Scandinavian Journal of Pain 17 (2017) 37–40

Contents lists available at ScienceDirect

Scandinavian Journal of Pain

journal homepage: www.ScandinavianJournalPain.com

Educational case report

Management of patients with pain and severe side effects while on intrathecal morphine therapy: A case study

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HIGHLIGHTS

- Intrathecal morphine therapy is deemed the last resort for chronic pain.
- Two patients experienced severe side effects and lack of optimal pain control.
- Treatment using a multidisciplinary approach and opioid tapering was effective.

ARTICLE INFO

Article history:
Received 25 April 2017
Received in revised form 26 June 2017
Accepted 5 July 2017

Keywords:
Intrathecal morphine therapy
Side effect
Multidisciplinary
Pain management
Opioid tapering

ABSTRACT

Background and aims: The use of intrathecal morphine therapy has been increasing. Intrathecal morphine therapy is deemed the last resort for patients with intractable chronic non-cancer pain (CNCP) who failed other treatments including surgery and pharmaceutical interventions. However, effective treatments for patients with CNCP who "failed" this last resort because of severe side effects and lack of optimal pain control remain unclear.
Methods and results: Here we report two successfully managed patients (Ms. S and Mr. T) who had intractable pain and significant complications years after the start of intrathecal morphine therapy. The two patients had intrathecal morphine pump implantation due to chronic consistent pain and multiple failed surgical operations in the spine. Years after morphine pump implantation, both patients had significant chronic pain and compromised function for activities of daily living. Additionally, Ms. S also had four episodes of small bowel obstruction while Mr. T was diagnosed with end stage severe "dementia". The successful management of these two patients included the simultaneous multidisciplinary approach for pain management, opioids tapering and discontinuation.
Conclusion: The case study indicates that for patients who fail to respond to intrathecal morphine pump therapy due to side effects and lack of optimal pain control, the simultaneous multidisciplinary pain management approach and opioids tapering seem appropriate.

1. Introduction

The clinical use of intrathecal morphine was firstly introduced as continuous spinal alagesia for obstetric analgesia in 1979 [1,2]. This was followed by the introduction of programmable intrathecal morphine pump (PIMP) for pain related to malignancies in 1981 [3,4]. The PIMP devices allow for non-invasive dose changes and refills and can decrease adverse effects of opioids such as sedation and constipation [4]. Since the 1980s, the use of intrathecal morphine therapy has been increasing [5], and has been expanded to the treatment of patients with intractable chronic non-cancer pain (CNCP) who failed other treatments including surgery and pharmaceutical interventions [6]. The increase in intrathecal morphine therapy use is supported by its effectiveness and ease of use, although large randomized control trials are still lacking [5,6].

Intrathecal morphine therapy is deemed the last resort for patients with CNCP. However, years after morphine pump implantation, adverse events of morphine, sometimes including small bowel obstruction and severe sedation, respiratory depression and even death, may become increasingly common [7]. Additionally,

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http://dx.doi.org/10.1016/j.sjpain.2017.07.006
1877-8860/

studies also found that patients with chronic morphine use may present with poor pain control, decreased quality of life, and frequent emergency room visits, all of which are common side effects from chronic morphine use [8,9].

While the emergent management of the patient with pain and severe side effects while on long-term intrathecal morphine therapy focuses on life saving with opioid antagonist for side effects and/or bolus opioid injection for pain, optimal management of these patients may include tapering of intrathecal morphine and the management of CNCP. Methadone taper is the most commonly used method for opioid tapering where patients on long-term opioids are firstly stabilized with a dose of methadone that mitigates withdrawal followed by gradual opioid taper [10]. For CNCP itself, a multidisciplinary approach is usually recommended [12]. Nonetheless, research studies on combining methadone taper with a multidisciplinary pain management approach for patients with pain and severe side effects while on long-term intrathecal morphine therapy are still scarce in the literature, and optimal treatments for these patients remain unclear. Here we report two patients with intractable pain and significant complications while on long-term intrathecal morphine therapy. The two patients were successfully treated with methadone taper in combination with the multidisciplinary pain management.

2. Case presentation

2.1. Case 1

Ms. S was 67 years old when she had the PIMP implantation for her prolonged consistent low back pain in 2004. Prior to that, Ms. S had 4 failed back surgeries and received the implantation of an implantable spinal cord stimulator. After the PIMP implantation, Ms. S was also given oxycodone and hydrocodone for breakthrough pain. With the highest intrathecal morphine dosage of 3.60 mg/day and bolus morphine dosing, the treatment protocol had become unsatisfactory as Ms. S had increased visits at hospital emergency departments for respiratory compromise-induced pneumonia, small bowel obstruction, constipation, on top of intolerable pain aggravation.

By the end of 2009, Ms. S restarted to use fentanyl patch with increasing doses as she believed that morphine no longer worked for her, despite the continuous treatment of intrathecal morphine. From 2009 to 2011, Ms. S received three additional surgeries for her back pain. In October, 2011, Ms. S was admitted to the hospital due to facial numbness, tingling, and sensory changes with anxiety and intractable lower back pain. We saw the patient on October 20th, 2011 for pain management and rehabilitation.

By that moment, Ms. S had been unable to sit or stand and had difficulties in transferring in and out of bed for more than two years. Besides morphine per pump (3.60 mg/day), Ms. S was also receiving fentanyl patch 50 mcg/h for pain control. After relevant examination and lab work, Ms. S was diagnosed with anxiety, trochanteric bursitis as well as lumbosacral radiculopathy and plexopathy. We thus treated the patient with bursa injection and lumbosacral plexus block. We also recommended methadone (2.5 mg, twice a day) for the tapering of both intrathecal morphine and fentanyl. After three days of methadone use, we discontinued fentanyl patch and increased methadone to 5 mg three times daily. We then decreased the dosing of morphine (initially 20% decrease monthly) while slightly modulating the dosing of methadone (5 mg given three to five times a day depending on patient's response).

Meanwhile, we adopted a multidisciplinary approach for pain management which included patient education and counselling, therapeutic exercises, fluoxetine, clonidine, lamotrigine, mirtazepine, and alternative and complementary medicine [heating and cold pad, acupuncture, and massage when appropriate]. Additionally, short-term meloxicam, naproxen, oxacarbazepine, and pregabalin had also been used separately or in combination during the long treatment course. We completely discontinued Ms. S's morphine per pump and started methadone weaning on June 27th, 2013. We slowly decreased methadone quantity and then frequency. By the time patient took methadone for the last time on July 20th, 2014, Ms. S's pain was well controlled and she was able to stand, sit, walk with rolling walker, and drive for community activities. She underwent another operation to remove her morphine pump in late 2014 after pain was under control with exercise and other non-opioid medications for around five months.

2.2. Case 2

Mr. T was 65 years old in 2004 when he had the PIMP implantation after multiple failed back and cervical surgeries for his work related injuries. Although the morphine pump originally provided some help, his pain over the lumbar and cervical spine increased over time. Since 2006, Mr. T had been receiving intrathecal morphine 3.373 mg/day and bupivicaine 0.8432 mg/day with the use of additional oral hydrocodone, oxycodone and hydromorphine for pain control. Mr. T had gradually lost his ability to stand and walk, and became totally wheelchair bound. Additionally, he also had gradually developed confusion, agitation, delirium, bowel and bladder incontinence, and frequent episodes of hypoxaemia from 2006 to 2011. In early 2011, Mr. T was diagnosed with end stage severe "dementia" and was under hospice care at a nursing home. On March 1st, 2012, Mr. T was brought in our office by her family for a second opinion.

After a close examination and evaluation, we found it was not sufficient to diagnose Mr. T with dementia while he was on large doses of opioids. We recommended weaning down the opioid medications using methadone taper while managing Mr. T's pain with the comprehensive multidisciplinary approach. Similar to the aforementioned case, we decreased the dosing of morphine (initially 20% decrease monthly) while slightly modulating the dosing of methadone (5 mg given three to five times a day depending on patient's response) after initially 2.5 mg twice a day for one week tolerance (allergy) test. Additionally, treatments including family education and counselling, physical therapy, tapering dose of methadone as well as adjuvant medications such as clonidine, lamotrigine, mirtazepine, oxcarbazepine, and citalopram were used.

During the methadone taper process, Mr. T's dementia-like symptoms improved gradually. By the summer of 2012, Mr. T was discharged home from nursing home. With pain well-controlled, on November 29th, 2012, we stopped the use of morphine per pump and started gradual methadone weaning via slowly decreasing methadone quantity and then frequency. On April 11th, 2013, his methadone use was completely discontinued when Mr. T had been tolerating well with standing and walking training with therapists, had no pain for most of the time, and was also able to ambulate with rolling walker inside his house with dementia-like symptoms completely resolved. The pump was later removed in early 2014.

3. Discussion

Both patients had unsatisfactory pain control and general weakness after years of opioid use. The suppressed endogenous opioid peptide system may be one of the potential culprits. The human body is constantly secreting endogenous opioid peptides [13]. The endogenous opioids participate in various physiological activities including the secretion of various hormones [13,14]. Van Bockstaele [15] reported decrease in endogenous opioid peptides in the rat medullo-coerulear pathway after chronic morphine treatment.