The British Pain Society's

Cancer Pain Management

A perspective from the British Pain Society, supported by the Association for Palliative Medicine and the Royal College of General Practitioners

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Chapter 8  Invasive procedures for cancer pain

Summary

Patient selection for an interventional procedure requires knowledge of the disease process, the prognosis, the expectations of patient and family, a careful assessment and discussion with the referring physicians. There is good evidence for the effectiveness of a coeliac plexus block and intrathecal drug delivery. Safety, aftercare and the management of possible complications have to be considered in the decision-making process. 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.

8.1 Introduction

- This chapter focuses on the interventional procedures that are considered to be the most effective. It deals with the pharmacological blockade of neural tissue by targeted injection or infusion; their destruction by chemical, physical or surgical methods; and the fixation of vertebral compression fractures.

- For a few procedures (coeliac plexus ablation, intrathecal infusions, see below), there is controlled trial evidence in cancer populations. For most procedures, there is less robust evidence of largely uncontrolled case series.

- A pragmatic approach is required when deciding whether to offer such therapies. The likely benefits and possible risks need to be considered and compared with those of continuing with pharmacological management. Typically, interventional management of cancer pain does not substitute for other modalities, but can improve pain relief and allow for a reduction in systemic medications and their side-effects.

- A careful assessment of the pain should be undertaken by an interdisciplinary team, usually including specialists in pain, palliative care and nursing, although the team might include others. Practical factors should be considered, such as the discharge home, as well as patient and family preferences. Complex situations will often require high-level discussion (Chapter 13).

- It has been traditional to consider exhausting oral or topical analgesia before considering invasive methods; however, this is not always in the patient’s best interests. Where there are unacceptable side-effects from opioids, such as drowsiness, then invasive methods may be preferred; while a pump implanted early in advanced cancer can allow for the maximum benefit to be obtained.

- This chapter aims to provide information related to benefits and adverse effects for interventional procedures commonly used in cancer pain management.

8.2 Types of interventional procedures

- These most typically involve interruption to or modification of nerve conduction, with the aim of diminishing pain from a target area. The nerves involved include those of the peripheral, autonomic and central nervous systems.
The procedures may be considered to be non-destructive or destructive. In non-destructive procedures, nerve blockade or modulation is achieved by the deposition of reversible pharmacological agents. These may be provided by bolus injection and most commonly involve local anaesthetic agents, often supplemented by depot steroids. Alternatively, catheter placement allows for the continuous delivery of agents. When placement is adjacent to peripheral or autonomic nerves, similar agents are used. For catheter placement in the spinal canal with the aim of modulating neuronal activity of the spinal cord, different agents are used. These are most commonly opioids, often supplemented by local anaesthetics and/or the alpha-2 adrenergic agonist, clonidine. More recently, the voltage gated calcium channel blocker, ziconotide, has been introduced (Staats, 2004).

- The destructive procedures involve the use of chemical agents (alcohol 50-100% and phenol 6-10%), physical methods of heat (radiofrequency) and cold (cryoablation) and surgery.

Destructive procedures must only be provided by appropriately trained personnel, and are best offered within a multidisciplinary framework of care that recognises the psychosocial components of the pain experience. Failure to do so is likely to reduce the efficacy of such procedures.

- Patients should be thoroughly informed about any likely sensory deficits and possible complications.

- In most cases, destructive procedures should first be simulated with a local anaesthetic to allow the patient to experience the sensory changes that may occur (Cousins, 1998).

- The patient should be closely followed as an inpatient for several days after the destructive procedure, with close monitoring and planned opioid reduction in order to avoid drowsiness and respiratory depression when the respiratory stimulation of pain is removed.

### 8.3 Peripheral nerve blockade

Peripheral nerve blocks have a limited role in cancer pain management. There is no controlled trial evidence, but case series describe pain relief for a short time with the local anaesthetic blockade of the regional nerve supply of a target area. They may therefore be useful for perioperative pain and other acute cancer pains, such as pathological rib fracture (intercostal nerve blockade). This may be achieved by the bolus injection of local anaesthetic. It is often supplemented with depot steroid with the aim of providing longer term relief, but there is no evidence to support this practice for peripheral nerves (McCarrberg, 2007). Alternatively, catheter infusions of local anaesthetic adjacent to the brachial plexus (Vranken, 2000) or other nerves may prolong the pain relief (Cooper, 1994; Amesbury, 1999).

- Neurolytic blockade of peripheral nerves produces short-term relief; for instance, intercostal neurolysis has a median duration of 3 weeks (Wong, 2007). Although this study found no incidences of neuritis, the survival time was short, and others have reported an incidence of neuritis of 30% (Doyle, 1982). Neurolytic agents should be limited to those with a short life expectancy.

### 8.4 Autonomic nerve blockade

It is known that the sympathetic nervous system carries pain afferents from the viscera and that blockading these can reduce pain.
8.4.1  Coeliac plexus ablation

- The coeliac plexus carries visceral afferents from several abdominal organs, including the pancreas, liver biliary tract, renal pelvis ureter, spleen and bowel up to the first part of the transverse colon.

- The injection of a neurolytic medication around the coeliac plexus has been most investigated for pancreatic cancer pain, but a role has been found for other upper gastrointestinal malignancies, such as gastric cancer, oesophageal cancer, colorectal cancer, liver metastasis, gallbladder cancer and cholangiocarcinoma (Eisenberg, 1995).

- Access to the plexus is most commonly posterior, with needle placement in front of or posterior to the crura of the diaphragm (Weber, 1996). However, other approaches are used such as anterior (Lieberman, 1988), endoscopic (Abeldi, 2001) and transdiscal (Ina, 1996). Imaging most commonly involves fluoroscopy, but some of the alternatives used include computerised tomography (Haaga, 1984) and MRI (Hol, 2000). Whilst there is no apparent difference in outcome between these methods, they do allow for access in certain individuals where fibrous infiltration or tumour invasion may distort the anatomy affecting neurolytic spread (Akhan, 1997; DeCicco, 2001), or may be valuable when patients cannot lie on their front (Perello, 1999).

- In a single blind randomised controlled trial of 100 patients with pancreatic cancer, neurolytic plexus ablation was compared with pharmacological management combined with sham procedure. Pain relief was better in the interventional group for 6 weeks (Wong, 2004). A meta-analysis (Yan, 2007) of 5 randomised controlled trials of coeliac plexus ablation found significantly improved pain relief when compared with pharmacological management or local blockade of the plexus for 8 weeks, with reduced opioid consumption in the ablation group.

- Up to 30% of patients experience hypotension after a coeliac plexus block due to the loss of sympathetic tone and splanchnic vasodilatation (Fugere, 1993). This reaction usually manifests itself within the first 12 hours. Up to 60% of patients report diarrhoea resulting from a sympathetic blockade and unopposed parasympathetic efferent influence after coeliac plexus block, which usually resolves within 48 hours (Hastings, 1991). Neurologic complications, including paraplegia, leg weakness, sensory deficits and paresthesias have been reported after coeliac plexus ablation, with a large study reporting four cases of paraplegia after 2730 coeliac plexus blocks (Davies, 1993). Paraplegia was attributed to either direct injury of the spinal cord during the procedure or spinal infarction secondary to spasm of the spinal artery.

- Theoretically, radiofrequency splanchnic denervation should avoid the risk of such paraplegia (Raj, 2002), but the outcome is less studied. It may be an option when the relative risks are discussed with the patient.

8.4.2  Superior hypogastric plexus block

- The superior hypogastric plexus carries afferent from the bladder, uterus, vagina, prostate, testes, urethra, descending colon and rectum. Superior hypogastric block may relieve pelvic pain and a block of these nerves has been described as reducing pain associated with pelvic malignancy (Plancarte, 1997). The posterior approach is commonest, but an anterior approach has been described (Kanazi, 1999).
8.4.3 **Ganglion impar block**

- This is the most inferior sympathetic ganglion, lying anterior to the sacrococcygeal junction. It has been shown in case series to provide pain relief for patients with advanced cancers of the pelvis and perineum, after abdominoperineal resection for rectal cancer (Plancarte, 1997) and following radiation proctitis (Rabah, 2001).

8.5 **Neuraxial blocks**

- Neuraxial blocks may be epidural (outside the theca or dura mater) or intrathecal (into the cerebrospinal fluid).

- Epidural local anaesthetic and steroid can provide temporary pain relief where a vertebral metastasis is associated with nerve compression.

- Care should be exercised if an impending cord compression or an invasion of the epidural canal by a tumour is suspected, and imaging may be advisable in such circumstances.

- Despite the lack of evidence to support these interventions, several experienced practitioners have used and continue to use these techniques with reported benefit to patients. Epidurals with steroid and local anaesthetic can provide temporary pain relief.

8.5.1 **Intrathecal and spinal nerve root neurolysis**

- A saddle block with heavy intrathecal phenol can be used for perineal pain of somatic origin in advanced pelvic cancers, especially where bladder and bowel function are already compromised.

- Chemical neurolysis of spinal nerve roots is used less frequently than in the past, since safer interventions (e.g. neuraxial infusions) have been developed. Whilst there are case series describing the effective relief of pain, the duration is limited and the incidence of neurological deficits is high (Lynch, 1992).

8.6 **Neuraxial infusions**

- Some patients with advanced cancer may have pain which cannot be controlled with systemic medications, or the use of these medications may be limited by unacceptable side-effects at doses below those required to give adequate relief. For these patients, the administration of drugs by the spinal route, either epidurally or intrathecally, may be required and gives good control in the majority of cases (Baker, 2004).

- There are different types of procedures, ranging from percutaneous lines to fully implanted programmable pumps. The fully implanted systems carry less risk of infection and have lower maintenance, but the operation is more prolonged (Williams, 2000). The costs of the therapy currently suggest that implanted systems are more cost effective than the percutaneous after 3 months (Mueller-Schwefe, 1999).

- There is evidence from randomised controlled trials of improved pain relief and less drug-related side-effects compared with medical therapy for fully implanted systems. The reversal of drowsiness associated with systemic opioids is of great practical significance (Smith, 2002, 2005; Staats, 2004).
• These procedures carry a moderate level of minor adverse effects and a low level of serious adverse effects (Williams, 2000). They should be reserved for those patients whose pain cannot be controlled with systemic analgesia and undertaken in centres experienced with the techniques and with aftercare (British Pain Society, 2008).

• The most effective drugs are opioids, commonly morphine, and generally patients who respond to spinal morphine are those who only partially respond to systemic morphine and/or are limited by dose-related side-effects. Patients who are unresponsive to large doses of systemic opioids are unlikely to respond to spinal opioids. Other drugs that appear to be effective spinally include local anaesthetics (typically bupivacaine) (Van Dongen, 1999), alpha-2 agonists (clonidine) (Eisenach, 1996) and ziconotide (Staats, 2004). In a randomised placebo controlled study of Ziconotide in ill patients, 50% on active therapy vs 17% on placebo achieved greater than 30% pain relief. However, 30% on ziconotide against 10% on placebo experienced “serious” side-effects, while 38% of those on ziconotide discontinued treatment and follow-up was generally thought to be too short. Fuller details of the use of intrathecal therapies can be found elsewhere (British Pain Society, 2008).

• Intraventricular opioids can be administered via an implanted pump and catheter for pain in the head and face. Cerebrospinal fluid diversion via a shunt or third ventriculostomy may be appropriate for palliation in some cases of obstructive hydrocephalus that are otherwise inoperable; craniotomy and subtotal removal of a malignant cerebral tumour is a routine neurosurgical palliative procedure.

8.7 Domiciliary Management of Spinal Catheters

Most patients want to die at home (Higginson, 1998), and while the safe management of spinal drug infusions does present challenges to this, these can be overcome to facilitate this aim (Gestin, 1997). In addition, with percutaneous drug delivery, intrathecal use allows lower dosage and therefore longer intervals between infusion refilling of ambulatory pumps, facilitating home care and reducing the risk of infection. Intrathecal catheters may be less prone to dislodgement and blockage due to fibrosis (Crul, 1991), and have been shown to be safer in the domiciliary setting (Nitescu, 1990).

8.7.1 Preparation

• Full involvement of the primary care team in the management of pain is vital. If, when considering the use of spinal drug delivery, management at home is identified as a priority, it is essential to establish that the patient and family are suitable and have appropriate goals and expectations. The community nursing and primary care teams should be happy to co-operate and be involved.

• Psychological assessment should be considered once pain has been relieved and sedation due to analgesics minimised, since some patients may be less distracted from the other psychological aspects of their illness. This can lead to difficulties with good symptom control. Full discussion and consent from the patient and family, taking factors such as these into consideration, is essential.

8.7.2 Procedure

• Percutaneous catheters, injection portals or fully implanted systems may be used, but a factor in patient selection is the shorter expectation of survival in this group compared with patients with non-malignant pain. Percutaneous catheters may be tunnelled or non-tunnelled; tunnelled catheters are less prone to displacement and infection (Baker, 2004).
• Implantation and other procedures are ideally undertaken in a sterile facility with resuscitation facilities in a hospital or hospice. Insertion as a domiciliary procedure has been reported (Mercadante, 1994), but this does raise issues with sterility and the ability to resuscitate in the event of side-effects.

• Very compact and reliable battery-powered infusion pumps are available that allow both continuous and patient-controlled bolus drug administration.

8.7.3  Aftercare

• It is imperative that those who will be involved in the patient’s management at home are fully trained and confident in the necessary techniques and knowledge before discharge. The patient’s management should also be stabilised as an inpatient or in a hospice prior to discharge home, with titration down of systemic analgesics to avoid opioid overdosage in particular (SIGN, 2000). The co-operation of the patient’s general practitioner and out-of-hours service is important, and this is supported by the availability of detailed guidelines or protocols and back-up from members of the specialist pain or palliative care team is essential (British Pain Society, 2008). This should be recognised in job plans.

• With appropriate training and compliance with competencies, the refilling of infusion reservoirs can be performed by community nursing staff, as well as monitoring of the patient’s condition, particularly pain relief, temperature and the state of implantation sites. Again, guidelines or protocols should support this.

8.10  Anterolateral cordotomy

• This can be undertaken as a percutaneous or open procedure, involving intervention on the side of the spinal cord opposite to that of the pain to ablate the spinothalamic tract fibres. Consequently, it reduces the sensation of touch and temperature in addition to pain.

• The awake percutaneous procedure ablates the spinothalamic tract using radiofrequency lesioning through a needle inserted between the first and second cervical vertebrae. Its value in mesothelioma is well documented (Jackson, 1999), and its use in other lateralised pains is recognised (Crul, 2005).

• Immediate pain relief is achieved in the majority, with 80% either stopping or reducing opioids; but pain recurs in a third of these after six to twelve months (Jackson, 1999). The main risk is of weakness of the leg contralateral to the side of the pain through damage to the corticospinal tract; mild effects are seen in up to 8-10% in the first few days, but prolonged effects are reported in only 1-2% (Crul, 2005). This risk increases, for topographical reasons, when the lower sacral dermatomes are targeted. Painful dysaethesias occur in about 5% of cases (Jackson, 1999).

• While percutaneous cordotomy can only be performed in the cervical area, the spinothalamic fibres can be divided by open operation in the thoracic cord. This avoids the risk to respiration and to the upper limb when the pain is below the waist (e.g. secondary to invasion of the lumbosacral plexus and is recommended for bilateral procedures to avoid fatal sleep apnoea). In a small series (Jones, 2003), no patients experienced motor weakness and all had complete or nearly complete and sustained relief of the target pain, allowing a substantial reduction in medication for all but one. This released them from being closely tied to the hospital/hospice, allowing greater freedom and independence, which was dramatic in some cases (e.g. holidays abroad). There were no new sphincter disturbances reported.
8.9 Midline myelotomy.

- Splitting the spinal cord in the midline posteriorly was intended to divide the spinothalamic fibres as they crossed, thereby controlling bilateral pain while simultaneously avoiding the risks of bilateral cordotomy. Introduced in 1926, it was not particularly successful until the serendipitous observation in 1970 that a single level myelotomy at C1 produced analgesia over a wide body area. It was subsequently found that a limited midline myelotomy at T10 was effective against pelvic visceral cancer pain (Gildenberg, 1991). The recent discovery of a specific pathway in the medial dorsal columns, which conduct visceral pain (Hirschberg, 1996), provides a possible substrate for this operation which appears to be very effective and safe (Nauta, 2000), but is rarely used.

8.10 Other neurosurgical procedures

In the past, many surgical targets in the brain have been tried with varying degrees of success and morbidity, but none is now used more than sporadically. They include sites in the medulla, pons, midbrain, thalamus and hypothalamus, as well as the somatosensory and cingulate cortices. The pituitary gland provided one of the most useful targets; transnasal alcohol-induced hypophysectomy was very effective against hormone-dependant and diffuse cancer pain, particularly when this resulted from bone metastases from breast and prostate. Diabetes insipidus occurred in half the patients and visual disturbances were common; pharmacological hormonal manipulation has made this redundant. Dorsal root entry zone (DREZ) lesions are rarely used for cancer pain. An extensive laminectomy is required, the morbidity is relatively high, only paroxysmal pain responds well and cordotomy or rhizotomy are likely to be preferable.

8.11 Vertebroplasty

Painful pathological fractures of vertebra that do not respond to the conservative therapies of medications, TENS or steroid epidurals can be considered for fixation by cemented vertebroplasty. Open studies in myeloma and metastatic cancers report pain relief that is often complete in around 80% of patients (Gangi, 1999; Fourney, 2003; Dudeney, 2002). Cement leak is the commonest risk at around 5%, and complications from this are rare but serious (Hentschel, 2005).

References


Further reading

