not least being the specific significance that the patient attaches to his or her pain at that time, will also influence the extent of an individual's distress. Thus, we observe intricate interactions between physiological, psychological, sociocultural, sensory, cognitive and behavioural dimensions.[9] It is never possible to treat pain in an abstract sense; one may only treat the person with the pain. Thus, patients require a multi-faceted approach to pain and symptom management utilising pharmacological and non-pharmacological strategies in conjunction with appropriate psychosocial therapies.[10]

Of course, we must understand the pathophysiology of each individual pain, recognising that cancer patients will typically have multiple pains.[11] But a detailed pain assessment demands that we undertake a more holistic review of each individual patient in the context of his or her unique circumstances. Pain management requires a multi-dimensional and inter-disciplinary approach to assessment, and thereafter, therapeutic strategies will require the use of both pharmacological and non-pharmacological interventions.

Meeting the patient, not the pain

Wolpaw and Shapiro[12] highlight the importance of establishing a connection with each individual patient that allows us to care for them as whole persons.

They identify four key components in this regard:

1. Seeing the patient as a unique individual;
2. Identifying shared experiences;
3. Demonstrating that we are observant and attentive to the patient's narrative and circumstances;

4. Indicating that we are open to a meaningful exchange/conversation.

In order to have a meaningful therapeutic relationship with a patient, we must allow patients the opportunity to say 'this is who I am'. The absolute need to combine a high level of technical competence with a more human and compassionate approach to patient care is eloquently and poignantly portrayed in Professor Kieran Sweeney's personal account of his cancer journey that was published in 2009.[13] Professor Sweeney was a medical academic who developed a mesothelioma. In this article, he describes with remarkable honesty his own individual experiences of living and dying with cancer. He commends the high level of technical competence that he so frequently encountered. Nevertheless, he also describes a profound sense of isolation because of perceived failings in the relational aspects of care.

Clearly, we need to develop an open, honest and trusting relationship of equals between physician and patient. This relationship, like all other relationships, must be characterised by mutual respect and understanding. We must always remember that, irrespective of how technologically advanced medicine may become, the practice of medicine is always a social act.[14] There is always a real person, with real fears and concerns, at the end of our needles and catheters and within the chambers of our increasingly advanced imaging devices.

Standard approach to cancer pain management

Dating back to the early work of Dame Cicely Saunders and colleagues in the 1960s and 1970s, the unique safety profile and efficacy of the regular administration of oral opioids in the management of cancer pain were clearly demonstrated. These core principles of cancer pain management were subsequently endorsed and promoted by the WHO in the now-famous 'analgesic ladder'. The regular administration of oral opioids, with careful attention to patient selection, drug selection and a proactive approach to ensure an optimal balance between analgesic effects and adverse effects, remains and will remain the basis of our approach to cancer pain management.

Extensive experience worldwide has confirmed the effectiveness of this approach in the vast majority of cancer patients. But therein lies a problem. If, as the available evidence confirms, we can achieve good or satisfactory analgesia by the application of relatively simple oral analgesic protocols in the vast majority of cases, one might be forgiven for starting to believe that the problem of cancer pain is largely a historical one. Nothing could be further from the truth.

Refractory pain

The published literature indicates that an acceptable level of analgesia is achievable using well-publicised protocols in 85–90% of cancer patients. This is undoubtedly good news for the majority of cancer patients. However, we must be mindful of the needs of those patients whose pain is refractory to standard approaches. Hoskin[15] reports that 10–30% of people with advanced cancer still have inadequate pain control, despite optimised use of systematic analgesics. The timely application of interventional therapies necessary to achieve and maintain good pain control is essential. Although interventional pain therapies are often effective in otherwise intractable pain, these therapies are often under-utilised or withheld until the very end of life.[16] The individual human and societal cost of uncontrolled pain in this significant cohort of patients is incalculable. Furthermore, if one practises medicine in the specialties of pain medicine or palliative medicine, one may expect to see a much higher proportion of patients with more complex pain needs. Such patients are referred to these services precisely because their pain is not responsive to simple management strategies.

Refractory pain may be defined as pain that responds poorly to standard, conventional treatments. In addition to uncontrolled pain, these patients may be further burdened by many unwanted adverse effects associated with the use of their medications.[17] Thus, the most unsatisfactory circumstance whereby a patient continues to experience uncontrolled pain and is additionally burdened by the undesirable adverse effects of opioid medications is one of the most challenging issues in both palliative medicine and pain medicine.

Interface between pain medicine and specialist palliative care

Many patients with more complex and refractory pain syndromes will benefit from timely assessment by a comprehensive, inter-disciplinary pain service. In terms of the interface between palliative medicine and pain medicine, the situation is evolving rapidly. In the past, many hospice and specialist palliative care services had limited access to or availed little of the particular expertise of colleagues in pain medicine. Historically, hospice services were particularly associated with the 'care of the dying', and the pervading culture was largely one of non-intervention. The culture has now changed such that the modern specialist palliative care service works in a more integrated fashion, embracing as appropriate all the technological developments in medicine. Nowhere is this more evident than in the application of interventional radiology techniques for the relief of burdensome symptoms. Such techniques include draining malignant pleural effusions or ascites, decompressing an obstructed renal or biliary tract, positioning a stent in an obstructed oesophagus or colon, enteral feeding devices, using a vascular stent in the superior vena cava (SVC) or inferior vena cava (IVC), tumour embolisation, vertebroplasty and so on.

But to what extent are pain specialist and palliative care specialists availing of each other's expertise? Several high-level reports have recommended closer ties between palliative care services, cancer services and pain services to improve patient experience and outcomes.[18–20] There is a scarcity of literature on the subject of the interface between pain services and palliative medicine services for cancer pain, with only two national surveys having been published since 2002.[21,22] As both these surveys are now fairly outdated, it is difficult to ascertain whether effective provision of services for cancer pain exists.

Linklater et al. in 2002 reported on a postal survey of palliative medicine physicians that revealed marked under-utilisation of specialist pain management teams by hospice services. While most palliative medicine respondents indicated that they had access to such services, over half had used the services of a pain specialist less than four times in the previous 12 months. Previous surveys of palliative medicine consultants have found that only 40% of respondents felt that regular contact with a pain specialist would be of benefit and only 65% felt that 'ad hoc' contact would be useful. While they thought that up to 8% of patients may benefit from an interventional procedure, only 20% of palliative care doctors believed that more input from pain specialists was required.[21]

A variety of reasons for this apparent under-utilisation are proposed, including a lack of formal structures, geographical isolation of hospice units, different management and governance structures between the services and a lack of experience among palliative medicine physicians.

In 2007, Kay et al.[22] reported on a similar postal survey of pain specialists across the United Kingdom. Again, referral rates from palliative medicine were low and joint consulting arrangements were 'rare'. The authors concluded that

> Although pain specialists have a vital role in the management of patients with advanced cancer, …. few anaesthetists are involved in the delivery of an integrated palliative care service and only a small proportion of patients who could benefit from advanced pain management techniques do so.

It is noteworthy that joint consultations were uncommon, with about 50% of pain specialists never having done a joint consultation. Two-thirds were using time outside their job plan to accommodate the ad hoc referrals of palliative patients to allow them to be seen more quickly. However, those who had formally allocated time had a significantly increased amount of referrals for the management of cancer pain.

More strikingly, 65% of respondents either stated there were no pain specialists available for the palliative medicine multi-disciplinary team (MDT) or they did not know if there was one.

There was also a significant variability between regions in the types of procedure performed. Contrary to the common belief among palliative medicine consultants that the role of the pain specialist should be limited to interventional procedures, pain specialists felt they had a significant role to play. Of those questioned, 10% did work jointly with palliative medicine, and this group saw a significant increase in referrals. This fact highlights the need to increase joint working and the importance of formal arrangements in order to best meet the needs of patients.

These surveys are now becoming outdated, and it is difficult to be precise as to the current picture, but there remains a consensus of opinion that patients are often referred too late to specialist pain services to benefit optimally from the available expertise. Anecdotally, there are reports of successful structured and funded collaboration between specialist palliative care and pain services, but this is not widespread. The scope for collaboration on clinical, research and teaching initiatives is enormous and remains seriously under-developed.

There is an apparent lack of understanding and awareness among colleagues from both specialties regarding the role and competencies of colleagues from the other. There is clearly a need for more interaction and shared education experiences between palliative medicine physicians and pain specialists, and this should begin during training years and at the earliest opportunity.

However, the previously mentioned studies may not fully capture the complexity and nuances of the problem. In a more traditional model defining the interface between palliative care and pain management teams, the pain specialist was typically invited to review only those patients who had failed every possible opioid therapy delivered over protracted periods of time. Not infrequently, clinicians followed the 'analgesic ladder' in a methodical way and considered a possible Step 4 of interventional pain services only after all other modalities of care had failed.

Worst-case scenario

Consider the following unsatisfactory scenario. A patient with complex pain needs that are proving refractory to multiple analgesic approaches is under the care of a palliative medicine service. In desperation, a colleague from pain medicine is now invited to review an increasingly distressed and frustrated patient, often accompanied by a very angry and despondent family, with escalating levels of distress and anxiety. In many instances, the pain specialist has no meaningful relationship with the palliative care service and is now meeting the patient and family for the first time. Unless the pain specialist has dedicated clinical sessions at the hospice, this review may be undertaken in the late evening when neither the patient nor the pain specialists are performing at their very best. To compound the issue, the referral to the pain service may be represented to the patient as a 'guarantee' of almost instant and sustained pain relief. Sometimes, the expectations created around interventional pain services are totally unrealistic. Surely, there must be a better way to organise matters.

Coming together – for better, for worse

At the outset, it is acknowledged that there is considerable overlap and complementarity between specialist palliative care and specialist pain management services. Each has a separate and distinct set of skills and competencies, and each shares a common 'middle-ground'. Both disciplines must establish close, professional and respectful relationships and gain an appreciation of their complementary roles. This will only be achieved if colleagues from specialist pain services are fully integrated into the specialist palliative care team. In this regard, the pain specialists must have a minimum number of defined sessions each week at the specialist palliative care unit or service. In the event that the specialist palliative care service and the pain service are funded separately and have different governance structures, it will be necessary to have a formal service agreement. This will create the opportunity for relationship building and understanding; for shared patient review and discussion and for collaborative research, audit and educational activity. Inviting colleagues from pain services to review only those patients with the most intractable and protracted pain management problems is an entirely inappropriate use of a pain service. The 'ad hoc' strategy is defunct, and we need to move forward to a fully integrated and accessible model of service provision.

As previously identified, palliative medicine specialists may view pain specialists as 'technicians' whose role is limited to performing 'nerve blocks' or establishing drug delivery systems for spinal analgesia. Again, this portrays a very limited and entirely inaccurate picture of the role of the pain specialist. Pain specialists need to be involved in the overall assessment and management of patients with more complex pain problems. They may advise on a range of investigative and therapeutic strategies that include, but are not limited to, interventional procedures. Equally, we all must get better at identifying those patients with more complex and challenging pain syndromes at an earlier stage in the disease trajectory. All such patients should have direct access to a comprehensive pain assessment with input from a fully integrated multi-professional team. And, as the pain specialists will gain a greater understanding and appreciation of palliative care strategies, so also will palliative care specialists gain a greater understanding of pain specialist approaches, including interventions. In addition to medical and nursing personnel, we must also remember the important function of pharmacy colleagues in supporting optimal patient care.

The British Pain Society[23] has developed chronic pain pathway maps for other forms of chronic noncancer pain. Their aim is to provide consensus-based pathways that reflect the best available evidence. As in many areas of pain management, robust scientific evidence to support specific strategies is all too frequently lacking. Thus, there is a self-evident need for more large-scale studies.

An inconsistent partnership

In terms of cancer pain management, the British Pain Society has produced, in association with the Royal College of General Practitioners and the Association for Palliative Medicine of Great Britain and Ireland, a 'perspective' document on cancer pain management.[24] The document notes the need for improved pain management in palliative care and observes '*an inconsistent partnership between the specialties of pain medicine and palliative medicine*'. The document summarises the barriers to links between specialist pain management and palliative medicine, and these are reproduced in Table 1.

Addressing the subject of invasive procedures for cancer pain, the British Pain Society's publication notes that

> There is good evidence for the effectiveness of a coeliac plexus block and intrathecal drug delivery; …..and, where applied appropriately and carefully at the right time, these procedures can contribute enhanced pain relief, reduction of medication use and a markedly improved quality of life.

In addition, the British Pain Society cancer pain document also cites relatively good results associated with the use of anterolateral cordotomy.

Clearly, we need more evidence-based protocols to inform and guide clinicians. However, notwithstanding the guidelines, each clinician must make his or her own decision with due regard to the individual patient's

Table 1. Barriers to links between specialist pain management and palliative medicine.

Short survival of patients following referral to palliative care services
Funding of the service
Time on the part of the pain specialists for proper assessment and discussion
Facilities for performing interventions may not be easily accessible
Complexity/lack of real understanding
Staff training in the management of pumps and catheters
Pharmacy issues; procurement of solutions/availability of preservative-free opioids/lack of sterile facilities for making up infusions
Cost of implanted devices
Who is going to manage neuraxial infusions at home
Lack of availability of pain specialists out-of-hours
The palliative care doctor may be unaware of potential benefits/unsure how to access expertise
The pain doctor may not be adequately trained in the management of cancer pain/selection of an appropriate technique

unique set of circumstances. Even if the clinician is happy to proceed to intervention, access to the necessary facilities may prove problematic as reported in a survey of Australian palliative medicine consultants who highlighted their difficulties in accessing services.[25] Access to theatre facilities with suitable imaging is indeed sometimes problematic and is not a uniquely Australian problem. Such access problems represent a block to timely interventions and treatment. It is not always ideal, or even possible, to transfer a frail palliative care patient from a hospice setting to a local or regional hospital for a pain intervention. Therefore, hospice units might usefully consider developing on-site facilities to support anaesthetic interventions. In addition to a suitably equipped theatre, waiting room and recovery rooms, pharmacy, secretarial and storage facilities will also be required. Such a facility may not be fully utilised by palliative care patients. As such, the hospice unit might make the facility available to other non-specialist palliative care patients who require such interventional treatments. At a regional level, not every procedure or intervention can be safely provided at every site. It will be necessary to concentrate the more complex procedures in a regional centre to ensure adequate expertise and competence.

Illustrative procedures/approaches

There are a plethora of interventional techniques available, but for the purposes of this article, we wish to focus on three interventions in particular – percutaneous coeliac plexus block, intrathecal drug delivery systems (ITDDs) and percutaneous cervical cordotomy (PCC). It is beyond the scope of this article to attempt to summarise the range of interventions that might be used.

Coeliac plexus block

The coeliac plexus contains pain fibres from the pancreas, spleen, small bowel, diaphragm liver, adrenals, kidneys aorta, and ascending and proximal transverse colon. As such, a coeliac plexus block may have some benefit in treating pain originating from these areas. It is most commonly used to treat direct invasion of the coeliac plexus from pancreatic cancer.[26]

A systematic review in 2013 of coeliac plexus block for upper abdominal cancer pain, which included a meta-analysis of five studies containing 295 patients in total (149 vs 146), showed that pain was improved significantly up to 1 month following treatment compared to those on pharmacotherapy alone. Even when pain scores were no longer significantly better a month after procedure, patients were on significantly less opiate compared to those who had not had the procedure. Although there was a transient increase in hypotension and diarrhoea following the procedure, the patient group also had less nausea, vomiting and constipation possibly related to reduced opioid consumption.[26] A review by the Cochrane collaboration of coeliac plexus blocks in pancreatic cancer concluded that there is evidence to show superiority of coeliac plexus block over standard therapy, although at present there are less adverse effects than those caused by opioids, which should be another important consideration.[27]

In terms of when the block should be performed, a randomised control trial in 2013 looked at patients with pancreatic cancer. One group had a coeliac plexus block performed after initial meeting and the other had medical management to reduce baseline pain, and then the block was performed. The latter group had better pain control, less opioid consumption and better quality of life scores compared with the early intervention group.[28]

It should be noted that these studies often do not compare the treatment with those on neuropathic agents, and this remains one area for further research. Palliative medicine professionals must be mindful of the need to reduce the baseline opioid dose following a successful coeliac plexus block to minimise the risk of emergent opioid toxicity. They must also be aware of the complications associated with coeliac plexus block, including hypotension, diarrhoea, and the more serious neurological complications of paraplegia, leg weakness, sensory deficits and paresthesias. Four cases of paraplegia were reported in one series of 2730 patients undergoing coeliac plexus block.[29] This devastating complication was attributed either to direct injury to the spinal cord or to spinal infarction secondary to spasm of the spinal artery. Although this was from a retrospective postal survey, the true prevalence is unclear.

This evidence highlights the importance of close working between pain and palliative medicine as a joint medical and interventional approach could be performed at an earlier stage, resulting in better pain control and better quality of life. Either service working individually would be unlikely to provide the same level of outcome.

ITDDs

ITDDs are appropriate for use in patients with a variety of pain pathologies related to cancer, including neuropathic pain. Consensus guidelines for the use of ITDDs were published in 2011, which promoted a phased approach from the most conservative management stepping up to ITDD systems for refractory cancer pain or where significant adverse effects existed.[30] Typically, patients whose cancer pain cannot be adequately controlled on less invasive therapies without unacceptable side effects should be considered for an ITDD system. Spinal analgesia has been shown to offer good palliation in palliative care patients.[31] A randomised controlled trial in 2002 showed that in patients with complex pain on high doses of opiates (equivalent to 260 mg oral morphine per day), the use of ITDD significantly improved pain scores and alertness while reducing drug toxicity and improving survival at 6 months compared to best medical management.[32] Patient-activated dosing using ITDD systems as opposed to continuous infusion also showed significantly reduced pain scores and adverse effects.[33] In continuous intrathecal infusions, the opioid is often combined with a local anaesthetic agent.

Despite this evidence base, there remain significant problems with the implementation of this approach into clinical practice. An audit of use in the United Kingdom in 2008 showed significant variation, with ITDD services having emerged in an ad hoc way. Thus, there is a geographical lottery in terms of accessing this pain management approach.[34] Implanted devices are the most convenient although they do require on-going support and management. They are compatible with the patient being at home if that is his or her choice.

While this is clearly an effective measure of pain control for some patients, it is also clear that it is only feasible in an environment that not only identifies suitable patients at an early enough stage to benefit from analgesia but also has on-going close connection between services to deal with them post-insertion. An integrated cancer pain service model in this situation would allow for training and education to be implemented with accessible support for those looking after these patients in the community.

PCC

PCC, a neurodestructive technique, is indicated for any unilateral pain below C5. In this procedure, an attempt is made to ablate the spinothalamic tract on the side of the spinal cord opposite to the site of the pain. Cordotomy can be particularly useful for chest wall pain associated with mesothelioma. Its evidence base is small but what exists suggests that significant pain control can be achieved.[35] It is discussed here as an example of both a problem and an example of integrated working.

Currently in the United Kingdom, only a few sites offer percutaneous cordotomy.[35] There is a consensus of opinion that a significant number of patients that may benefit from it are never referred for practical and logistic reasons. This demonstrates the need for not only a local or regional structure for integrated working, but it is also required at a national level to ensure that centres providing all procedures are distributed evenly across the country.

It is also an area where coordinated thinking is likely to increase both knowledge and understanding of the use, benefits and risks of this procedure. In 2011, a pilot study of the invasive neurodestructive procedures in cancer pain (INPiC) conducted a systematic review of cordotomy use for mesothelioma and concluded that good pain relief in most patients on all pain outcome measures was achieved.[36]

Notably though, in order to provide governance for the clinicians performing these procedures and to gain a larger evidence base for on-going research, a national cordotomy registry was developed. This should negate some of the innate problems in gaining evidence to support implementation of cordotomy services in other areas.[36]

Conclusion

The above interventions highlight three different examples of circumstances in which interventional pain techniques may yield significant and meaningful benefit for patients. Indeed, many patients will undoubtedly continue to experience uncontrolled pain and/or suffer unacceptable side effects without such interventions. Thus, such approaches to service development are not an optional extra, they are an absolute necessity.

There is an urgent need to develop national policy in this regard that will provide the blueprint for loco-regional development and integration of pain management and specialist palliative care services. This will support enhanced educational, audit and research activity in addition to ensuring better patient outcomes. Thus, we must develop clear local, regional and national structures to support a fully comprehensive and integrated pain management service within all specialist palliative care services. Equally, all pain management services must have easy access to specialist palliative care support as and when required. The era of 'ad hoc' arrangements is over.

> There is always more to analgesia than analgesics. (Robert Twycross)

Conflict of interest

The authors declare that there is no conflict of interest.

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