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SURGICAL METHODS FOR IMPLANTING INTRATHECAL MEDICATION DELIVERY DEVICES

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Abstract
Patients with chronic pain that is not responding to treatment may benefit from intrathecal drug delivery systems (IDDDS). Current developments in technology, novel therapeutic uses, documented side effects, and the expenses and upkeep associated with this treatment need staying current with new guidelines that could enhance results. When used by qualified practitioners and with medications that have a documented safety record, intrathecal drug delivery devices may be beneficial for patients with a narrow therapeutic safety margin. We go over the most widely used medications (both opioids and non-opiods), their pharmacokinetic and pharmacodynamic properties, and their recommended uses. Morphine, hydromorphone, methadone, fentanyl, bupivacaine, clonidine, and ketamine are the most commonly utilized medications. This chapter examines all technological concerns related to the implantation of IDDS devices, along with follow-up and pharmaceutical recommendations released in recent years that offer an evidence-based approach to decision-making for the treatment of patients' chronic pain and spasticity.

Keywords: Intrathecal drug delivery, chronic pain, opioids.

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Introduction

Intrathecal drug delivery (IDD) is well established as an effective treatment of patients with chronic nonmalignant or malignant pain, and as a tool for controlling of patients with severe spasticity. It is involved in processes for treating patients with comfortable to severe pain, when other conventional options have failed.(9) Since the spinal cord is a dispensation center for pain signals, it advantage lies in the possibility of attaining high drug concentrations at the site of action, with a lower dose requirement than with other routes of administration, leading to better symptom control with a lower incidence of side effects. The role of intrathecal drug delivery in treating refractory pain has become a standard of care. The risk to benefit ratio of IDD makes it a relatively safe therapy for both cancer- and no cancer-related pain, but it is not free of risks, so it should be managed at specific centers. (13) All these issues, together with the financial and human cost of setting up and maintaining this type of therapy, make it essential to keep up to date with new aspects of management in order to optimize outcomes. The 2016 Polyanalgesic Consensus Conference (PACC 2016) Consensus Documents were published in 2017, with the aim of updating previously published in guidelines issued in 2007 and 2012, providing indications, standards of use, and updated management for intrathecal drug infusion devices. (9,10)

Multiple compressions fractures

- Discogenic pain
- Spinal stenosis
- Diffuse multiple - level spondylosis
- Failed back surgery syndrome
- Abdominal/pelvic pain
- Somatic
- Extremity pain
- Radicular pain
- Joint pain, Trunk pain

History of Intrathecal Analgesia Intrathecal Drug DelivarySystem:

In 1898, soon after the discovery of cocaine as a local anesthetic, August Bier documented the first spinal analgesia by injecting cocaine into his own intrathecal space as well as that of six patients whowere to undergo lower extremity surgery, thus creating immense interest in this technique.(4) Soon after, Rudolph Matas showed

that mixing morphine with cocaine was able to mitigate the adverse symptoms associated with intrathecal cocaine Continuous spinal analgesia was first used in the 1940s, but it was the discovery of opiate receptors in the spinal cord in 1973 that provided a scientificrationale for this form of treatment. The development of infusion pumps in the early 1970s allowed for greater flexibility in administering intrathecal opiates. In 1991, externally programmable, battery-powered IDDS pumps were introduced, allowing for noninvasive dose changes of these medications using an external programmer. This allowed for an easier means of changing patients' analgesic therapies in response to the dynamic changes in pain. (4)

Types of Intrathecal Drug Delivery System:

IT administration of drugs requires the placement of an infusion pump that includes a drug reservoir, amechanical pump and a catheter implanted in the IT space. e. In addition to a wide variety of catheter systems, there are both nonprogrammable and programmable pumps on the market. A non- programmable fixed flow pump provides a continuous volume of drug in the IT space, maintaining constant flow and ensuring fixed daily drug delivery. Although these systems are less expensive, any dose change requires a change in the concentration of the drug in the reservoir. On the other hand, the flow rate of the drug can be regulated by a programmable pump that deliver different doses. The two most frequently used variable flow pumps on the market are the continuous peristaltic pump and the valve bolus pump. SynchroMed II Pump (Medtronic Inc., Minneapolis, MN, USA) is a peristaltic pump, which consists of a system of roller rotors and gears that introduces agents from the reservoir through an internal catheter, in a peristaltic sequence. (14) Drug delivery is obtained by positive pressure that pushes the drug through the opening inlet to the dosing chamber. Moreover, it can deliver a precise dosage, without dosage fluctuations caused by external factors such as pressure and temperature variations

Drugs Used in Intrathecal Therapy

The FDA and EMA (European Medicines Agency) have approved ziconotide and morphine for IT infusion for the treatment of pain. Hydromorphone from Mallinckrodt is undergoing a clinical trial for potential IT labeling (finished in February 2018, not yet publish). Off-label monotherapy or combination therapy should be considered after failure of FDA-approved medications. these medications are contraindicated; in cancer patients. It has been agreed to use an admixture with bupivacaine or the primary use of fentanyl. (12) The PACC 2012 divided the level of evidence between neuropathic, nociceptive, and mixed pain. Neuropathic pain generally responds to ziconotide, opioid plus local anesthetic, local anesthetic alone, clonidine plus opioid, and clonidine alone.

Pharmacokinetics of IT drugs

The higher analgesic efficacy and lower rates of treatment failures and technical complications compared to epidural administration. (13) The advantage of IT involves bypassing the blood–brain barrier, which results in higher concentration of administered agents in the cerebrospinal fluid (CSF), using fewer amounts of medication. Hydrophilic agents have longer half-lives, reflecting the faster clearance into the vasculature demonstrated by lipophilic agents and smaller volumes of distribution, resulting in potentially deeper cord penetration and more rostral spread (3), which may have a clinical advantage over lipophilic IT agents. However, lipophilic medications have the advantage of limited spread when precise the targeted delivery is desired.

Non-opioids:

Ziconotide. This is the first-line drug in chronic nociceptive and neuropathic pain. It mechanism of spinal action is to block presynaptic N-type calcium channels in the dorsal horn of the spinal cord. Successful use of combined ziconotide and morphine is recognized in patients with chronic cancer pain refractory to systemic treatment. The advantages of using ziconotide include its morphine independent mechanism of action, absence of respiratory depression, and the low doses needed to achieve clinical effects..

Ketamine. In a case report of a 49-year-old woman with severe cancer-related upper back and abdominal pain, IT ketamine was added to her regimen of morphine and bupivacaine and her NRS score decreased from 6 to 3. There were no signs of motor paralysis, psychomimetic alteration or neurological dysfunction Clonidine. Is an alpha2 adrenergic agonist; it produces antiallodynic effects by inhibiting the activation of glial cells and by activation of nuclear factor κB and p38 (MAP kinase), thus inhibiting the production of proinflammatory cytokines. Clonidine has been evaluated in many clinical studies, with improvement in analgesia and opioid-mitigating effects. (4)

Baclofen. This γ-aminobutyric acid (GABA) agonist is a fourth line treatment in chronic neuropathic pain. Use of baclofen in severe, progressive spasticity that is refractory to conventional medical treatment is considered a good treatment option, for example, in spinal injury, brain damage,
amyotrophic lateral sclerosis, cerebral palsy, stiff-man syndrome, children with progressive neurologic disease, patients with dystonia, myoclonus, dysautonomia and hypertonia following severe head injury. [11]

Intrathecal Drug Delivery System Devices

There are four methods of delivering medications intrathecal: two include the use of an external pump while the other two represent fully implantable devices.

- Third, a fully implanted fixed-rate (or constant flow) IDDS may be beneficial for long- term delivery of analgesia. Codman 3000 (Codman and Shurtleff, Inc., Raynham, MA, USA) is an example of such a system. Fixed rate delivery systems are less expensive than

variable- rate delivery systems and do not require a battery to operate, so should theoretically last the lifetime of the patient.it lacks the flexibility to change medication delivery or allow fora patient-controlled bolus

- The fourth method of spinal medication delivery consists of a fully implanted programmable IDDS, such as the Medtronic Synchro Med II infusion system.

The fourth method of system is Codman 3000 intrathecal puma with progressively increasing reservoir sizes. These numbers are stored, analyzed, and used to reprogram the system for optimum dosing. Symptoms resolve, and then repeat imaging is recommended in 6 months. Animal work with morphine has shown that the concentration of the drug used is important rather than the actual total dose. Problematic leg edema has been described with IT opioid 2008 study looking at 168 patients found that 85% of patients were satisfied with this technology.

Device implantation

IDDS implantation involves of two parts needing two separate incisions. the first entails placements of the catheter into the intrathecal space of the thoracolumbar region. Typically, this incision occurs in the lower back for catheter insertion into the intrathecal space, and catheter adherence to the underlying fascia via anchoring devices. The second part consists of placing the pump/reservoir into the abdominal region. Several aspects must be considered when deciding where to place the pump reservoir. Alternatively, the pump can be placed in the buttock region when abdominal pocket sites are unavailable. The major in the majority of patients, the pump is surgically placed on either the left or right lower quadrant of the abdominal.

After securely connecting the catheter to the pump, the pump reservoir is anchored within the pocket and the incision sites are closed. Patient in the lateral decubitus position for implantation of intrathecal drug delivery system implantation. The blue surgical mark indicates anticipated lumber incision for intrathecal catheter placement.

Delivery programing and outcome

As reviewed in the previous section, the development of systems, which can deliver programmed infusion as boluses and/or continuous delivery at different rates, suggest the potential impact that programming can have on neuraxial drug distribution. An important question is whether these programming choices, indeed, lead to changes in a clinical outcome. on-cancer pain treated by intrathecal drug application by means of programmable pumps and the abase reviewed in the previous section, the development of systems, which can deliver programmed infusion as boluses and/or continuous delivery at different rates, suggest the potential impact that programming can have on neuraxial drug distribution. The influence of the injection rate on drug distribution is well- known by anesthesiologists performing spinal anesthesia.

Conclusion

Treating persistent intractable pain that is typically poorly controlled by systemic medical therapy may benefit from the introduction of medicines through the IT route. The IDDDs' available technology, like as catheters and pumps, have been significantly improved recently. For this therapy to be successful, it is essential to apply appropriate clinical practices, follow guidelines, engage in ongoing improvement, and do clinical research. In terms of pain relief, a decrease in side effects, and cost-effectiveness, the statistics highlight the importance of intrathecal therapy for cancer pain. Especially with intrathecal opioids, implanting physicians should be aware of the necessity to monitor changes in specific serum hormones and the possibility of granuloma development. In order to provide more comprehensive pain relief, increased safety, and improved long-term outcomes in terms of quality of life, studies combining innovative intrathecal agents with cutting-edge IDDS technology promise surgical procedures for intrathecal medication delivery system installation.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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