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Review Article

The Future of Pain Management: Implantable Devices

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ABSTRACT

Pain management strategies can be used to treat chronic pain, including the use of implant devices like spinal cord stimulators, intrathecal medication therapy, and peripheral nerve stimulators as well as pain evaluation scales. Despite widespread agreement that these are effective pain management, a comprehensive pain evaluation and frequent reassessments are frequently overlooked. The pain treatment continuum is a suggested algorithm for the appropriate use of possible pain management therapies. In this review, we discuss the current state of the art of pain management strategies for chronic pain. In addition, we review the recent advancements in injectable solid implants for non-invasive implant administration; fluorouracil-based implants, in particular, the promise as adjuvant therapy for cancer patients

INTRODUCTION

Pain is a vital health alarm for human beings that could inform them of future health problems. However, pain is often prolonged and exceeds the normal healing process, which can lead to unpleasant feelings and harmful effects on their life. [1] Acute pain is typically accompanied by tissue injury, inflammation, or a very brief illness phase (days or weeks). Chronic pain occurs when pain remains for a lengthy period of time, either as a result of a disease process or after the typical period of time that is indicated for the injury to heal. Chronic pain is defined by the International Association for the Study of Pain (IASP) as pain that lasts more than three months. The pain lasts long after it has served its functional purpose, and it is no longer merely a sign of damage or sickness but a medical concern.[2] The International Classification of Diseases (ICD-11) officially recognised two types of chronic pain in 2019: "chronic primary pain," which is characterised by physical or emotional distress unrelated to another diagnosis, and "chronic secondary pain," which occurs when the pain is a symptom of a diagnosable underlying condition.[3] Analgesia, pain control, and pain alleviation are all terms used

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to describe the process of managing pain, which can take many forms, ranging from acute and manageable to chronic and difficult. During their routine care, many doctors and other healthcare providers offer some form of pain management. For more complicated cases of pain, however, they may also seek further assistance from pain medicine, a branch of medicine that is only concerned with treating pain. The Joint Commission and the World Health Organization, along with many national professional organisations and agencies, have recognised that pain management is an essential aspect of patient care.[4] The pain treatment continuum is a suggested algorithm for the appropriate use of possible pain management therapies. These therapies are listed in order of increasing invasiveness. The algorithm is used when appropriate, in parallel and not in series. Multiple therapies can and should be used at the same time. Therapies that don't work should be abandoned and new invasive therapy should be introduced. [5]

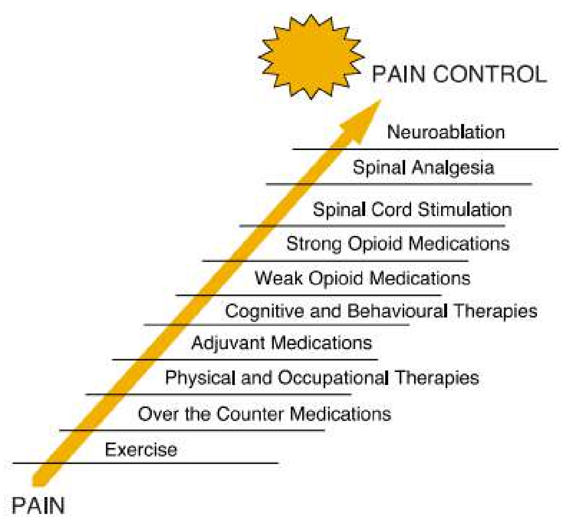

Fig 1 [pain treatment continuum]

To promote self-efficacy, pain management is described as the goal of modifying a patient's pain or reaction to pain via the use of multimodal techniques in a collaborative manner. Since people with chronic pain are more likely to become inactive and concentrate on their pain all day long, those with the condition must receive appropriate pain management to preserve as much of their daily routine as possible.[6]

For those suffering from persistent and frequently incapacitating pain, pain management implants have become a game-changer. There are many significant advantages they offer. By lowering pain intensity and promoting better sleep and mobility, these implants improve overall quality of life by providing precise and targeted pain treatment. Additionally, they lessen the need for systemic drugs, especially opioids, which lowers the hazards involved. In such cases, implants have emerged as a revolutionary approach to pain management.

Pain Assessment

When dealing with acute pain or pain as a sign of trauma or sickness, assessing pain can be a simple and uncomplicated procedure. In clinical practice, an assessment of the location and degree of pain is frequently adequate. Other significant features of acute pain, in addition to pain intensity at rest, must be defined and assessed when clinical trials of acute pain therapy are planned. False conclusions and nonsensical data might ensue otherwise. Assessing chronic pain and treatment outcomes is more difficult for individuals with cancer as well as those with pain from non-cancerous reasons. Clinical studies and efficient pain management depend on valid and trustworthy pain assessment. Pain cannot be objectively measured due to its nature. [7] The basis for treating pain methodically is an accurate assessment of the patient's discomfort. Nevertheless, despite widespread agreement that these are effective pain management, a comprehensive pain evaluation and frequent reassessments are frequently overlooked. For instance, a study of 1454 patients over 65 receiving hip fracture treatment in the emergency room revealed inconsistent pain evaluations. A significant proportion of the study population—

40%—did not obtain an analgesic prescription, despite the prevalence of intense pain (the mean pain intensifying to the absence of acknowledgement of pain). Of those surveyed, 34% did not receive an objective evaluation of pain, and only 59% were assessed using self-report measures of pain. [8] A thorough examination of the patient's physical condition, a thorough investigation of their medical history and pain, and any necessary diagnostic testing should all be part of a comprehensive assessment for all demographics. The identification of the origin of pain is one of the primary goals of the physical examination and history.[8] Healthcare providers need to use pain assessment scales to assess and measure their patients' discomfort. For this reason, a variety of scales are employed, and the selection of a scale is influenced by the patient's age, cognitive capacity, and kind of pain. Pain assessment scales encompass various types, including Visual Analog Scale (VAS), Numeric Rating Scale (NRS), Faces Pain Scale (FPS), Verbal Rating Scale (VRS), FLACC Scale, PAINAD Scale, COMFORT Scale, Behavioural Pain Scale (BPS), McGill Pain Questionnaire, and Wong-Baker FACES Pain Rating Scale, each tailored for different patient populations and communication abilities.

Visual Analogue Scale

The VAS measures either pain alleviation or pain severity, and is frequently used to assess the analgesic qualities of different treatments. The VAS is a straight line with the limits carrying a verbal description of each extreme of the symptom to be evaluated. It provides a continuous scale for subjective magnitude measurement. The line is typically 10 cm long and vertical, however it has been successfully used at other lengths and orientations. This "comparative" scale has extreme boundaries that are described in terms of pain alleviation: "no relief" at the upper end and "complete relief" at the lower end. Patients are asked to mark the line between the two extremes to indicate how much their pain has subsided after receiving therapy. To calculate pain relief scores, measure the distance between the patient's mark and the upper end of the scale. Alternatively, place a linear graduated scale next to the VAPRS, numbered sequentially from 1 to 20, and record the pain relief score as the number that corresponds to the patient's mark. [9]

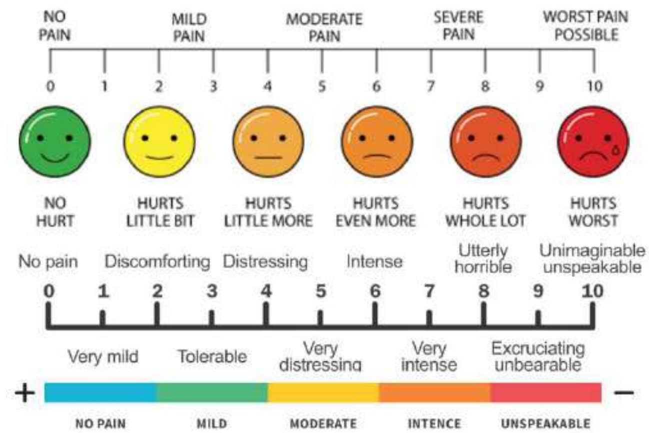

Figure 2 [representing VAS scale]

Numerical Rating Scale

With the NRS, pain is measured on a scale of 11, 21, or 101 points, with no pain and pain at its worst or as severe as it may be at the end points. The NRS may be presented orally or visually. Depending on how many levels of discrimination the patient is given, the scale is referred to as an 11- or 21-point box scale when the values are shown visually and encased in boxes. [10]

Figure 3[numerical rating scale]

Implants in pain management

Implants provide an option in situations where conventional methods of pain treatment are not effective. Two well-known implant-based methods have become more well-known: intrathecal pumps and spinal stimulators. In the field of pain treatment, implants are cutting-edge tools inserted into the body via surgery to relieve persistent pain. These implants are targeted remedies that provide long-lasting pain relief by going straight to the site of the problem.

Spinal Cord Stimulator

The goal of spinal cord stimulation as a pain management technique is to lessen the frequency, duration, and intensity of pain perception. Even though Melzack and Wall's gate control theory of pain served as its foundation during development. Peripheral vascular illness, complex regional pain syndrome, failed back surgery syndrome, and refractory angina pectoris are among the main indications for conventional SCS. [11] Dorsal column function in the spinal cord appears to be required for a therapy known as dorsal column stimulation. Spinal cord stimulation (SCS) causes inhibitory neuronal responses that limit pain transmission in dorsal-horn neurons or close the pain "gate" by selectively depolarizing dorsal-column large-fibre afferent neurons. Research on animals has shown that SCS modifies the concentrations of neurotransmitters in cerebrospinal fluid and that sympathetic and GABAergic interneurons are involved in stimulation-induced pain alleviation. Targeted SCS produces a pleasant tingling or paraesthesia that "covers" typical pain locations in vivo (e.g., around T9–L1 for lower limb pain), and it may be useful in providing analgesia for chronic pain that has been resistant for a long time. [12] The following criteria are used to choose patients who are in pain: 1) the discomfort cannot be linked to cancer; 2) the patient has not improved after at least six months of conservative treatment; and 3) corrective surgery is not advised. 4) no significant psychological illness, including symptoms of somatization; 5) readiness to cease using drugs improperly before implantation; 6) no litigation or secondary gain; and 7) capacity to provide informed permission for the surgery.[11] Because SCS is reversible and less invasive, it is reported to be a safe procedure. Catastrophic problems are extremely uncommon, even though they are feasible. On the other hand, reports place the incidence of mild SCS problems at 30% and 40%. These mild side effects usually go away after a year or so of implantation and are easily corrected. The three primary categories of complications are connected to techniques, biology, and mechanics. Compared to biological origins, mechanical origins are more likely to result in complications. In the past, adverse biological events happened in 7.5% of instances, while hardware-related issues happened in 24% to 50% of cases. Lead migration has a reported incidence of between 0% and 27%, lead fracture or disconnection has a reported incidence of between 5% and 9%, and implantable pulse generator failure has been documented to occur 1.7% of the time. With the right leads, anchoring, and suturing methods, these issues can be reduced to a minimum. Additionally, limiting patient movements in the first three months following surgery enables leads to be permanently scarred into position. [13]

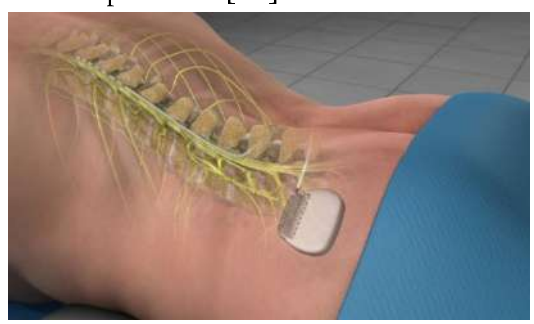

Figure 4 [describing placing of SCS in the spinal cord]

Spinal cord stimulators are ineffective in treating certain types of pain, including nociceptive pain, central neuropathic pain (also known as central post-stroke pain), pain after spinal cord injury linked to total loss of posterior column function, and pain related to de-affirmation. Coagulationopathy, sepsis, immunosuppression, poor overall health, active mental disease, substance abuse problems, incapacity to comply or operate the device, and demand pacemaker are among the conditions that preclude the use of SCS. [12]

Intrathecal drug therapy

Patients with persistent non-cancer pain, cancer pain, and spasticity may be managed using intrathecal drug delivery (ITDD) devices. It has been said that intrathecal drug delivery (ITDD) is a "last resort" option that is usually offered to patients who have endured protracted periods of agony, sometimes lasting up to 40 years. [14]

To manage pain and stiffness, intrathecal treatment entails injecting analgesic and antispasmodic drugs straight into the spinal fluid. To reduce the side effect load associated with greater dosages of systemic analgesics, physicians frequently apply considerably lower doses of analgesics when employing intrathecal treatment to manage pain. The intrathecal method also has the advantage of allowing the administration of other kinds of drugs that cannot be delivered orally or systemically. Function and pain management improve at lower dosages when administered intrathecally, and the adverse effect profile is reduced.[15] By dose-dependently inhibiting the release of neurotransmitters from primary afferent nociceptors in the C and Aδ fibres and hyperpolarizing pain-transmitting neurons in the dorsal horn of the spinal cord, intrathecal opioids produce "selective spinal analgesia." Due to the cephalad migration of medications in cerebrospinal fluid, intrathecal opioids also have analgesic effects via binding to opioid receptors in specific brain regions. [12]

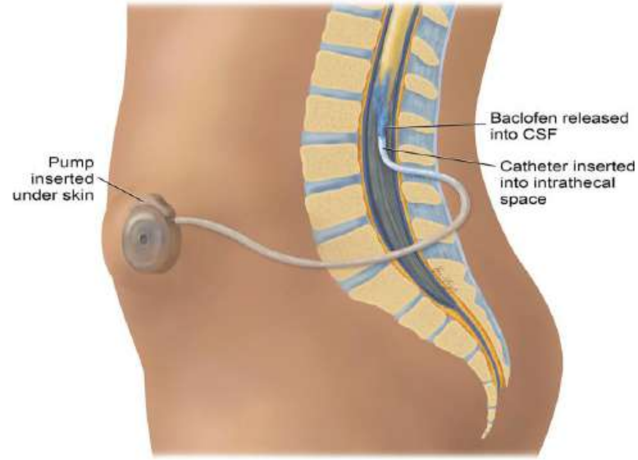

Fig 5 [intrathecal pump inserted containing baclofen]

Intrathecal treatment has a few hazards, such as drug-related adverse events, coexisting medical illnesses, and IDDS issues. Meningitis, catheter-tip inflammatory masses, and postoperative subarachnoid haemorrhage are among the worst side effects following the implantation of an intrathecal catheter. Adverse occurrences associated with medication frequently include giving the wrong medication or dosage, using the incorrect method while refilling, or the pump malfunctioning and causing withdrawal. Preventing issues with pump installation and long-term therapy requires identifying people who may experience difficulties. Healthcare providers using implanted intrathecal pump treatment need to be aware of precautionary measures and medication regimens to reduce the possibility of side effects. [16]

Peripheral Nerve Stimulators

Neuromodulation was first used in peripheral nerve stimulation (PNS). There is a lot of research being done on the neuromodulation of peripheral nerves to relieve pain. Peripheral nerve stimulation (PNS) precedes both spinal cord and deep brain stimulation, despite the latter two having more public and clinical knowledge today. It is crucial to make clear that, despite the consensus about anatomy, the dorsal root ganglion (DRG) is considered to be in the periphery, but stimulation of the DRG is not included in the PNS for the Food and Drug Administration (FDA). According to the suggested mode of action, pain signals are transmitted from small nociceptive fibres to the brain less often when large-diameter sensory neurons are stimulated. To selectively activate Aa/b fibres while preventing the activation of Ad/C fibres, stimulation is provided by a system that is positioned close to but still apart from the nerve; this technique is known as distant selective targeting. The greatest sensory afferents can usually be selectively activated by stimulating mixed nerves at a frequency of 100 Hz. On the other hand, muscular efferent fibres can be equally stimulated by stimulating mixed nerves at a low frequency, like 12 Hz, resulting in remote selective targeting. It has been proposed that percutaneous PNS systems, as opposed to traditional "intimate" electrode implantation, may activate a higher percentage of large-diameter fibres without unintentionally activating nociceptive afferents. Percutaneous and open lead implantation were employed in the early PNS experiments.[17]

Paddle leads inserted surgically were tested in the middle of the 1980s. Percutaneous leads were first utilized in 1999 to treat conditions including occipital headaches. PNS has been used to treat a variety of illnesses, such as headaches, sacroiliac joint pain, post-amputation pain, plexus injuries, mononeuropathies, facial discomfort, arm and limb pain, and joint pain. Additionally, it has been used to treat faecal incontinence, overactive bladder, and postoperative discomfort.

BIOMATERIALS FOR PAIN IMPLANTS

Biomaterials are a variety of materials that may replace or innocuously interact with biological tissues. They include metals, alloys, polyester-based polymers, and other goods used for tissue repair or reconstruction. They are intended to heal (or perhaps even cure) a multitude of severe illnesses and to replace some permanently damaged anatomical elements without being rejected. Lopez provided the following extensive characterization of contemporary surgical biomaterials recently: "substances and products with the ability to interact with live tissue while still avoiding the body's rejection. After these biomaterials accomplish their intended purpose, they are either gradually absorbed by the body and removed by biological processes, or they remain permanently in the environment. [18] The idea behind biomaterials is that they should, on the one hand, work in concert with biological processes that occur naturally (such as regeneration in wound healing); furthermore, they should stimulate cellular responses that might not occur naturally, such as the healing of various damaged structures in a diseased subject or the creation of a new vascular bed to receive a cell transplant); and, on the other hand, they should prevent natural phenomena that occur naturally, such as the immune system rejecting xenotransplants or the growth factor signals that encourage the formation of scars. [19] Polyaryletherketones (PAEKs) have been increasingly employed as biomaterials for orthopaedic, trauma, and spinal implants. Commercialized for the industry in the 1980s, PAEK is a relatively new family of high-temperature thermoplastic polymers, consisting of an aromatic backbone molecular chain, interconnected by ketone and ether functional groups. [20] Poly(aryl-ether-ether-ketone) (PEEK) and poly(aryl-ether-ketone-ether-ketone-ketone) (PEKEKK) are two PAEK polymers that were formerly utilised for orthopaedic and spinal implants. Because of their chemical makeup, polyaromatic ketones are highly desirable for use in industrial applications like turbine blades and aircraft because they are stable at temperatures above 300 degrees Celsius, resistant to damage from chemicals and radiation, and compatible with a wide range of reinforcing agents, including glass and carbon fibres. They also have greater strength per mass than many metals. [20,21]

Advances in implants for pain relief

The use of injectable solid implants for non-invasive implant administration is a result of technological advancement. A study claims that pellets made of fluorouracil were created and extruded to a size that could be injected, allowing the anti-neoplastic drug to be delivered. It demonstrated strong in vitro-in vivo correlation and good in vivo release. It took 14 days to see almost 100% medication released. As a result, it was discovered that fluorouracil-based implants might be used as adjuvant therapy in cancer patients and those having tumour excision. Technology progressed to the point where 3-dimensional (3D) printing was creatively used to create a drug delivery system that offers patient-specific personalized medicine and has also been used in the production of implants. Highly intended products made from various materials are possible with 3D printing. [22] Early in the 1990s, a 3D printer was initially used for something called "binder jetting," which is another name for the drop-on powder method used in traditional inkjet printers. The nozzle of a traditional 2D inkjet printer swerves to both sides to accelerate the printing of materials in two dimensions: breadth and length. Similar technology is used by the 3D printer, however, instead of moving in only one plane, it can move 90 degrees to both sides, top and bottom. It is therefore three-dimensional due to the inclusion of this height. These days, 3D printers use a liquid binder solution that is selectively deposited onto a powdered bed instead of paper, giving it features similar to those of a 2D inkjet printer instead of ink. The first step involves placing the powdered bed, which varies depending on the substance employed, onto the structural platform and uniformly spreading it with a roller system. [23] As instructed by CAD, the nozzle sprays the binding solution onto the exact powdery area. The surplus powder is blown out as soon as the powder and binder solution combine. After shrinking the platform under study, a second layer of powder is added and equally distributed. This method is then continually carried out until the finished structure is constructed. Electrical pulses are normally delivered by conventional SCS at a frequency of less than 1200 Hz, more frequently 50 Hz. Some patients may find it intolerable, but it creates paraesthesia (usually at frequencies below 300 Hz) to "map" the painful area. Axial back pain is difficult to cover with conventional SCS, even though it usually reliably covers leg pain. Recently, HF-10 SCS (high-frequency, 10,000 Hz) was brought into clinical practice to address these problems. Because the stimulation intensity in HF-10 SCS is below the paraesthesia threshold, patients do not experience paraesthesia. Because "paraesthesia mapping" is not required, the process is streamlined and "wake-up" testing is not required during implant surgery. For the first time, placebo-controlled trials were made feasible by the stimulation free of paraesthesia. [24] With the introduction of devices that supply power to the lead directly over the implant site through percutaneous means, PNS has now entered a fourth phase. By avoiding applying a lead (or extension) across a joint, this significant development reduces the possibility of lead fatigue and migration.[17]

CONCLUSION

A number of pain management strategies can be used to treat chronic pain, including the use of implant devices like spinal cord stimulators, intrathecal medication therapy, and peripheral nerve stimulators, as well as pain evaluation scales. For people with chronic and frequently incapacitating pain, these implants offer focused pain relief and enhance overall quality of life.

To repair or replace damaged anatomical components, biomaterials are a broad class of materials that can interact with biological tissues without being rejected. Polyaryletherketones (PAEKs), including PEEK and PEKEKK, have shown great promise as biomaterials for spinal and orthopaedic implants because of their durability, stability, and ability to work with reinforcing agents. Technology has led to advancements in injectable solid implants for non-invasive implant administration; fluorouracil-based implants, in particular, show promise as adjuvant therapy for cancer patients. 3D printing has also made it possible to create implants and medication delivery systems that are customized for each patient. To address pain management difficulties without requiring paresthesia mapping, high-frequency SCS has also been introduced. Due to percutaneous devices, lead fatigue and migration have been less common in PNS.

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