Does pethidine still have a place in therapy?

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SYNOPSIS

In chronic pain management, the general consensus at present is that pethidine has no role to play. There is a myriad of other options including spinal implants, long-acting opioid preparations for nociceptive pain or the newer drugs for neuropathic pain. In all cases ruling out new or undiagnosed pathology and early consideration of the role of psychosocial factors is important. Pethidine can be used to treat acute pain for a short time. After this time other options should be considered due to the risk of accumulation of norpethidine and the potential adverse sequelae. If pethidine is used in episodes of recurrent pain such as migraine, patients can become overly reliant on this medication. The resultant drug-seeking behaviour can be very difficult to treat.

Index words: analgesia, morphine, pain.

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Introduction

Pethidine is a synthetic opioid analgesic. There is no doubt that it is an effective analgesic but there is a significant potential for the development of dependence and drug-seeking behaviours. Once these are established they may be very difficult to address. The other significant concern is the potential for toxicity due to the accumulation of its metabolite norpethidine after repeated administration.

Pharmacology

The effects of pethidine are generally similar to those of morphine, despite its different structure. It also has local anaesthetic and atropine-like effects. Pethidine is readily absorbed orally, but its bioavailability is only about 50%. In the acute pain setting, pethidine can be administered by intramuscular injection, patient controlled analgesia, and also intraspinally, for example epidurally after Caesarean section.

Pethidine has a half-life of 3–5 hours and useful analgesia lasts between 2 and 4 hours after parenteral administration. Given at this frequency the active metabolite norpethidine (half-life 8–21 hours) accumulates (particularly in renal failure). This may lead to potentially serious adverse effects including tremor, twitching, agitation, confusion and (rarely) fitting. Norpethidine is estimated to possess half the analgesic potency of pethidine but twice the convulsive potency.[1]

Pethidine has some clinically significant drug interactions. Phenobarbitone and chlorpromazine enhance the production of norpethidine, and pethidine should not be given to patients taking monoamine oxidase inhibitors because of the risks of respiratory depression, hypertension and possibly coma.

Acute pain

Pethidine is effective for intra-operative and postoperative analgesia and is used as a premedication. In acute pain pethidine acts on opioid receptors to inhibit pain-generating impulses in afferent Aδ and C fibres. At equi-analgesic doses pethidine produces less smooth muscle contraction in the biliary tract and less of a rise in the common bile duct pressure than morphine.[1] It also causes less urinary retention and constipation than morphine. Pethidine is not recommended for conditions such as migraine.[2]

Alternatives to pethidine for acute pain

For acute pain states there are a number of alternatives including other opioid analgesics, non-steroidal anti-inflammatory drugs, simple analgesics, regional anaesthetic techniques and intraspinal techniques (intrathecal and epidural administration). While pethidine remains a useful drug in the peri- and postoperative period it should not be used for more than 72 hours, with further caution exercised in those patients requiring higher than normal doses, or in those with renal failure.[3] Such patients should be changed to a different analgesic regimen and if necessary assessed by an acute pain team if one is available. However, the evidence for the risk of adverse events attributable to norpethidine is not clear. Patients may experience adverse effects due to norpethidine toxicity in shorter time frames and with relatively low concentrations of norpethidine.[3]

Chronic pain

Epidemiological data show that 20% of the population experience chronic pain and that approximately 10% of the population are significantly distressed and disabled by chronic pain.[4] In contrast to acute pain, research suggests that chronic pain is likely to be less sensitive to opioids. For example, nerve injuries are associated with up to a 70% reduction in presynaptic opioid receptors and the presence of substances such as cholecystokinin, which may reduce opioid sensitivity.[5]

There is a surprising lack of clinical studies showing that opioids reduce pain and improve function in patients with chronic pain. One study found nearly 60% of patients attending a pain clinic were taking opioid analgesics. Many reported taking above the recommended dose despite no reported benefit. In this study the use of opioids correlated well with

measures of distress and disability, but not with objective physical signs.[6]

There are no long-term controlled studies on the efficacy or adverse effects associated with the use of opioids in chronic non-malignant pain.[7] An Australian review found that opioids were often prescribed for patients with social problems, high levels of emotional distress and unclear medical diagnoses. Escalation occurred in those patients prescribed short-acting opioids such as pethidine or dextromoramide.[8]

Guidelines on management strategies for the use of oral opioids in patients with chronic non-malignant pain were published in 1997.[9] This followed an earlier consensus statement on the 'Use of opioids for the treatment of chronic pain' by the American Academy of Pain Medicine and the American Pain Society.[10] These guidelines do not support the use of regular parenteral opioids in the management of chronic pain.

Alternatives to pethidine for chronic non-malignant pain

Those receiving regular pethidine for chronic pain should have their condition re-evaluated. Preferably this re-evaluation should be by a multidisciplinary pain management team where one is available. If there is a delay in obtaining a multidisciplinary assessment, attempts should be made to identify and start to address any unhelpful beliefs and behaviours in addition to any nociception or neuropathy present. In most cases this approach will broaden the treatment options to include a clinical psychologist or psychiatrist with expertise in pain management.

If the patient has evidence of tissue damage such as lytic lesions associated with cancer or joint degeneration (e.g. rheumatoid arthritis) then nociceptive pain can be inferred. Treatment options include non-steroidal anti-inflammatory drugs, simple analgesics such as paracetamol and long-acting opioid preparations providing steady blood concentrations of opioids such as morphine, oxycodone, hydromorphone or fentanyl. In the same way, a patient who has had a major nerve or spinal cord injury should be assessed for neuropathic pain and consideration given to drugs such as sodium valproate[11], gabapentin[11] or mexiletine. In carefully selected cases an intrathecal drug delivery system or spinal cord stimulator may be considered.

Pethidine is often used for conditions such as low back pain and radicular pain which may have nociceptive or neuropathic components or be a combination of both. A similar approach to that described above is recommended. These patients will require the early involvement of a multidisciplinary pain management team.

Self-help

As pain is a multidimensional experience, treatment should not be continued with one modality unless there is a rapid and sustained response. Failure to instruct patients on self-management approaches risks reinforcing an external locus of control (excessive reliance on others instead of managing their own pain). Usually this is the province of a clinical psychologist but medical practitioners can make a start with self-help books such as *Manage your pain* which is written to be used as a manual for patients to work with their doctor, physiotherapist or other health care worker.[12] In many cases this approach will not be sufficiently intensive and treatment may be required in a good quality pain management program.[13]

Summary

Pethidine is an effective analgesic for acute pain, but has no role in chronic pain. Patients reliant on regular pethidine require a multidisciplinary assessment. A round-table conference should follow to consider treatment options. There may be options to address the pain and also options to help the individual to manage their pain more successfully. In many cases a co-ordinated multidisciplinary cognitive behavioural pain management program will be required. Maintenance of gains made during such programs requires an understanding that patients will continue to experience pain and that their function and quality of life requires the active use of pain management strategies that they have learnt. This requires the support of their doctor or other healthcare worker. As this approach aims to 'de-medicalise' the management of their pain, practitioners have to be careful not to inadvertently undermine this approach by switching the focus back to pain, rather than promoting function by encouraging the use of 'well behaviours'.

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FURTHER READING

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See resources on the following web site: www.painmgmt.usyd.edu.au

Dr Molloy is a co-author of 'Manage your pain'.