Overview

Interventional Techniques for Cancer Pain Management

J.G. de Courcy

Cheltenham General Hospital, Cheltenham, UK

Received 7 October 2009; received in revised form 13 December 2010; accepted 5 April 2011

Abstract

Patients with cancer frequently experience pain, and even with increased modern knowledge and skills in drug and other therapy, this pain is poorly controlled in a significant proportion. For these patients, a range of interventional techniques can play a significant role in providing pain relief. These include neuraxial administration of opioids and other drugs, temporary or permanent blockade of nerve pathways and minimally invasive management of bony and other metastases. Those involved in the treatment of pain from cancer should be aware of the scope of these techniques and ready to call upon specialists in their use.

Statement of Search Strategies Used and Sources of Information

Literature searches were carried out using Embase and Medline via the NHS Evidence Healthcare Database in August and September 2009 and November 2010. Search terms included interventional pain cancer; epidural cancer pain; intrathecal pain cancer; nerve block cancer pain; radiofrequency cancer pain, as well as multiple individual searches for particular procedures and drugs. Further papers were included from the author’s own database and selected references from authors’ citations.

Introduction

Since the publication of the World Health Organization pain ladder and with greater understanding of appropriate multimodal analgesia, the management of cancer pain has improved dramatically: the World Health Organization method is effective in most patients [1], but 5–14% do not have their pain controlled adequately, even with optimised systemic medical therapy [2]. Even with further improvements in recent years, a significant proportion still remain poorly controlled, with recent surveys suggesting that the above figures are an underestimate [3–5]. This has led to the suggestion [6] that the World Health Organization ladder should be modified with a fourth step, that of interventional procedures and techniques. This overview focuses on interventional procedures commonly used in UK practice.

The specialty of pain medicine evolved out of the use of invasive approaches to provide permanent or temporary interruption of nerve transmission. Over the years, particularly from the point of view of destructive lesioning, this perspective has changed, in part due to increased awareness of the risks of deafferentation and post-block neuropathic pain, but also due to increased experience and skills in pharmacological management of pain and in implant and infusion techniques.

Nevertheless, interventional techniques remain an important and frequently underused part of the multimodal management of cancer pain— it has been suggested that 8–11% of cancer patients could benefit from interventional procedures [1,7].

One issue impeding this is the availability of time and resources for the involvement of pain medicine specialists, most of whom are anaesthetists, in this area. This has been revealed by surveys of palliative care and pain specialists.
Joint consultations with palliative care and regular resourced sessions in a palliative care facility are uncommon [8]. The availability of specialist pain input to the palliative care multidisciplinary team has been shown to result in an increase in referrals and procedures carried out [7]. The UK National Institute of Health and Clinical Excellence guidance on supportive and palliative care in cancer [9] highlighted that each local specialist palliative care multidisciplinary team should have access to pain specialists with expertise in nerve blocking and neuro-modulation techniques. Recent guidelines [10] recommend the assessment of patients with difficult to control pain by an anaesthetist with expertise in pain medicine.

General Considerations

The main groups of patients in whom interventional procedures may be appropriate are those with pain responding poorly to systemic medications or those in whom adequate titration of these medications is prevented by adverse effects. The major pain types in this group are neuropathic and cancer-induced bone pain, although these techniques can be applicable to a wide range of other pain sources.

Interventional procedures will rarely give adequate benefit to be the sole treatment of the patient’s pain, and must be viewed as a part of multimodal analgesia and patient care. Nevertheless, these procedures can give very substantial benefit and allow the reduction of other analgesic drugs and their side-effects [11].

Many of these patients will have been treated with high-dose opioids and other medications before an interventional procedure. This may lead to initial excessive sedation once the pain is reversed: conversely, over-rapid withdrawal of opioid treatment may lead to withdrawal phenomena. It is therefore necessary to observe these patients closely in the period after the procedure in order to prevent these problems, and to titrate systemic medications downwards according to their response – a common approach is to halve the systemic opioid immediately after the procedure and to continue to reduce it thereafter.

These large doses of medications may also lead to impairment of cognition. In preparation for carrying out interventions, it is therefore particularly important to ensure adequate consent, discussion of targets of treatment and potential side-effects and to involve relatives in decisions, with careful documentation of this.

Patients in this group will frequently have significant comorbidities and before carrying out interventional procedures it is important to be aware of, and to document, neurological examinations and investigations, including clotting, platelet and neutrophil count. However, the context in which these procedures and their risks are being considered is very different from the non-cancer population, and this will affect treatment decisions [12], relative contraindications and consent [13]. A number of the treatments discussed involve off-licence use of drugs, useful guidance for which is given elsewhere [14].

Potential Interventional Techniques

There are a wide range of potential interventional procedures: this review concentrates mainly on those in common use in the UK. These include neuraxial delivery of analgesic drugs, and destruction of spinal and radicular nerve pathways; interruption of pain pathways travelling via the sympathetic nervous system, local anaesthetic and destructive techniques directed to peripheral nerves, and other procedures, including minimally invasive treatments directed at bony metastases and other pain sources.

Neuraxial Analgesia

General Considerations

In situations where pain control cannot be obtained using systemic opioid and other medications, or where control is limited by the side-effects of higher doses of systemic medications, it may be advantageous to target the dorsal horn mechanisms [15] of analgesia by administration of drugs by epidural or intrathecal routes. This may be with opioids, most commonly morphine, alone or in combination with other groups of agents. It has been estimated that 1–3% of patients with cancer pain may be suitable for spinal drug delivery [1,16].

Clinical spinal administration of opioids was introduced not long after the initial demonstration of spinal opioid receptors [17] and has been used increasingly commonly in recent years, with a substantial number of studies supporting its use: the use of spinal administration of opioids alone or combined with other drugs has been discussed in detail elsewhere [12,18–20].

Spinal Opioids

The most common drug used for spinal administration is morphine [21,22], although drugs such as diamorphine, fentanyl, sufentanil and hydromorphone have also been used.

Spinal use allows targeting of action at opioid receptors on dorsal horn pre- and post-synaptic neurons to modulate pain impulse transmission. Concentrating actions at the spinal level allows the use of smaller doses with fewer adverse effects than are caused by systemic administration of higher doses.

With epidural administration, the opioid must cross the dura and spread via the cerebrospinal fluid (CSF) into the spinal cord. Particularly with lipid-soluble opioids, epidural administration will result in uptake into epidural blood vessels and loss into the systemic circulation. As a result of this, dose requirements of epidural opioids will be greater than intrathecal: dose equivalences for morphine of 1 intrathecal: 10 epidural: 100 intravenous/subcutaneous or 300 orally are often used.

Less lipid-soluble opioids, such as morphine, which take longer to penetrate the cord, have a slower onset and longer duration and allow greater rostral spread within the CSF, increasing the potential for analgesia and avoiding the need
of the drug to be given at the spinal segmental level of the pain. Lipid-soluble opioids, such as fentanyl or sufentanil, have more localised actions and need to be administered closer to the appropriate spinal segmental level.

A number of studies have established that spinal administration of morphine [23] provides good to excellent pain relief, with increased activity and quality of life in patients with intractable cancer pain. A systematic review [24] supports intrathecal opioid therapy for pain inadequately controlled by systemic therapy.

A prospective, randomised, multicentre clinical trial [25] compared intrathecal drug delivery plus comprehensive medical management with comprehensive medical management alone, showing a reduction in pain and its improved control, reduced adverse effects and improved 6 month survival. Increased survival [26] may be associated with increased mobility and alertness, reduced anorexia and other adverse effects [25], and possibly the effects of systemic morphine on the immune system. (Similar effects have been noted with interventions such as coeliac plexus block [27].)

Opioids may be administered into the cerebral ventricular system [24,28], although this approach is not commonly used.

**Adverse effects of spinal opioids**

The most worrying side-effect is the potential for late respiratory depression, due to cephalad spread of opioids in the CSF [21]. However, this is very rare in these patients and may, in addition to a direct effect of the opioid in the CSF, be due to continuing effects of opioids given before the institution of the block, whose effect is potentiated once the pain is reversed. These patients are non-opioid naive and are less prone than the opioid-naive population to develop respiratory depression from spinal opioids.

Urinary retention, pruritus and endocrine abnormalities in chronic administration may also occur. In addition, similar side-effects to those seen in systemic opioid administration may occur, although in many studies the incidence and severity of these is lower given the reduced total doses given.

A rare complication is catheter tip-related granuloma formation in the cord [12,22], which is rare and related to a high opioid concentration in the infusate and increasing infusion duration: this is more a consideration for long-term administration in non-malignant pain rather than in the shorter-term cancer pain context. Although mostly reported with morphine, there have been reports with other opioids [29].

Morphine used alone spinally, although giving good analgesia in many patients, may be inadequate in up to 10–30% of patients [30]. In these circumstances, combination with other drugs, most commonly local anaesthetics or clonidine, may improve analgesia. Indeed, many centres now routinely start with combinations of drugs [31]. The use of other agents is reviewed in detail elsewhere [12,19,32].

**Local Anaesthetics**

The most common agent used is bupivacaine: there is little advantage to the use of other agents in this context. Local anaesthetics may be particularly useful in neuropathic pain. They act by blocking sodium channels and reducing nerve transmission: at a low dose their actions may be more through membrane stabilisation than sodium channel blockade [12].

Combination of opioids with local anaesthetics plus or minus clonidine can offer synergism [32,33] to allow lower overall doses and a reduced risk of side-effects, such as motor blockade, and can prevent morphine dose progression [34]. There is now considerable experience and evidence of safety in combination and prolonged use [35].

A further potential advantage of the addition of bupivacaine to the spinal infusion is its weak bacteriostatic effect [36], which may help to reduce the risk of infection.

Local anaesthetic needs to be administered in the spine close to the dermatomal level of the patient's pain. Catheters are often inserted at the lumbar level, but can successfully be placed at any level [37,38], although if the catheter is inserted at levels above the conus at L2, this is potentially at increased risk of cord damage. It is possible, particularly with reinforced catheters, to insert the catheter at lumbar levels and thread upwards successfully with imaging guidance.

Local anaesthetics may, at higher doses, give rise to weakness and sensory disturbance. At lower doses below 30–60 mg/day, however, this can normally be avoided [39]: it is more likely in patients with pre-existing nerve dysfunction from, for instance, lumbar plexus involvement with pelvic malignancies. There is also a potential risk of cord compression being wrongly attributed to the local anaesthetic: it is essential that in the event of unexpected worsening of weakness or sensory deficit, the infusion is turned off to ensure rapid recovery takes place.

In the event of very severe pain in the terminal stages of disease, when motor loss is less of an issue, the local anaesthetic dose can be increased to anaesthetic levels if necessary.

**Other Agents**

Clonidine is another commonly used secondary analgesic agent used in combination with morphine and local anaesthetics, with which it has synergistic effects. It has been shown to be effective in cancer pain [40]. It acts at alpha-2 receptors on pre-synaptic primary afferents and post-synaptic dorsal horn neurons, reducing the release of neurotransmitters, such as substance P and calcitonin gene-related peptide (CGRP), and pre-ganglionic sympathetic transmission. At higher doses it may cause postural hypotension and sedation.

A large number of other agents have been used as part of combined spinal analgesia, the use of which is reviewed in detail elsewhere [12,18,20]. These include midazolam and ketamine [41], although there are concerns about toxicity [42] and other adverse effects with their use. Baclofen [19] may be of use for spasticity. The voltage gated N-type calcium channel blocker ziconotide [43] shows benefit though this is limited by side-effects [44] (and cost) although recent consensus guidelines [12] suggested a role for its increased use.
Practical Considerations in Spinal Analgesia

Studies have suggested that opioids and other drugs administered intrathecally may give better pain relief than when given epidurally [31,39,45] and be less prone to complications [46,47]. In particular, epidural catheters are prone to blockage due to encapsulation and fibrosis around the tip of the catheter [39,48]. This may occur within 2 or 3 weeks of insertion and require resiting of the catheter or conversion to an intrathecal.

The larger dose and (of local anaesthetics) volume requirements of epidurals may prevent the use of implanted pumps and necessitate more frequent changes of reservoirs of percutaneous systems, with increased potential for infection and complexity of care [39].

Spinal drugs may be given using percutaneous catheters with external pumps, or fully implanted systems [21]. The latter may be constant flow or programmable pumps. External pumps are more commonly used in the management of cancer pain than implanted systems. This is related to the considerably greater costs involved in the latter, but also to the greater complexity of their implantation process in sick patients. It is often quoted that there is a threshold at around 3 months where the use of fully implanted systems, which carry lower risks of infection and technical complications, becomes preferable [49–51]. In our centre, the mean survival of patients after implantation of percutaneous tunnelled catheters has been 2.5 months (range up to 10 months); prediction of survival at the time of technique choice is difficult.

Percutaneous catheters can be maintained for considerable durations with meticulous care to monitor for, and avoid, sepsis [34,35]. This can be aided by the in-line use of 0.2 μm bacterial filters, strict asepsis and monitoring for signs of infection [39,52], minimum changes of tubing and the use of pre-prepared drug infusion bags.

Tunnelling catheters reduces the risk of displacement or infection [31]. Tunnelling to an exit site on the anterior upper chest allows easier hygiene and bathing, and is easier to manage.

Small and very portable battery-powered infusion pumps facilitate patients’ mobility: some have the facility for patient-controlled bolus doses, which can be beneficial for breakthrough pain [53,54] and can also increase a patient’s feeling of control over their pain.

Most patients with cancer wish to be managed and to die at home [55]. If it is proposed to discharge a patient home and to manage their pain there using continuous spinal analgesia, it is critical, before the procedure, to ensure that the home situation is suitable, and to ensure that the primary care team are trained and happy to manage the infusion. Clear lines of availability of the pain management or palliative care teams are critical to avoid problems and to ensure safety [22]. Nevertheless, these techniques can be very successfully managed on a domiciliary basis [35,56,57].

Safety and Complications of Spinal Drug Administration

Long-term use of intrathecal drug delivery is well established, with a number of reviews of safety and efficacy [21,22,36,39,48,57–60].

Post-mortem examinations of 15 patients who had received intrathecal infusion of bupivacaine and morphine (with preservatives) for a median of 81 days [61] showed subdural fibrosis (six), subarachnoid mononuclear cell infiltrates (10) and other changes, although no patient had shown any new neurological deficits related to the infusion. The preservatives in drug preparations may contribute to toxicity, and it is advisable that the solutions used are preservative-free [12].

In a prospective study of 209 cancer patients [62] using implanted pumps, catheter-related and other complications occurred at a rate of 0.45 events per patient year.

A prospective cohort study reviewed the management of 200 patients with cancer [57] who received spinal analgesics via tunnelled percutaneous catheters with bacterial filters over 14 485 days, both in hospital and at home. A standardised protocol for nursing care with careful asepsis was followed. Ninety-three per cent of the patients had what was described as perfect function of the system. Post-dural puncture headache occurred in 15.5% and other complications were unusual, including meningitis (0.5%), epidural haematoma from injury of an unknown tumour (0.5%) and displacement (1.5%). These figures broadly concur with other publications [63]. More recent studies and systematic reviews [56,64] also show a very low incidence of infection, CSF leak or other complications.

Infection and potential meningitis [65], although relatively unusual, are a major concern. A systematic review of 12 studies on indwelling epidural catheters, including a total of 4628 patients [66], revealed 257 catheter-related infections in total: 211 superficial and 57 deep – the incidence of deep infection was 0.4 per 1000 catheter treatment days.

Meticulous aseptic management and attention to detail are essential in the management of these patients [67]. There is little published evidence about the use of antibiotic prophylaxis [22]. If infection does occur it may be necessary to remove the catheter, although in some circumstances at the end of life it may be appropriate to take the decision to continue rather than lose control of pain: intrathecal and systemic antibiotic treatment may be given [18].

In patients implanted with intrathecal catheters, with breach of the dura, there is the potential for more severe infective complications and meningitis, although epidural abscesses too may be difficult to manage.

CSF leaks and post-dural puncture headaches may occur with intrathecal catheters [39]. These headaches are normally self-limiting to within days after insertion [22], although on occasion an autologous epidural blood patch [18] may be necessary: fibrin glue has been used as an alternative to this [68].

Contraindications

Clotting abnormalities should be corrected before implantation, and local sepsis near the insertion site, or
systemic sepsis, are contraindications to implantation in non-malignant pain and normally in malignant pain. As discussed above, the context in which these procedures are being considered differs from that of non-malignant pain, and some conditions may be relative rather than absolute contraindications: a documented thorough and detailed discussion and consent with the patient and relatives is important.

Spinal and epidural metastases have been reported as a reason for failure of spinal analgesia [22,69]. In patients with these it may be advisable to insert the catheter cephalad to the tumour in case of obstruction.

**Nerve Block and Destructive Techniques**

Blockade of nerves is a common practice in pain medicine and a range of nerves can be targeted, from peripheral nerves to sympathetic nerves and proximally to the spinal nerve roots. Blockade may be with local anaesthetic with or without the addition of corticosteroid, and local anaesthetic blocks to areas such as the brachial plexus [70] may be extended with the use of implanted catheter techniques. Although not supported by strong evidence, procedures such as epidural or paravertebral blocks with local anaesthetic and steroid are commonly carried out for vertebral cancer-induced bone pain [22,71], and can give useful duration of benefit in a number of patients.

It has been observed that both central [72] and peripheral [73–75] nerve blocks can give analgesia of duration considerably in excess of that of the local block – possible mechanisms for this include a reduction in central sensitisation mechanisms or a reduction in local nerve excitability. There is some evidence that the duration of benefit from nerve blockade may be prolonged by the addition of corticosteroid to the local anaesthetic [76,77], particularly when the nerve itself is involved in a pathological process; possible mechanisms include suppression of ectopic neural discharges from injured nerve fibres [78].

More permanent blockade of neural tissue may be carried out using neurolytic agents or with thermal methods using heat (radiofrequency ablation) or cold (cryoneurolysis) [79]. These methods aim to cause Wallerian degeneration of the nerve fibre, interrupting pain impulse transmission. The damaged nerves tend to regrow over months, with the potential for the return of pain.

The main chemical neurolytic agents used include phenol (7–12%) and ethanol (50–100%). These agents also have a potential, particularly when used on somatic rather than sympathetic nerves, to give rise to neuritis, which can itself give pain. In addition, the loss of afferent sensation and the nerve destruction process can itself lead, after some months, to the development of neuropathic pain.

Cryoneurolysis uses a probe whose tip is cooled towards –70 °C by the expansion of pressurised nitrous oxide in its tip, which causes freezing and ice crystal formation within the axon. Radiofrequency ablation is the destruction of neural tissue with heat generated within tissues by a high-frequency electrical current. Feedback via a thermocouple in the needle tip allows accurate control of the temperature, normally 44–80 °C. Radiofrequency ablation is used in lesioning in the central nervous system, notably percutaneous cordotomy.

A more recent modification of radiofrequency ablation is the use of pulsed radiofrequency [80,81], where the temperature at the needle tip is held below 42 °C to avoid neural damage. Its mechanism is unclear, possibly altering descending or dorsal horn modulation of pain impulse traffic or selectively impairing C fibre transmission of pain. There have been no controlled studies on pulsed radiofrequency in cancer specifically: a report of three cases [82] described the benefit.

Radiofrequency ablation of other areas, such as the trigeminal ganglion, has been extensively used for trigeminal neuralgia, and has also been used with benefit in head and neck cancer [83]. Radiofrequency ablation and cryolesioning have also been used for the treatment of lesions such as bone metastases, as discussed below.

**Neuraxial Neurolytic Blockade**

The use of spinal neurolysis [84] has become less common in recent years [85], largely because of increasing expertise in neuraxial analgesic infusion, but also because of the potential for inadvertent motor blockade and interference with bladder or bowel function. The relative hyperbaricity of phenol in glycerin can be used in the semisupine patient to aim to give selective unilateral sensory root block. Another specific use can be in carrying out a saddle block [86,87], preferentially for the sacral nerve roots in advanced perineal malignancy, this being appropriate in patients where urinary and bowel control is not an issue. In addition, neurolytic agents may be introduced into the epidural space [85] to target spinal nerve roots as they exit through it, either by bolus injection or by the introduction of catheters into this space, or by transfemoral injection [88].

**Percutaneous Cordotomy**

Percutaneous cervical cordotomy is applicable to unilateral pain below the level of C5, and is achieved by inserting a needle into the anterolateral aspect of the cord on the side opposite the pain, into the spinothalamic tract, under image intensification. Radiofrequency thermal lesioning is carried out after ensuring correct positioning by electrical stimulation.

Bilateral procedures are more prone to adverse effects [89], particularly interference with respiratory control with the potential for sleep apnoea, and are not normally carried out. Cordotomy at lower spinal levels is a far more invasive procedure and is rarely carried out. Other techniques have been reported [90] in attempts to avoid adverse effects.

This procedure can be particularly useful for conditions such as mesothelioma [91]. In a series of 43 patients with severe unilateral pain due to cancer [92], resistant to systemic therapy, a good result was obtained in 95%, sustained in 69% at the end of life.
Unfortunately, expertise in cordotomy is only available in a few centres in the UK and access to the procedure is difficult or impossible in many localities [7,8].

Spinal Cord Stimulation

Spinal cord stimulation [93] involves the implantation of stimulating electrodes in the epidural space at a spinal level where evoked sensations refer to the area of the pain. Its mechanism is unclear, but it probably works by recruiting inhibitory mechanisms in the cord. Electrodes are normally inserted percutaneously and then connected to an implanted pulse generator. Spinal cord stimulation is not often used in the cancer pain context [94], and its use is not supported by randomised controlled trial evidence, although there have been some individual case reports [95,96].

Neurolytic Sympathetic Blocks

Pain from malignant involvement of visceral organs is conveyed along sympathetic pathways and may be amenable to interruption of these pathways [97]: this is most commonly by chemical neurolysis using alcohol or phenol or alternatively using radiofrequency thermal lesioning [98]. The two main areas that may be interrupted in this way are the coeliac plexus and splanchnic nerves, and the superior hypogastric plexus. Although there have been reports of destructive lesioning of the stellate ganglion for cancer pain, this is not commonly used, particularly given the risk of damage to neighbouring structures. Interruption of these pathways, although often not fully removing pain, will frequently allow improved analgesia and a reduction in analgesic drug doses and resultant side-effects.

Coeliac plexus and splanchnic nerves

The most common neurolytic sympathetic block carried out in this context, and for which there is the strongest evidence, is of the coeliac plexus [99]: this may be used for relief of pain from pancreatic and other upper abdominal malignancies.

The splanchnic nerves arise bilaterally from the sympathetic chain on the lateral aspect of the lower thoracic vertebrae and pass anteriorly through the crura of the diaphragm to form the coeliac plexus, which lies retroperitoneally anterior to the aorta around the origin of the coeliac artery at the level of the T12 and L1 vertebrae. This carries afferents, which traverse the plexus without synapse, from the pancreas, liver and biliary tract, upper renal tract and bowel down to the mid-transverse colon.

Various approaches have been reported for access to the coeliac plexus [100,101], commonly used ones being posterior transcrural with fluoroscopy guidance, or alternatively to the splanchic nerves, although other approaches, such as with ultrasound guidance either percutaneously or endoscopically [102,103], or using an anterior approach with computed tomography [104] or magnetic resonance imaging guidance, have been reported. Needle positioning may be confirmed by the spread of radiological contrast medium. For neurolytic blocks, the most commonly used agent is 50–100% alcohol, 20–25 ml per side. Because this is painful, it is preceded by an injection of local anaesthetic.

A number of studies have examined the benefits and risks of coeliac plexus neurolytic blockade. A meta-analysis [99] examining data on 1145 patients from 24 studies concluded that this intervention provided long-lasting benefit for 70–90% of patients with pancreatic (63%) and other upper abdominal cancers. Good to excellent pain relief was reported in 89% of patients during the first 2 weeks after block performance. Pain relief persisted in 90% of the patients who were alive at 3 months after the procedure. A randomised placebo-controlled double-blind prospective study [105] of 100 patients showed significant sustained improvement in pain relief or until death. A comparison with oral opioid therapy [106] concluded that coeliac plexus neurolysis resulted in a reduction in visual analogue scale pain scores equal to oral treatment with non-steroidal anti-inflammatory drugs and opioids, but the oral therapy group had higher opioid consumption and a greater incidence of side-effects. A similar study comparing early sympathetic blockade with systemic treatment gave similar results with, in addition, a significantly better quality of life in the neurolytic block groups [107].

The side-effects of coeliac plexus block [99] may include diarrhoea, more common with retrocrural techniques; temporary postural hypotension, more common with retrocrural techniques [101]; back pain and dysaesthesia. More severe adverse effects include temporary or (considerably rarer) permanent motor deficit, probably due to spasm of the anterior spinal artery causing anterior spinal cord ischaemia. Haematuria, haemorrhage, aortic dissection and impotence have been reported. In a review of complications of 2730 patients [108], the overall incidence of major complications was one in 683 procedures, with paralysis as high as one in 700.

There has been debate about the need to carry out a diagnostic local anaesthetic block before neurolytic blockade: its predictive value is questioned and this block is often omitted.

Superior hypogastric plexus and lumbar sympathetic chain

The superior hypogastric plexus carries afferents from the viscer of the lower abdomen and pelvis, and is positioned retroperitoneally bilaterally anterior to the L5/S1 disc and vertebrae. Neurolytic blockade of this plexus may be used to reduce pain resulting from malignancy in these organs.

A cohort study of 227 patients [109] with advanced pelvic cancer of gynaecological, colorectal or genito urinary origins examined the effect of superior hypogastric plexus block. A diagnostic local anaesthetic block failed to give relief in 21%: the remaining patients were treated with one or two neurolytic blocks. Of the group receiving blockade, 72% had good and 28% moderate pain control. Benefit was maintained at 3 months, and of the responders, all patients significantly reduced their opioid intake. Similar results were reported in a previous study on a smaller cohort reported by the same group [110]. No complications related to the block were detected in either of this group's studies, and this has been the case in other reports [111].
Bilateral L5 sympathetic neurolysis has been used as an alternative to superior hypogastric plexus block and may be technically easier. Neurolytic blockade of the lumbar sympathetic chain [112] has been used for pain from urological cancers and for renal pain, as well as pain resulting from critical ischaemia of the lower limbs.

The ganglion impar or Walther’s ganglion, the unpaired midline termination of the sympathetic chains, is located in the post-rectal space just anterior to the sacrococcygeal junction and receives afferents from the rectum and lower bowel. Neurolytic blockade of this ganglion has been used in rectal malignant pain [113,114] and for the pain of radiation proctitis.

**Peripheral Sites**

Overall, ‘one shot’ peripheral nerve blocks have only a limited role in cancer pain. However, they can be of use in providing short-term analgesia, while control of pain is gained by other means, and as noted above they have on occasion been noted to give prolonged analgesia.

Catheterisation and prolonged blockade of nerve plexuses and other peripheral nerves for the management of cancer pain have been reported [13,41,115], as well as implantation of catheters into the interpleural space [116,117] to allow diffusion of agent through the parietal pleura to anaesthetise the intercostal nerves: this may also diffuse onto and block the thoracic sympathetic chain on the lateral aspects of the vertebral bodies.

The only commonly used site for peripheral neurolysis is the intercostal nerves, which may be of use for relatively short periods of several weeks [118]. This carries a risk of neuritis, which may approach 30% [119]; this may be less with cryoneurolysis, although chemical neurolysis was more effective than cryoneurolysis in one case series [120].

**Myofascial trigger points**

The development of myofascial trigger points, localised painful areas of contraction in skeletal muscles, is a common secondary phenomenon in patients with cancer pain. Local anaesthetic infiltration of trigger points may give prolonged relief of pain [121]. Botulinum toxin and dry needling techniques similar to those used in acupuncture have also been used for trigger point deactivation: acupuncture in general, while sometimes being useful particularly for secondary myofascial trigger point pain, is not supported by strong evidence in malignant pain [122].

**Bony metastases**

There has been increasing interest in the use of minimally invasive techniques in the management of bony metastases, this falling within the remit of interventional radiologists, orthopaedic surgeons and pain physicians.

Bony metastases are a common source of pain. Case series of intraleisional injection with steroids [123,124] have given up to 70% prolonged relief. A case series of intraleisonal injection of ethanol [125] under computed tomography guidance gave a reduction in analgesic requirements in 74% of patients.

Other minimally invasive approaches have also been reported for bony metastases, such as radiofrequency with or without cementoplasty [126,127] and acetabuloplasty for pain from metastatic involvement in this area [10]. Pain arising from metastases close to joints such as the sacroiliac or hip may also be helped by local injection of the joint with steroid [128].

Vertebral metastases may give rise to severe movement-related pain, which is often very difficult to manage with radiotherapy or drugs. These are increasingly being managed with percutaneous vertebral augmentation [129]. These techniques involve percutaneous insertion of a cannula under image guidance into the vertebral body, normally via the pedicle, although an anterior approach can be used in the cervical spine. Once the correct position is confirmed, polymethyl methacrylate cement is injected (vertebroplasty [130]) or this is preceded by expansion of the vertebra by inflation of a balloon (kyphoplasty).

A case series of 283 patients [131] showed substantial pain relief in 86% over a median follow-up of 7 months. A systematic review of studies with these procedures [132] showed a high proportion of pain relief, including 87% with vertebroplasty and 92% with kyphoplasty. The degree of relief may be marked or complete [133]. Cement leaks are commonly reported [132], although complications of these, although potentially severe, are rare.

The benefit of these procedures is not solely explained by treating vertebral collapse, as very small doses of methylmethacrylate may give good pain relief [134] — other postulated mechanisms include microfracture stabilisation, thermal or cytotoxic destruction of tumour cells or interference with tumour blood supply.

Although it carries a higher risk of cement leak than kyphoplasty, vertebroplasty is less time consuming, and more likely to be carried out under local anaesthetic/sedation and therefore to be appropriate for patients with advanced disease [10]. It has recently been recommended that patients with difficulty controlling pain from vertebral secondaries should be referred for consideration of vertebroplasty if locally available [10].

**Conclusion**

Although most patients with cancer pain are well managed with traditional and adjuvant analgesics, there are a significant minority in whom this is inadequate or limited by adverse effects. For these patients the use of interventional techniques may prove an important and successful part of multimodal symptom control. The range of potential techniques is wide, and an awareness of these is important for all those involved in the management of these patients. Pain medicine specialists will continue to play a significant role in this management [135].

**Conflict of Interest**

The author confirms that there is no conflict of interest.


