Intrathecal Polyanalgesia

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Abstract

Drugs when deposited central neuraxially produces effect at a much smaller dose so as to prevent systemic toxicity. A single analgesic drug may be less effective and different drug combination for treatment of chronic pain with the help of an implantable intrathecal drug delivery system is an attractive modern day choice for treatment of various malignant and non malignant painful conditions though it has their own complications and limitations.

INTRODUCTION

The concept of Intrathecal Polyanalgesia was started in 1979 following intrathecal injection of morphine. Wang et al conducted a double blind study and injected intrathecal morphine in eight cancer patients with intractable pain. The result was encouraging. They predicted that the technique may be useful in labour analgesia and postoperative pain. They also speculated that prolong pain control is possible with a drug reservoir or with an indwelling catheter[1] .The concept has travelled a long way. Now a days it is a standard protocol to treat chronic malignant and non malignant pain patients with intrathecal drugs. The growing knowledge of pain pathways, receptors, neurotransmitters, neuromodulation, and availability of newer drugs has helped to understand the subject and revolutionize treatment. The other equally important factor without which Intrathecal (IT) Polyanalgesia could never have become a success is the development of intrathecal drug delivery systems (IDDS) or various intrathecal pumps.

INDICATION

Main indications of intrathecal polyanalgesia are

1. Pain not subsided with comprehensive medical management (CMM). That means pain is not responding to systemic analgesic and adjuvant drugs.
2. Pain is responding to systemic analgesic drugs at the expense of unacceptable severe side effects.

Other indications are

1. Fear of addiction to narcotic analgesic drugs.
2. Patients on aggressive chemotherapy with high toxicity profile.
3. Plexopathy i.e. involvement of neural plexus.
4. Impending fracture of skeletal bones.
5. Low life expectancy.

PHYSIOLOGY

Pain stimulus produces impulse which travels down from periphery to Cerebral cortex via spinal cord. The spinal cord is very rich in different types of receptors for pain and analgesia. Any painful stimulation causes release of various chemical substances in the spinal cord - the neurotransmitters which carries the painful impulse in the central neuraxial system. The spinal drugs mimic or act through inhibitory neurotransmitter or they antagonize excitatory neurotransmitter. This system undergoes lot of modulation from supraspinal descending pathways, reticular activating system, limbic system and other areas CNS.

Intrathecal Polyanalgesia provides aggressive pain control by direct instillation of drugs into CNS. The dosage is usually much less than systemic dose with minimum amount of systemic drug concentration and toxicity[2]. There are mainly two types of pain- nocicptive and neuropathic. If untreated nociceptive pain often changes to neuropathic pain and gives rise to chronic pain syndrome. Often both remains together. The mechanism is quite complex and involves sensitization of multiple different receptors, functional

reorganization of receptive field in the dorsal horn of spinal cord, release of various neurotransmitters. So it can be well postulated that simultaneous delivery of multiple drugs with different mechanisms of action may be therapeutically advantageous. In many painful states there are multiple mechanisms of pain where a single analgesic drug may not be very effective and association of another drug to modulate other component of pain may be advantageous. There is evidence that several agents may not display cross tolerance and in fact prevent development of tolerance otherwise associated with the use of equipotent dose of a single drug[3]. Newer IDDS and newer drugs further improve the situation. Effective titration of the dosage at a short time is possible with less unanticipated and breakthrough pain. The overall effect is better analgesia with lesser side effects.

PHARMACOLOGY

Drugs commonly used are

1. OPIOIDS

- Morphine, Hydromorphone
- Fentanyl, Sufentanyl.
- Meperidine, Buprenorphine

Opioid receptors are abundant in CNS. In spinal cord opioid receptors exist primarily in the substantia gelatinosa of dorsal horn (Rexed's Lamina II).Spinally delivered opioid acts on opioid receptor to produce dose dependent analgesia[4,5]. Opioids may act through multiple mechanisms including presynaptic inhibition of release of excitatory neurotransmitter, coupling with G protein and opening up of K+ channels to produce neuronal hyperpolarization. Spinal opioid also acts on descending inhibitory pathway and may be associated with release of other neurotransmitters like acetylcholine, adenosine[6,7].

Morphine is the gold standard therapy and can be started at a dose as low as 0.1mg/day which can be adjusted to as much as 15 mg/day. Hydromorphone is very popular for intrathecal analgesia especially in breakthrough pain. This is equianalgesic in a dose 20% of that of morphine. The drug acts on mu receptor primarily but also on kappa and delta receptor. Hydromorphone is more lipid soluble, has less active metabolite than morphine , has a smaller supraspinal distribution and fewer side effects. The potency of fentanyl and sufentanyl administered intrathecally are 10-20 times greater than when administered systemically indicative of high lipophilicity and lesser side effects. These two drugs are not seen to be associated with granuloma formation. Meperidine alone or with Clonidine is found to be helpful in intractable neuropathic cancer pain. Long use of meperidine can cause neurotoxicity of the central nervous system[8]. Buprenorphine is a partial mu receptor agonist with long duration of action. There is not enough evidence of its use in long term intrathecal therapy.

2. ADRENERGICS

Alpha2 (a2) stimulants : Clonidine, Dexmedetomidine

Alpha2 agonists are non opioid pain modulating drugs which acts on alpha2 adrenoreceptors reducing noradrenaline release by a negative feedback mechanism[9]. They also activate descending inhibitory pathway and act synergistically with local analgesic, opioid, neostigmine[10]. Dexmedetomidine is a highly selective a2 stimulant.

Clonidine is FDA approved for epidural use in cancer patients. However it is mostly used intrathecally for the treatment of chronic neuropathic pain. Intrathecally dose of Clonidine needs titration and commonly starts from 50 to 75 microgram/day. The dose may be as high as 300 microgram/day. Side effect includes bradycardia (especially when the catheter tip is in upper thoracic region), hypotension, dry mouth.

GABA RECEPTOR AGONISTS

- Midazolam (GABA A)
- Baclofen (GABA B)

GABA an amino acid is a inhibitory neurotransmitter in CNS. Intrathecal GABAergic drugs and Gabapentine are currently researched. GABA B receptor agonist Baclofen is the drug of choice for spasticity[11].

CALCIUM CHANNEL ANTAGONST ZICONOTIDE

Ziconotide is a highly selective reversible blocker of N type of voltage dependent calcium channels which are active in the dorsal horn of spinal cord, cerebral cortex and neurohypophysis[12]. Ziconotide is effective in both nociceptive and neuropathic pain. Clinical experience suggests that ziconotide should be started at a lower dose than2.4 microgram/day (0.1mcg/hour), titrate the dose once per week and use an overall period longer than three weeks upto a recommended maximum of 19.2mcg/day (0.8mcg/hr).

LOCAL ANALGESIC DRUGS

BUPIVACAINE, ROPIVACAINE

Local analgesic drugs when given neuraxially blocks autonomic, sensory, motor all types of transmission depending upon dosage and concentration. They cause axonal membrane blockade predominantly of spinal nerve roots[13].The efficacy of Bupivacaine depends on the site of administration or its rate and form of delivery. Bupivacaine when given in a very low dose with morphine shows analgesic improvement and sometimes a reduced tolerance to morphine. It was felt that low dose Bupivacaine acts mainly by membrane stabilization inhibiting calcium channel rather than sodium channel. Sodium channel blockade is seen with high dose administration. Bupivacaine less than 20 mg/day is well tolerated where as high dose is associated with tachyphylaxis, motor paralysis, urinary retention and orthostatic hypotension[25]. There is no long term study with Ropivacaine as yet.

NMDA ANTAGONISTS

KETAMINE

Intrathecally administered NMDA antagonist produce antinociception in patients with neuropathic pain[14]. These drugs prevent spinal "wind up" and help preventing development of chronic pain syndromes.

MISCELLANEOUS DRUGS

ADENOSINE

Adenosine is an endogenous ligand that acts on four types of receptors. Adenosine receptors are found in substantia gelatinosa of spinal cord. The antinociceptive effect is mediated by A1 receptor subtype. Intrathecal adenosine is more effective at reducing allodynia and hyperalgesia than spontaneous pain[15,16].Intrathecal adenosine 500 to 2000 microgram in human volunteers was shown to decrease allodynia in phase I clinical trials. The side effect reported was transient lumber pain after a dose od 2000 microgram[17,18]. Adenosine can be given as a bolus dose between 1-2 mg or infusion of 0.05 -0.1 mg/hour.

CYCLOOXYGENASE INHIBITOR-KETOROLAC

Prostaglandins are known to be responsible for pain and inflammation. Spinally synthesized prostaglandin effects can be reversed with non selective cyclooxygenase inhibitor drug Ketorolac which produces analgesia and may reverse the hypersensitivity seen with chronic spinal opioid exposure[19].

GABAPENTINE

Gabapentine a GABA analogue is thought to act on voltage dependent calcium channels resulting in inhibition of glutamate release in the spinal dorsal horn and effective in neuropathic pain[20.] It activates the noradrenergic system after nerve injury[21].The vast majority of preclinical studies with impressive result has necessitated human trial and a phase 2 clinical trial for intrathecal delivery is in progress[22].

OCTREOTIDE

Octreotide is a synthetic octapeptide of somatostatin. Somatostatin is located in substantia gelatinosa and mitigates nociception. Octreptide is found to have similar effect[22].

ANTICHOLINESTERASE DRUG- NEOSTIGMINE

Neostigmine administered spinally inhibits nociception by increasing endogenous acetylcholine an inhibitory neurotransmitter and can be an adjunct to other spinal medications[23].

XEN 2174 / CGX 1160

These drugs are conopeptides like ziconotide and presently the undergoing extensive investigations. Drugs found to inhibit noradrenaline transport and activate noradrenaline inhibitory pathways[24].

RESINIFERATOXIN

Resiniferatoxin desensitizes dorsal root ganglion[25.].

P-SAPORIN

P-Saporin is a neurotoxin which selectively destroys cells of neurokinin-1 receptors responsible for signaling pain signals from dorsal horn to brain and is currently under trial[26].

POLYANALGESIC CONSENSUS CONFERENCE

Hassenbusch and Portenoy reviewed four hundred and thirteen physicians who use intraspinal infusion device and found out that physicians who use intrathecal analgesia and device for years do not have universal drug protocol and their usage of different drugs in different painful conditions vary according to their knowledge and experience without clear indication[27].To make a uniform drug policy for intrathecal administration three Polyanalgesic Consensus Conference of expert panelists have convened since 2000. These guidelines were published in 2000,2003 and 2007 and were based on "best evidence" and expert opinion. This algorhthm is for treatment of chronic pain refractory to conventional therapies. They have taken into accounts of different new molecules designed specifically for intrathecal

therapeutic use, new devices (IDDS) , compatibility of the medication with the drug delivery system on " best available evidence" inclusive of both an updated literature review and expert consensus and not necessarily by "type A evidence " of large gold standard randomized clinical trials. The recommendations presented represent consensus of expert opinion regarding what is old and what is new and not what is standard of care. This is only to help treating physicians to formulate knowledge-based decisions when using intrathecal analgesic therapies[28].

THE CONCLUSIONS AND RECOMMENDATIONS OF POLYANALGESIC CONFERENCE 2007

Algorithm: Selection of Medications for Long-Term Intrathecal Infusion

The consensus and recommendation of a panel of experts on intrathecal polyanalgesia is to follow a definite protocol on the basis of preclinical and clinical available data. The committee recommends a six tier drug therapy for chronic pain patients. If a lower tier drug fails then the patient should get next tier drugs.

Figure 1

Treatment category	Intrathecal drugs
First line drugs	Morphine (a) Hydromorphone (b) Ziconotide (c)
Second line drugs	Fentanyl (d) Morphine/Hydromorphone + ziconotide (e) Morphine/Hydromorphone + Bupivacaine/Clonidine (f)
Third line drugs	Clonidine (g) Morphine/Hydromorphone/Fentanyl/Bupivacain + Clonidine +Ziconotide (h)
Fourth line drugs	Sufentanyl (i) Sufentanyl + Bupivacaine + /Clonidine + Ziconotide (j)
Fifth line drugs	Ropivacaine Buprenorphine Midazolam Meperidine Ketorolac (k)
Sixth line drugs	Experimental drugs Gabapentine Octreotide Neostigmine Adenosine Xen 2174 ZGK 160

Line 1: Morphine (a) and ziconotide (c) are approved by the Food and Drug Administration of the United States for intrathecal analgesic use and are recommended for first line therapy for nociceptive, mixed, and neuropathic pain. Hydromorphone (b) is recommended based on clinical widespread usage and apparent safety.

Line 2: The apparent granuloma sparing effect and because of its wide apparent use and identified safety, fentanyl (d) has been upgraded to a line 2 agent by the consensus conference when the use of the more hydrophilic agents of line 1 (a,b) result in intractable supraspinal side-effects.

Combinations of opioid + ziconotide (e) or opioid + bupivacaine or clonidine (f) are recommended for mixed and neuropathic pain and may be used interchangeably. When admixing opioids with ziconotide, attention must be made to the guidelines for admixing ziconotide with other agents.

Line 3: Clonidine (g) alone or opioids such as morphine/hydromorphone/fentanyl with bupivacaine and/or clonidine mixed with ziconotide (h) may be used when agents in line 2 fail to provide analgesia or side-effects occur when these agents are used.

Line 4: Its proven safety in animals and humans and because of its apparent granuloma-sparing effects, sufentanyl alone (i) or mixed with bupivacaine and/or clonidine plus ziconotide (j) is recommended in this line. The addition of clonidine, bupivacaine, and or ziconotide is to be used in patients with mixed or neuropathic pain.

Line 5: These agents (k), although not experimental, have little information about them in theliterature and use is recommended with caution and obvious informed consent regarding the paucity of information regarding the safety and efficacy of their use.

Line 6: Experimental agents (l) must only be used experimentally and with appropriate Independent Review Board (IRB) approved protocols.

*In patients with end of life, the panelists felt that midazolam and octreotide should be tried when all other agents in line 1-4 was tried and failed (not recommended for non malignant pain).The physician " do no harm" mandate should be superseded by a mandate to relief pain and discomfort at the end of life.

CONCENTRATIONS AND DOSES OF INTRATHECAL AGENTS RECOMMENDED BY THE POLYANALGESIC CONSENSUS PANELISTS, 2007

Figure 2

Drug	Maximum concentration	Maximum dose/day
Morphine	20 mg/mL	15 mg
Hydromorphone	10 mg/mL	4 mg
Fentanyl	2 mg/mL	No known upper limit
Sufentanil	50 µg/mL (not available for compounding)	Not known
Bupivacaine	40 mg/mL	30 mg
Clonidine	2 mg/mL	1.0 mg
Ziconotide	100 µg/mL	19.2 µg (Elan)

Intrathecal cocktails need further evaluation regarding the physio-chemical properties of the mixture. As such small volume of IDDS reservoir may necessitate compounding of the drug which may itself be unsafe. Compounding means mixing of ingredients to prepare a medication for patient use, including dilution, admixture, repackaging, reconstitution and other manipulations of sterile products. Mixing of different drugs may not be stable. Morphine and hydromorphone favors ziconotide degradation though clinical effects of the combination do not reflect a decreased efficiency. Another important point in choosing a certain drug or combination takes into account of the fact whether exposure of the drugs in a device and tubings and under a surrounding temperature of more than 37degree C influence the stability of the drug or mixture. It has been also found that the degraded drugs may not necessarily be biologically inactive. The pH, tonicity , solubility, sterility of the drugs have immense importance on the success of intrathecal polyanalgesia. The United States Pharmacopia (USP) and the American society of Health System Pharmacists (ASHP) have independently issued standards on compounded sterile products.

EQUIANALGESIC CONVERSION FACTORS FOR INTRATHECAL MEDICATION

The conversion of opioid from one route to another is highly individualized and depends on age, pain intensity, disease. With morphine pump it is calculated as follows : Oral morphine 300 mg = Parenteral morphine 100 mg = Epidural morphine 10 mg = Intrathecal morphine 1 mg[29].

There is no true conversion factor for calculating dose changes from one opioids to another. There may be increased chance of respiratory depression when changing from a more lipophilic opioids to a less lipophilic opioids using conventional equipotent analgesic charts.

BEST PRACTICE TITRATION RECOMMENDATIONS

For management of cancer pain Stearns et al recommended that the titration should be guided according to patients pain level as determined by visual analog scale (VAS) and according to functional status[30].

Figure 3

OPIOID TITRATION DIRECTED BY PAIN LEVEL	IMPLANTABLE	EXTERNAL
VAS 2-4 (If patient desired reduction And has unacceptable function)	Increase dose by 10%-25% over 3-4 days	Increase 10%-25% per hour Per day
VAS 5-6	Increase 25%-50% Daily (consider thera-peutic bolus carefully)	Increase 35%-50% per hour twice daily
VAS 7-10	Increase 50%-100% per day	Titrate to efficacy

Safety must be balanced against the need to relieve pain and suffering. The dose change can be accelerated in the cancer patients and young and robust but kept to changes weekly in the frail and the old. The polyanalgesic consensus panel recommend between 20% and 30% changes in the nonend of life population and upto 50% changes in end of life population depending on individual characteristics[28].

THE MACHINE : IMPLANTABLE INTRATHECAL DEVICE SYSTEM (IDDS)

The first implanted continuous epidural infusion system was reported by Harbaugh RE et al in 1982 where two patients received epidural morphine by implanted pump . The system worked well without infection or respiratory complication[31]. Soon after the first US Food and Drug Administration (FDA) approved implantable pump (Infusaid Model 400, Norwood, MA, USA) was launched. The first generation pumps were gas driven and constant flow type. It became apparent that patients of chronic pain of various intensity with sudden increase of pain level cannot be effectively managed with a constant flow type of pump. The programmable pumps were developed which can give bolus dose along with constant flow. Predictive pain level changes due to physical activity or emotional stress as well as circadian rhythm now can be controlled by “Personal Infusion Scheme”. However this system needed further modification when unpredictive pain level changes were considered. A combination of PCA and implantable device type of thing was needed. The device so developed (SynchroMed EL, Medtronic Inc.) allows the patient to recall bolus infusion in advance of expected increase of pain (prophylactic) or in response to sudden break through pain (therapeutic). As in the usual PCA devices, the dose, infusion time, lock out interval, maximum repetitions of boluses can be programmed. Each boluses are counted as

successful, rejected, unsuccessful and stored in pump memory for readeptation of basic infusion dose and bolus dose for "individualization of therapy". The next generation (Synchromed II and PTM=Patient Therapy Manager, Medtronic Inc.) have additional features such as registering Visual analogue pain Scale (VAS) before and after a bolus. The values are stored and analyzed for reprogramming of daily doses. Optimum dose range is reflected by a reduction in daily bolus calls. In a multi centre open level registry recording 168 patients it was found that 85% patients were satisfied with PTM[32].

These complicated machines have mechanical and electronic parts as well as drug reservoir. At present on account of the bulk of the machine drug reservoir may be made small. A large reservoir and a good battery life is what is aimed to be developed other than fancy programmability. The membrane pumps driven by piezo-electric mini crystals seem to meet both demands. A number of new devices like Prometra Programmable Pump System (InSet Technologies, Inc.), Medstream Programmable Infusion System (Codman and Shurtleff, Inc.), The Medallion (Advanced Bionics, Valencia, CA)etc. are awaiting for FDA approval.

COMPLICATION

Complications of Intrathecal Polyanalgesia are due to

- Procedure related
- Drug related
- Instrument related.

Procedure related complications include subcutaneous tissue necrosis, seroma with the risk of infection and loss of device especially in patients with low subcutaneous fat, small abdominal area or atrophic (cortisone) skin. Turner et al described complications derived from 10 reports. An wound infection of 12% across 3 studies, meningitis of 2% in 3 studies, pump malposition of 17% in 2 studies was seen[33]. CSF leak around catheter resulting post dural puncture headache is another potential complication. Transverse myelitis due to catheter tip infection is reported. While the device related infection is low a strict guideline for prevention and management of infection related to intrathecal therapy have been published[34]. For other complications like seromas, local hematomas, a conservative management with abdominal binder and external pressure is recommended. Meningitis may need removal of device and pump. The patient who refuses removal of IDDS may be treated with intrathecal vancomycin 10 mg/day. It is worth noting the complete lack of control studies on implantation techniques. There is only a recommendation for the devices that the tissue layer between the device and the skin surface should not exceed 20 mm in order to provide effective remote control of the device.

Drug related complications are quite serious. Intrathecal granuloma at the tip of the spinal catheter has the potential to cause spinal cord compression with all its squeals. Over 100 cases have been reported-the first was in 1991 [35].It is commonly seen with morphine and appears to be a function of concentration (>25 mg/ml), dosage (>10 mg/day) and duration of therapy[36,37,38].Amongst opioid fentanyl and sufentanyl has apparent granuloma sparing effect[39].Signs suggestive of granuloma formation include loss of analgesic effect and progressive neurologic symptoms. Small granulomas which are diagnosed early require cessation of drug and observation along with pulling back of the spinal catheter two segments or change of catheter while large granulomas need surgical removal.

Instrument related complications arise from faulty programming of the instrument or due to instrument failure (battery failure, motor failure etc). Serious complication can arise from spinal catheter also. Spinal catheter has a thinner wall spinal segment and a thicker wall proximal segment which are subjected to different physical stress. Catheter disconnection , breakage, occlusion, microfracture, microleak is quite possible which will result in gross underdosing. This catheter has a dead space or inner space which must need to be calculated and filled. Faulty estimation of catheter volume will cause sudden over or under dosing both of which are dangerous. Misses of refill ports while refilling the instrument with medicine resulting paravasates is another possibilities. In January 14, 2011 — The US Food and Drug Administration (FDA) has issued a Class I recall for certain lots of implantable infusion pumps manufactured by Medtronic. The recall was issued for Medtronic SynchroMed II (model number 8637) and SynchroMed EL Implantable Infusion Pump (model numbers 8626 and 8627) and Refill Kits (model numbers 8551, 8555, 8561, 8562, 8564, 8565, and 8566). The problem with the devices is the potential for "pocket fills" to occur, in which the drug is injected into the pump pocket (the area under the skin where the pump is placed) instead of the pump. Between 1996 and 2010, 8 deaths and 270 events requiring medical intervention were reported related to the occurrence of pocket fills, according to the FDA. The rate of

occurrence per refill opportunity is at least 1 in 10,000[40].

Whatever happens the result is either overdosage or underdosage of drugs , both of which are dangerous and seeks immediate attention. In underdosage patient presents with withdrawal symptoms, pain. Baclofen withdrawal may be fatal as the patient presents with fever, altered mental status and profound muscular rigidity[41].Whereas over dosage of drug can cause respiratory depression, hypotension,coma. A complication needs immediate hospitalization, careful diagnosis and sensitive management as they are quite serious and often fatal.

Prompt diagnosis of unexpected pain or other symptoms are important to prevent complications.

The diagnostic approaches can be followed are

- Initial evaluation, including patient history will often identify the source of the problem.
- Verification of pump contents, volume and pump settings is the critical initial step.
- Plain X Ray (PA and LAT to visualize the entire catheter).
- Serial X Ray or fluoroscopy to confirm that the pump roller is moving at the expected rate.
- Myelography to see CSF flow around catheter.
- Nuclear Medicine Scan.
- Magnetic Resonance Imaging (MRI) study.

Diagnosis and treatment makes intrathecal therapy safe and effective. A randomised multicentric trial investigated the safety and efficacy of IDDS plus CMM versus CMM alone in patients with refractory cancer pain[42]. The authors concluded that patients receiving IDDS plus CMM had reduced pain, fewer drug toxicity and improved survival. After institution or reinstitution of intrathecal therapy patients should be monitored in an adequately equipped facility having sufficient monitoring equipment for a sufficient amount of time. A period of 24 hours is considered appropriate for evaluating potential complications in vulnerable patients which include the elderly, the very young, opiate naïve patient, patient with poor cardiac reserve or respiratory reserve.

DISCUSSION AND CONCLUSION

Intrathecal Polyanalgesia is indicated in chronic pain therapy where CMM fails.

Development of IDDS and various opioid and non opioid drugs along with growing knowledge of pain physiology made Intrathecal Polyanalgesia a highly successful modality of pain therapy in clinical scenario with very good patient acceptance. A panel of experts convened three Polyanalgesic Consensus Conferences since 2000. The last Polyanalgesic Concensus Conference was held in 2007 which has formulated an algorithm for drug selection in Intrathecal Polyanalgesia. Intrathecal baclofen a USFDA approved drug however has not been included in the algorithm for unknown reason. There are other experimental drugs like cannbinoids, calcitonin which the panelists did not include. The panel opined that clinical research on intrathecal analgesics that meets the “gold standard” of evidenced based studies has not kept pace with the growing need for innovative approaches to pain management. Vast majority of clinical experience is with the off-label use of various agents and large multicentre studies are required to establish the proven safety and efficacy. Until this is achieved the clinicians will have to depend on guidelines created from limited data and their own clinical experience. The success of intrathecal Polyanalgesia depends on issues like patient selection, screening trials, long term management issues and drug utilization. Recalling of devices by USFDA showed that intrathecal therapy is not a completely harmless technique. The evidence for IDDS is strong for short term improvement of cancer pain or neuropathic pain. Relatively strong evidence exists for the use of long term intrathecal analgesic therapy in alleviation of cancer pain. However the evidence supporting long term efficacy in persistent non cancer pain is less convincing.

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