

## Programmable morphine pump (an intrathecal drug delivery system) – A promising option for pain relief and palliation in cancer patients

Sir,

By following the World Health Organization guidelines, in about 80–90% of the cancer patients, pain can be well controlled, while the remaining 10–20% terminally ill cancer patients with refractory pain will require more intensive measures to control pain.<sup>[1,2]</sup> Totally implanted, programmable morphine pump is an intrathecal drug delivery system (IDDS) that delivers opioid or non-opioid drugs directly into the cerebrospinal fluid (CSF) around the spinal cord.<sup>[1,3]</sup> Morphine delivered directly into the intrathecal space is particularly effective because it does not have to circulate systemically to reach the CSF and the dorsal horn of the spinal cord and may provide a good option for pain relief.<sup>[1,3]</sup> Programmable morphine pump is a continuous, controlled and reversible drug delivery system in which the drug dosage can be adjusted as per the requirement for pain relief and refilled without any major procedure on an outpatient department basis.<sup>[1,3]</sup> After the pump is implanted, clinicians are able to use a programmer to interrogate and program the pump non-invasively.<sup>[1,3]</sup> It can also be programmed to release different amounts of medication at different times of the day, depending on the need, and the clinician can easily review this information with the programmer.<sup>[1,3]</sup> There are many benefits of this system compared with others. It may reduce the risk of infection compared with the long-term use of external systems.<sup>[1]</sup> To provide the same amount of pain relief, intrathecal morphine requires a much lower dosage than oral, intramuscular, intravenous or epidural injections and, consequently, has much less systemic side-effects.<sup>[4,1]</sup> Its response can be evaluated by a screening test prior to system implantation. In non-neurodestructive procedures, cancer pain is significantly improved by the IDDS in up to 90% patients as compared with intraventricular morphine administration in up to 70% patients only.<sup>[4]</sup> However, spinal cord stimulation does not have any proven role in relieving cancer pain.<sup>[4]</sup>

Destructive neurosurgical procedures are irreversible. For example, cordotomy, rhizotomy, thalamotomy or chemical destruction (alcohol nerve blocks, intrathecal phenol) of nervous structures may often bring about sensory or motor dysfunction, and relief is often only temporary as the pain usually switches to a different pathway or

redevelops later.<sup>[4,1]</sup> This makes chemical neuromodulation a more established means of pain management, possibly eliminating the need for neurodestructive procedures in those terminal cancer pain patients with a high operative risk.<sup>[1,3]</sup> The patient is functional, able to live without pain or minimum residual pain and capable of performing the basic, everyday activities (walking, eating, sleeping, etc.). Patients might not be as active as they were before having cancer, but they may not be bedridden either.<sup>[1]</sup> In cases where the patient is expected to live more than 3 months, and responds to a trial dose of intraspinal morphine, it may be more cost-effective to implant a drug pump to reduce the need to go to the hospital for frequent injections.<sup>[1,3]</sup>

The principle indication for using IDDS in cancer patients is failure of conventional routes of administration of analgesics to provide adequate analgesia despite maximum doses of strong opioids, dose-limiting and intolerable side-effects.<sup>[1,3]</sup> It can be used as first-line therapy if the patient is concerned about dependence or addiction or, if the cancer patient is receiving highly toxic chemotherapy regimens, the use of IDDS for pain control has a lower risk of additive adverse effects compared with conventional pain treatments and, therefore, the patient is more likely to maintain performance scores and is able to tolerate aggressive anticancer toxic chemotherapy regimens.<sup>[3]</sup> Pump should only be implanted if the patient has successful pain control (>50%) with a screening test injection of spinal epidural (5–10 mg) or intrathecal (0.5–2 mg) morphine after stopping all analgesics<sup>[4,1]</sup> and the life expectancy of the patient should be more than 3 months.<sup>[4]</sup>

The contraindications for IDDS include high CSF pressure, central nervous system or operative site infection, bleeding disorders, allergy to morphine, a failed trial of spinal opioid therapy, untreated depression, mental confusion, spinal deformity and an uncooperative family.<sup>[1,3]</sup>

Procedure- and device-related serious complications are rare, but minor complications are common. In cancer patients, catheter, procedure, device-related and illness-associated adverse incidents occurred at a rate of 0.45 events per patient year.<sup>[5,1]</sup>

Smith *et al.*, in a multicenter, international, randomized controlled trial, showed improved quality of life, by

reason of pain control, and significantly less drug toxicity with the IDDS as compared with comprehensive medical management (CMM). Although longevity was not the outcome measure, in 2005, Smith *et al.* demonstrated that at 180 days, 53% of the IDDS group was still alive as compared with 32% of the CMM group.<sup>[6]</sup>

In Bedder's 1991 study, the cost of intrathecal morphine administered via the Synchroned<sup>®</sup> infusion system was compared with the cost of epidural morphine administered via an external continuous automatic drug delivery (CADD) pump. The study indicates that an implantable pump becomes more cost-effective than the tunneled epidural catheter and external CADD pump after 3 months.<sup>[7]</sup>

Erdine and Talu *et al.* analyzed the cost issues by four methods of economic analysis: Cost-minimization, cost-utility, cost-benefit and cost-effectiveness, and compared bolus administration through an epidural port with the algomed system and exteriorized systems with implanted infusion pumps. They concluded that within 3–7 months, the implantable systems became cost-effective.<sup>[8]</sup>

After reviewing the literature on pain management in cancer patients, programmable morphine pump, an IDDS, is a better option of pain management and palliation in patients with intolerable side-effects due to oral or injectable medications. Because of better pain relief, lower side-effects and fewer complications as compared with oral or injectable medications and other pain-relieving neurosurgical procedures, it can be used with promising results in properly selected patients.<sup>[4-6,8]</sup>

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