



Role of Intrathecal Non-Opioid Analgesics in Cancer Pain



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Background

- Intrathecal drug delivery (ITDD) of analgesic agents, a type of targeted drug delivery, has been used for decades for the treatment of chronic pain that has become refractory to initial conventional approaches, such as systemic opioid therapy¹
- Long-term use of systemic opioids correlates to higher risk of systemic toxicity and side effects. In addition, 10-20% of patients being treated for cancer pain experience refractory pain that does not respond to conventional systemic opioid treatments².
- Morphine is the gold standard for treating chronic pain and the only opioid approved for intrathecal (IT) use by the FDA.
- Intrathecal clonidine and ziconotide are the only two non-opioid analgesics approved by the FDA for chronic pain. In addition, intrathecal bupivacaine and ketamine have also shown supporting data for pain relief.
- It has been suggested that using intrathecal non-opioids in conjunction with opioid therapy can reduce the overall dose of opioids, resulting in reduced risk of adverse effects, decrease in opioid associated toxicity and better pain control.
- As cancer survivorship increases, the need to manage chronic pain has correspondingly increased, so it is important to be aware of the different options available to manage pain safely, effectively and ultimately improve the patient's quality of life.
- Complications associated with intrathecal drug delivery system includes minor and serious infections, equipment malfunction, catheter related and psychological (distorted body image) category.

Objective

- The purpose of this study is to evaluate the available literature for the efficacy of intrathecal non-opioid analgesic agents in cancer-related chronic pain.

Methods

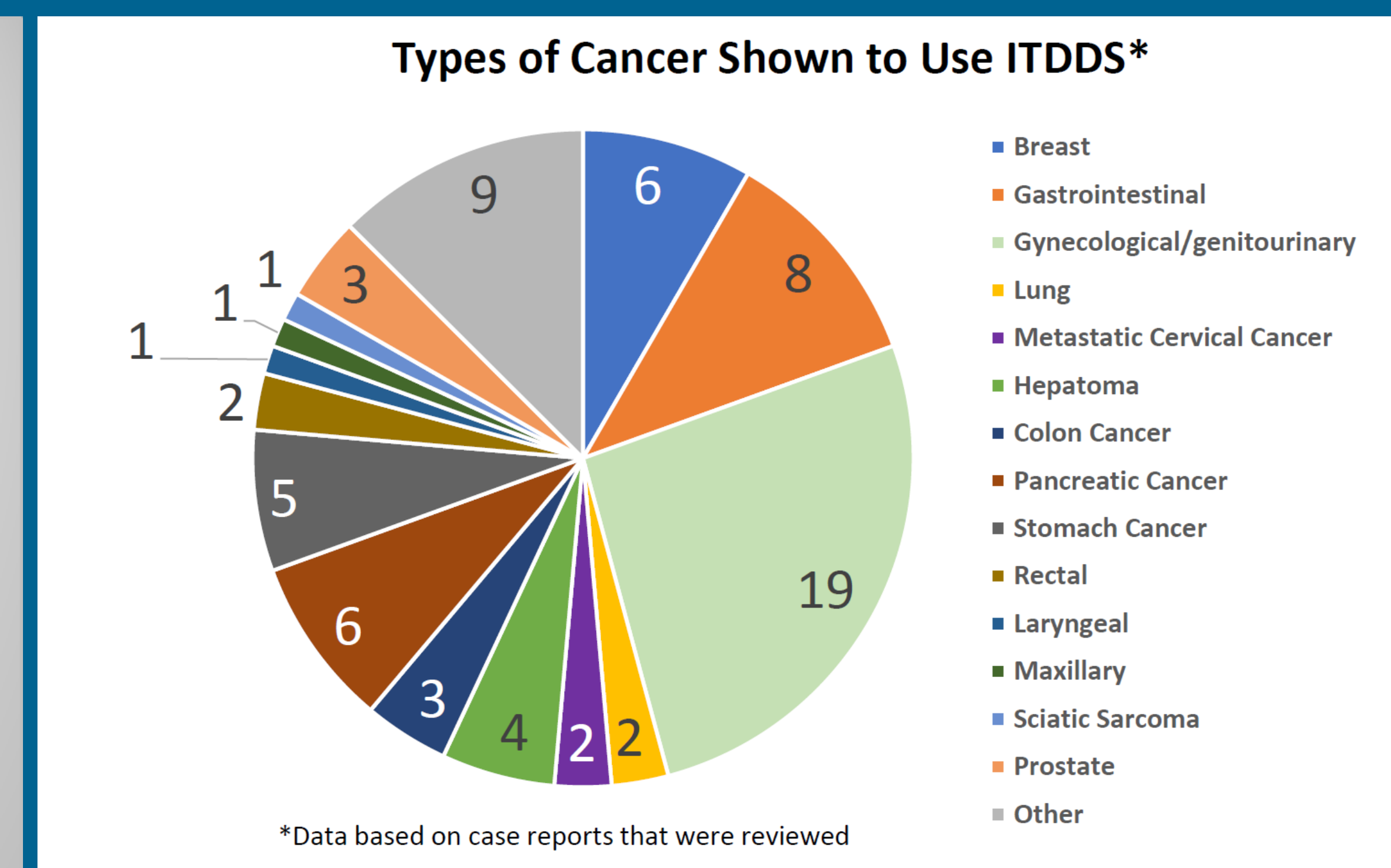
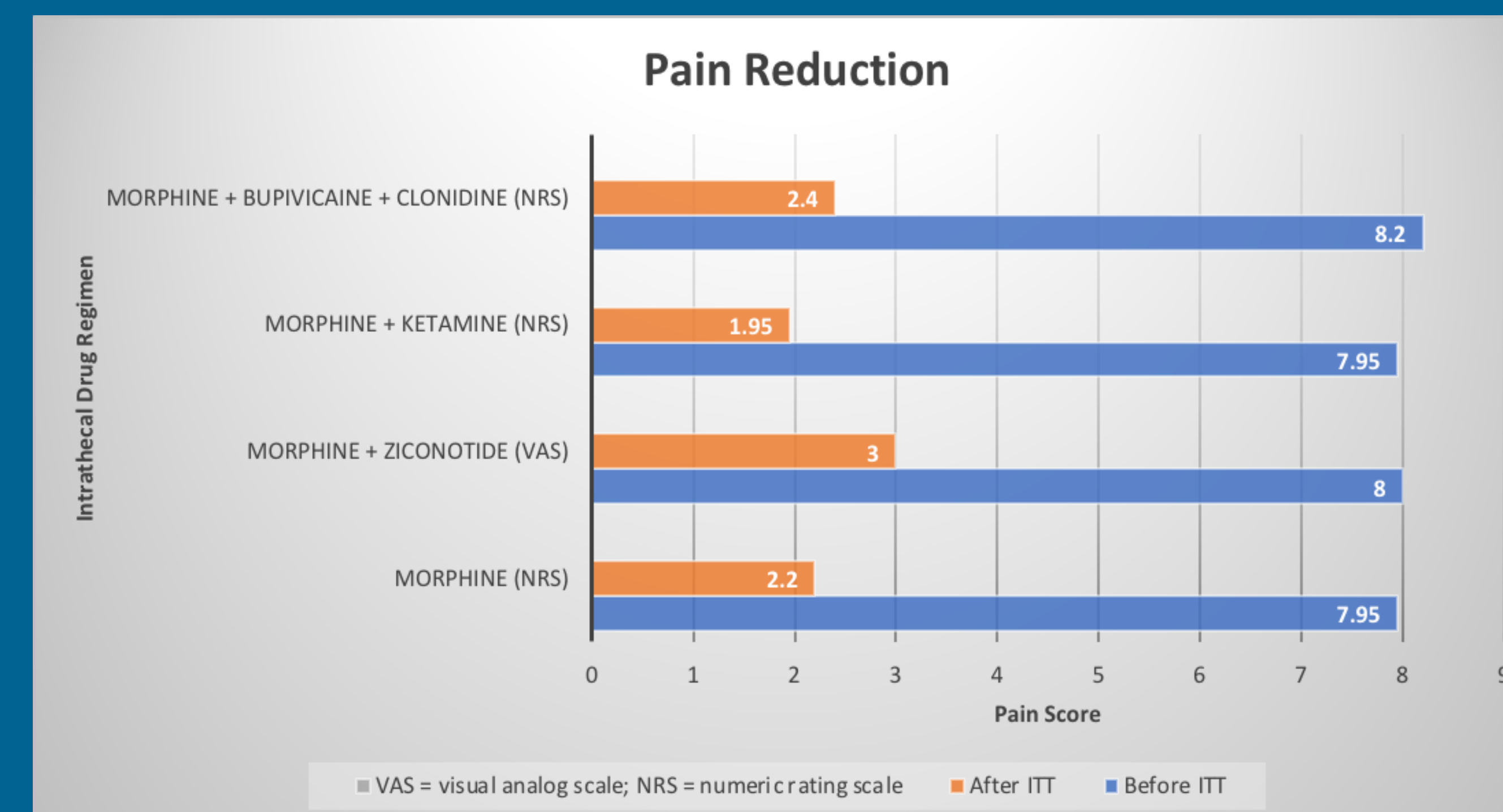
- A series of case reports, case series, and retrospective analyses on intrathecal drug delivery using various opioid and non-opioid combinations in patients with cancer associated chronic pain was reviewed to provide an idea of what available literature recommends.
- The Medline database was searched for studies that included "ketamine", "clonidine", "bupivacaine" and "ziconotide" AND ("cancer" OR "malignant") AND "intrathecal" in title or abstract.

Disclosure and Contact

All authors have nothing to disclose: brenden.pupi@ttuhsc.edu, saj.gowani@ttuhsc.edu

Results

Agent	Agent category	Typical use	Common adverse reactions	IT Adjuvants Used in the Studies
Clonidine	Alpha-2 Adrenergic Agonist	Combination	Hypotension and sedation	Morphine, ketamine
Bupivacaine	Local anesthetic	Alone or in combination	Motor weakness, sensory deficits, hypotension, and urinary retention	Morphine, midazolam propofol
Ketamine	N-methyl-D-aspartate antagonist	Combination	Nausea/vomiting, dysphoria, hypotension, and motor weakness	Morphine, bupivacaine, clonidine
Ziconotide	Calcium channel antagonist	Alone or in combination	Nausea/vomiting, dizziness, confusion, mental slowing, psychiatric reactions, hypotension, and ataxia	Morphine



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Discussion

- Intrathecal drug delivery systems (IDDS) for cancer pain remain little employed despite high level of efficiency and benefits. The case series presented shows the safety and efficacy of intrathecal targeted drug therapy. Palliative care patients who are suffering from chronic pain due to cancer are usually started on oral formulation for pain management; with time the patient stops responding to the medication and other forms of administration are needed to relieve the pain and provide comfort.
- The data suggests the use of analgesic cocktails in conjunction with opioids to be successful in reducing pain when administered intrathecally. There are wide ranges of dosing regimen seen throughout the different case reports. Intrathecal analgesic delivery is well-documented in terms of non-cancer pain; luckily, the data/interpretations in terms of safety and side effect profile of agents used intrathecally can be assumed to have a similar effect between non-cancer and cancer pain to represent the minimum expected negative effects when considering its use.
- It is difficult to gauge the efficacy of a single agent, as these case studies use a combination of different agents, making it difficult to individually evaluate an agent. In addition, the type of pain is different depending on the cancer - which can vary by cancer type - the etiology and pathology of the pain can also vary greatly between patients with the same type of cancer.
- Most of the drugs used in these case reports were not FDA approved for intrathecal administration. Limited data is also available on intrathecal medication use for cancer patients.

Conclusion

- Targeted intrathecal drug therapy for patients with cancer may be an alternate option when all resorts have failed to achieve optimal pain control. Multiple opioids and non-opioids agents have been considered in numerous case studies besides the gold standard of therapy, morphine.
- Alternative agents should be considered based on patients' needs and physicians comfort level with the treatment regimen to help achieve better pain control in patients whose chronic cancer pain is not being managed by their current regimen.
- Through these case series we have discovered that the use of non-opioid IT targeted drug therapies in conjunction with opioids IT have helped patients achieve optimal pain control and better quality of life.
- When opioids and non-opioids are used in combination via intrathecal delivery, greater pain relief can be achieved at significantly lower opioid doses, ultimately decreasing the risk of adverse effects that are commonly associated with systemic opioids.