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 on the rise for the treatment of chronic pain that has become refractory to initial conventional approaches, such as systemic opioid therapy.
- 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 experience pain refractory to both systemic and opioid therapy.
- 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 non-opioid in nature 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.

Results

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

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 delivery. Palliative care patients who are suffering from chronic pain due to cancer are usually started on oral formulation of pain medication only when 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 targeted drug delivery is the option of choice in reducing pain with opioids in patients who are suffering significantly lower opioid doses, ultimately decreasing the risk of adverse effects that are commonly associated with systemic opioids.

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.

References


Disclosure and Contact

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