Intrathecal Opioid Pump in the Treatment of Pain in Oncologic Patients: case series and literature review

Bomba de Opioide Intratecal no Tratamento da Dor em Pacientes Oncológicos: série de casos e revisão de literatura

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ABSTRACT

Introduction: Intractable pain in cancer patients reduces the quality of life and increases the use of oral opioids without effectiveness in treatment. Therefore, the intrathecal opioid pump becomes an option, allowing a reduction in drug dose and mortality while increasing treatment efficacy. 

Method: Systematic review of literature in PubMed searching for “intrathecal opioid” and “cancer pain”. The main points for the follow-up of an oncologic patient, who underwent an intrathecal opioid pump implantation were included.

Results: Case 1: Male patient, 63 years old, prostate cancer with bone metastasis and refractory bone pain preoperatively 7/10 and postoperatively 3/10 (NRS). Case 2: Female patient, 21 years old, rhabdomyosarcoma in the left mandible, refractory pain 7/10 in mandibular nerve territory and 3/10 (NRS) post-procedure. Case 3: Male patient, 31 years old, anal cancer, intense anorectal and lower limb pain refractory to odd ganglion block, with no improvement after the procedure.

Discussion: Refractoriness to other drug therapies and the trial of intrathecal therapies should be considered before the procedure. The case series presented shows the potential of the treatment, which was able to reduce pain intensity by more than 50%, in two patients. However, the technique has limitations, and one of the reported patients did not achieve symptomatic improvement even with the use of intrathecal morphine.

Conclusion: The implantation of an intrathecal opioid pump is undoubtedly an option with great therapeutic potential in refractory pain.

Keywords: Intrathecal Opioids; Cancer Pain; Oncologic treatment

RESUMO

Introdução: A dor intratável em pacientes oncológicos reduz a qualidade de vida e aumenta a utilização de opioides orais sem eficácia. Assim, a bomba de opioide intratecal torna-se uma opção, permitindo uma redução na dose de medicamentos orais e na mortalidade, ao mesmo tempo em que aumenta a eficácia do tratamento. 

Método: Revisão sistemática da literatura na base de dados PubMed buscando por “intrathecal opioid” e “cancer pain”. Foram incluídos os principais pontos para o acompanhamento de um paciente oncológico que foi submetido ao implante de bomba de opioide intratecal.

Resultados: Caso 1: paciente masculino, 63 anos de idade,
Many oncological patients suffer from intractable pain, which is associated with a reduction in their quality of life. According to the International Association for the Study of Pain (IASP), more than 10 million people worldwide who are diagnosed with some form of cancer each year suffer from pain, which is worrying. However, pain is not always avoidable for all of these patients, so the consequences of unrelieved pain are devastating\(^1\)\(^-\)\(^2\).

Some patients complain that this pain leads to concentration problems and impacts their daily activities. Besides the cancer alone, almost 30% of the patients described their pain as an intolerable aspect of their disease\(^3\). Nevertheless, cancer pain remains undertreated in 25 to 70% of the cases\(^4\)-\(^6\).

To deal with this issue, some procedures, whether invasive or not, were developed to manage this type of pain and to improve the quality of life of the patients. The first step for pain management in cancer patients would be the use of oral opioids, which, however, fail in several cases. The intrathecal opioid pump can be used in this context, but their long-term results cannot be predicted with certainty, since it varies to different types of cancer pain mechanisms\(^7\). However, a benefit of using intrathecal morphine is that this mechanism allows the dosage of the drug to be lower compared to the oral one, which reduces its side effects and shows greater effectiveness in the treatment, making it more tolerable to patients\(^8\).

In fact, the use of intrathecal medication has already been associated with a reduction in mortality, with an increase in survival in six months about 20% when compared to conservative treatment\(^9\). Thus, the use of such systems not only increases quality of life and the functional profile of patients, but it can also increase their survival, which greatly impacts their interpersonal and family relationships.

In this context, the aim of this study is to review the most recent work regarding the use of intrathecal opioid pumps in oncological pain and to summarize the improvement of patients’ profile and their possible side effects. We also intend to compare the literature with our personal data and experience.

### METHODS

Systematic literature review on PubMed searching for ‘intrathecal opioid’ and ‘cancer pain’, in which we included the main data of the follow-up of an oncologic patient submitted to intrathecal opioid pump: age, visual analogue scale (VAS) and numerical scale (Numeric Pain Rating Scale – NRS) pre- and postoperative and adverse effects of the treatment. For better visualization, data was organized (Table 1). The selection of articles was determined by the authors according to relevance. No period was established for the search of materials. In addition, three patients underwent surgery for implantation of intrathecal opioid pump for treatment of refractory pain. A comparison was made between the data in the literature and those of the three patients presented.
Table 1. Cases presented in the literature review.

<table>
<thead>
<tr>
<th>Authors, year</th>
<th>N**</th>
<th>Age (years)</th>
<th>Preoperative pain</th>
<th>Postoperative pain</th>
<th>Postoperative side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stearns et al. (2020)</td>
<td>1403</td>
<td>Average of 59</td>
<td>VAS‡ 6,8±2,4/10</td>
<td>VAS‡ 5,4±2,5/10</td>
<td>Infections and psychiatric, mediastinal, thoracic, nervous, and respiratory system disorders.</td>
</tr>
<tr>
<td>Becker et al. (2000)</td>
<td>43</td>
<td>Average of 64</td>
<td>VAS‡ 9/10</td>
<td>VAS‡ 3/10</td>
<td>Nausea and vomiting</td>
</tr>
<tr>
<td>Gogia et al. (2012)</td>
<td>1</td>
<td>61</td>
<td>At rest, VAS‡ 7/10; in movement, VAS‡ 10/10</td>
<td>VAS‡ 0-3/10</td>
<td>None</td>
</tr>
<tr>
<td>Bengali et al. (2014)</td>
<td>1</td>
<td>15</td>
<td>NRS† 8/10</td>
<td>No NRS† data, but there was pain relief</td>
<td>Transient urinary retention</td>
</tr>
<tr>
<td>Choi et al. (1989)</td>
<td>50</td>
<td>Between 40 and 72</td>
<td>-</td>
<td>-</td>
<td>Cardiorespiratory depression</td>
</tr>
<tr>
<td>Mercadante et al. (2007)</td>
<td>55</td>
<td>Average of 60</td>
<td>-</td>
<td>-</td>
<td>Nausea, drowsiness, confusion, constipation, urinary retention, and progressive paralysis.</td>
</tr>
<tr>
<td>Dennis and DeWitty (1987)</td>
<td>1</td>
<td>49</td>
<td>25% pain relief with oral medications</td>
<td>90% pain relief</td>
<td>None</td>
</tr>
<tr>
<td>Greenberg et al. (1982)</td>
<td>1</td>
<td>54</td>
<td>-</td>
<td>No VAS‡/NRS† data, but there was pain relief</td>
<td>Morphine tolerance</td>
</tr>
<tr>
<td>Sato et al. (2010)</td>
<td>1</td>
<td>49</td>
<td>NRS† 3/10</td>
<td>NRS† 3/10</td>
<td>None</td>
</tr>
<tr>
<td>Bentley et al. (2014)</td>
<td>5</td>
<td>Average of 54.8</td>
<td>VAS‡ 10/10</td>
<td>VAS‡ 8.8/10</td>
<td>Recurrence and/or permanence of pain, paraparesis and urinary retention.</td>
</tr>
<tr>
<td>Crul et al. (1994)</td>
<td>2</td>
<td>1) 50</td>
<td>1) VAS‡ 9-10/10; 2) VAS‡ 7-8/10</td>
<td>1) VAS‡ 5/10; 2) VAS‡ 1-2/10</td>
<td>None</td>
</tr>
<tr>
<td>Hawley et al. (2009)</td>
<td>6</td>
<td>Between 22 and 67</td>
<td>NRS† 9/10</td>
<td>NRS† 1/10 (60%); NRS† 2/10 (20%); NRS† 3/10 (20%)</td>
<td>None</td>
</tr>
<tr>
<td>Hochberg and Perez (2018)</td>
<td>3</td>
<td>1) 84, 2) 78, 3) 73</td>
<td>-</td>
<td>No VAS‡/NRS† data, but there was pain relief</td>
<td>Death because of neoplasia</td>
</tr>
<tr>
<td>Huang et al. (2015)</td>
<td>36</td>
<td>Average of 63</td>
<td>-</td>
<td>-</td>
<td>Transient urinary retention, constipation, nausea and vomiting.</td>
</tr>
<tr>
<td>Ju et al. (2018)</td>
<td>1</td>
<td>73</td>
<td>NRS† 8/10</td>
<td>At rest, NRS† 2-3/10; with irruptive pain NRS† 5-6/10</td>
<td>None</td>
</tr>
<tr>
<td>Ma et al. (2020)</td>
<td>233</td>
<td>Average of 60.41</td>
<td>-</td>
<td>VAS‡ 6.33/10</td>
<td>Respiratory depression, sensorimotor disturbances, low intracranial pressure, CSF* leak, anorexia, vomiting, dizziness, pruritus, nausea, urinary retention, constipation, and infection.</td>
</tr>
<tr>
<td>Moman et al. (2019)</td>
<td>1</td>
<td>59</td>
<td>NRS† 8-10/10</td>
<td>No NRS† data, but there was pain relief</td>
<td>Infection around the reservoir pocket, requiring an explant.</td>
</tr>
<tr>
<td>Rauck et al. (2003)</td>
<td>119</td>
<td>Average of 60.6</td>
<td>NRS† 6.1</td>
<td>NRS† 4.2/10</td>
<td>Almost all complications were implant-related: spinal headache, seroma, infections, wound healing problems.</td>
</tr>
<tr>
<td>Reddy et al. (2012)</td>
<td>1</td>
<td>30</td>
<td>VAS‡ 8/10</td>
<td>VAS‡ 5/10</td>
<td>-</td>
</tr>
<tr>
<td>Yamaguchi et al. (2018)</td>
<td>1</td>
<td>61</td>
<td>NRS† 6/10</td>
<td>NRS† 0/10</td>
<td>None</td>
</tr>
</tbody>
</table>

*CSF = cerebrospinal fluid; **N = number of patients; †NRS = Numeric Pain Rating Scale; ‡VAS = Visual Analogue Scale.
RESULTS

A series of oncology patients who underwent surgical implantation of an intrathecal opioid pump for the treatment of cancer pain was presented. The procedure was performed under general anesthesia, and the patients were arranged in left lateral decubitus position. A median incision was made at L3-L4 level, and a thorough dissection of all tissue layers, exposing the interspinous ligament. An intrathecal puncture was performed using a Tuohy needle, allowing the passage of an intrathecal catheter. Another incision was made in the right dorsal flank area and a dissection was done forming a subcutaneous pocket where the opioid pump was properly anchored. The catheter was positioned in a subcutaneous tunnel and connected to the pump.

Patient 1
A 63-year-old man was diagnosed with prostate cancer and bone metastasis, presenting with continuous bone pain. Oral opioids and analgesics were not able to provide adequate pain control. Thus, the patient was selected for surgical implantation of an intrathecal opioid pump. Preoperative pain was rated as 7/10 according to the Numerical Rating Scale (NRS). The surgery was uneventfully, and an intrathecal morphine pump (0.5 mg/mL) was installed and administered 0.4 mg morphine daily. After the procedure, there was no complete remission of symptoms, but the patient reported a significant decrease in pain intensity, with a postoperative pain score of 3/10 (NRS).

Patient 2
A 21-year-old woman was diagnosed with a rhabdomyosarcoma of the left mandible. On admission, the patient presented with severe pain in the left mandibular nerve region (V3) refractory to oral opioids. Preoperative pain was characterized as 7/10 (NRS). An intrathecal morphine pump was successfully inserted. Intrathecal morphine (10 mg/mL) was administered at 1.5 mg/day, providing immediate pain relief. Postoperative pain was rated as 3/10 (NRS).

Patient 3
A 31-year-old man was diagnosed with anal cancer, presenting with severe refractory anorectal pain. Oral opioids and analgesics did not provide adequate pain management. The patient underwent an odd ganglion block, but the procedure did not improve pain control. Thereafter, the pain was progressively more intense, and the patient progressed with diffuse bilateral lower limb pain. An intrathecal morphine pump was surgically implanted, but adequate pain control was not achieved on any morphine dosage.

To compile the data from the literature review, Table 1 was made.

DISCUSSION

Pain is one of the most common, burdensome, and distressing symptom for patients and is a significant factor underlying deterioration in quality of life. In this context, patients diagnosed with cancer may experience pain prior to their cancer diagnosis, which may then be aggravated by treatments.

The morphine pump is indicated for pain relief in patients with terminal cancer, in patients with reflex sympathetic dystrophy in whom the epidural electrode is no longer taking effect, or in patients who have disabling pain due to degenerative lumbar or thoracic changes. The surgeon must confirm that the chronic pain is refractory to more conservative therapies and that psychiatric disorders and psychosocial issues that could adversely affect the outcome of treatment have been adequately addressed.

Intrathecal therapy (IT) should be considered in patients with intractable focal pain or those intolerant of the side effects of systemic opioids. In cancer patients, especially, those patients undergoing long-term toxic chemotherapy regimens may particularly have benefit from IT therapy rather than systemic analgesics due to the lower additive risk of adverse events.

Prior to the procedure, a trial of IT may be considered prior to actual device implantation to assess medication tolerability, response, and patient acceptance of the IT delivery method. The trial may be performed using a bolus injection or continuous infusion via the IT pump, if already implanted for use with other treatments, or an extramural pump in patients without an implanted IT pump.

The surgery is relatively simple and consists first of a lumbar puncture, in which the catheter is directed upwards, with the bag already pre-established between the costal arch and the iliac crest.
in the subcutaneous space. As the cerebrospinal fluid (CSF) is withdrawn, the pump is connected. The pump is electronic and has an externally controlled flow rate of 0.048 mg/day.

Analyzing the case series, two of the three patients obtained satisfactory pain control after the operation. When compared to the literature, 1963 patients divided into 20 studies were analyzed. Of these, it was not possible to quantify exactly how many patients obtained significant pain relief, as different scales were used (NRS and VAS) or the patient's own report in the studies. Furthermore, the interpretation of these scales by the patient has a subjective load. However, even though this disparity exists, it is possible to note that in most patients there was significant pain relief with concomitant reduction of oral analgesic and opioid medication. It is also worth mentioning that, as in this study, rarely in the literature there was a complete remission of pain and, in some patients, there was a recurrence of pain.

The most common side effects include urinary retention, nausea and vomiting. Some patients developed tolerance to intrathecal medication, requiring a progressive increase in dose to maintain pain control. Moreover, cases of pain in the lower and upper limbs are considered a challenge in pain management after the use of the morphine pump, presenting little or no improvement of the pain, as it happened in patient 3 of this present study; therefore, a good choice of the patient is necessary.

Considering the pain relief in most patients, the use of morphine pump should be considered in the treatment of patients with advanced cancer and who present with chronic pain refractory to oral medications, aiming at improving the quality of life of such patient.

### CONCLUSION

The implantation of an intrathecal opioid pump is with no doubts an option with great therapeutic potential in refractory and chronic pain secondary to cancer. A precise anatomical knowledge of the procedure is necessary to minimize intraoperative risks and decrease postoperative side effects. The final objective of this surgical procedure is to promote pain relief as demonstrated in the patients of this study and in the respective comparison of patients described in the literature.

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