Analysis of complications that occur after intrathecal morphine trial or pump implantation

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Objective: A few cases of postoperative spinal syndrome (PSSS) provide very little pain relief even with standard treatment. Intrathecal morphine therapy (ITMT) has fewer side effects and can be used to improve pain control compared to systemic analgesic monotherapy, but ITMT-related complications may occur.

Introduction: Systemic opioids are considered an effective treatment option for patients with PSSS in whom severe pain cannot be controlled despite general treatment, such as drug therapy and nerve block, for pain relief. However, it can cause several side effects. Intrathecal morphine (ITM) treatment can reduce drug interventions, minimize side effects, and increase therapeutic effects.

Morphine is a hydrophilic opioid analgesic used to treat acute and chronic pain; thus, when injected intrathecally, morphine spreads gradually through the cerebrospinal fluid (CSF) circulation pathway, including the periaqueductal-periventricular gray matter, ventromedial medulla, and mu-receptors in the spinal cord, rapidly binding to several opiate receptors and ion channel. It can also suppress pain and produce an adequate analgesic effect, even at low doses.

However, aside from the positive effects of ITM, side effects have also been reported, including respiratory depression, nausea, vomiting, hypotension, bradycardia, pruritus, and urinary retention. Although morphine-related side effects are the most common with ITM treatment, device- or procedure-related complications may also rarely occur. In this study, patients with PSSS who underwent an ITM trial or pump implantation were classified into three categories—drug side effects, instrument, and procedure-related complications—and were analyzed.

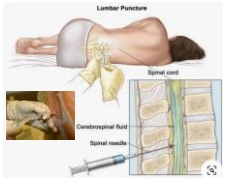
Methods: Thirty patients with PSSS were retrospectively evaluated. All patients had a visual analogue scale (VAS) score of 7 or higher and pain persisted for more than 6 months. If the VAS score decreased by more than 50% after a single dose of the ITM trial and there were no adverse events in the trial, ITM pump (ITMP) implantation was performed for continuous morphine injections for pain control.

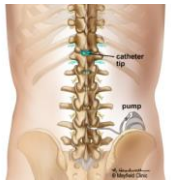
Of the 30 patients, 22 received only the ITM trial, and 8 patients received ITMP implantation, with a VAS reduction of more than 50% after the trial. Patients who received the trial only were observed for an average of 5.8 days (range: 4–15 days), while patients who received ITMP implantation were observed for an average of 53.3 months (range: 16–123 months). We analyzed adverse events after ITM injections or complications associated with ITM trial or ITMP implants. We used Highmol (Bio & Chemical R&D, Korea), a morphine free of preservatives and determined the dose considering the degree of pain relief and occurrence of side effects.

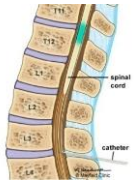
The ITM trial was performed with patients in the lateral decubitus position. After skin preparation and draping, a 25-gauge 10-cm spinal needle was inserted into the L2–3, L3–4, or L4–5 interspinous space to check the CSF flow. Subsequently, a bolus of 0.1–1 mg Highmol and 0.9% saline mixed solution was injected intrathecally over 5–10 seconds, and the spinal needle was removed.

After the ITM trial, no further ITM administration or pump implantation was performed if side effects occurred or if the VAS score was not reduced by more than 50%. No ITM-related side effects related to the trial were experienced underwent ITMP implantation for continuous morphine injection to control the pain. ITMP implantation was performed with the patients in the lateral position under general anesthesia.

After we performed dural puncture at the L2–3, L3–4, or L4–5 interspinous area and checked for CSF flow, the catheter tip was inserted up to L1–2 or T7–10, and the catheter was anchored to the fascia of the paraspinal muscle and fixed. A morphine pump pocket was created in the abdomen, an implantable pulse generator (IPG) was inserted, and the IPG and distal catheter were connected via subcutaneous tunneling.

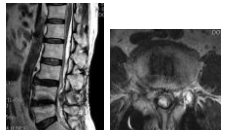




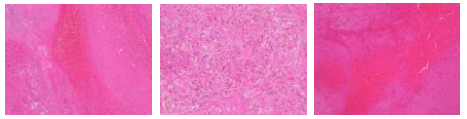


Results: Adverse drug events (n=12) were the most common complication, followed by procedural adverse events (n=1) and equipment adverse events (n=1). Dysuria (n = 9) was the most common side effect of the drug, followed by pruritus (n = 3). A rare but serious complication included a large lumbosacral subdural hematoma (n=1). There was catheter occlusion (n=1) by precipitated morphine crystals and skin infection at the implantable pulse generator (IPG) site (n=1). Skin necrosis was observed at the lumbar surgery site (n=1). Adverse drug events (n = 12) were the most common complications, followed by procedural adverse events (n = 1) and equipment adverse events (n = 1).

Saline injection into lumen, yellow crystal material exuded. Precipitated morphine crystal

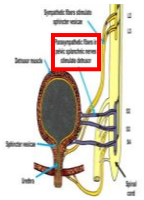


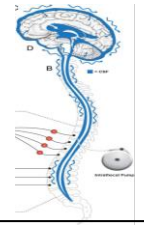
Subdural hematoma



Microscopic examination shows fibrous tissue & old hemorrhage. In the fibrous tissue, mild inflammatory cell infiltration and hemosiderin-laden macrophages are observed

Opioid-related side-effects and other complications (n=30)		
	Number	%
Opioid-related		
Urinary retention	9	3
Pruritus	3	1
Procedure-related		
Subdural hematoma	1	0.3
Back skin necrosis	1	0.3
Device-related		
Cather blockage	1	0.3





Discussion: Pensdi et al. reported that the use of ITM in spine surgery significantly lowered postoperative morphine consumption and VAS score, and was shown to increase pruritus for 24 hours after surgery in a meta-analysis of eight randomized controlled trials including 393 patients in 2017. Regarding ITM, 12 (40%) of the 30 patients had drug-related complications, of which urinary retention was occurring in 9 patients (30%), followed by pruritus in 3 patients (10%).

Urinary retention and pruritus were temporary adverse reactions that improved with conservative treatment. Overall, 27 patients (90%) had no or only transient adverse reactions. Urinary retention develops in 42%–80% of patients and is more common in older patients with an enlarged prostate. The underlying mechanism involves stimulation of the detrusor muscle by the sacral parasympathetic fiber to induce bladder contraction. This inhibits sacral parasympathetic outflow via an interaction with opioid receptors of the sacral cord, particularly the mu and delta receptors, and induces urinary retention through detrusor relaxation.

Pruritus is one of the common side effects that can appear on the face, neck, and upper chest. It develops several hours after drug administration and is usually mild. Owing to morphine's high hydrophilicity, it exhibits cephalad migration in the CSF. Its interaction with the trigeminal nucleus of the medulla reportedly causes an itch reflex by connecting with the substantia gelatinosa of the dorsal horn, and can induce changes in central nervous system-related pain perception. According to one study, the analgesic effect is maintained and pruritus can be improved when an intravenous drip of 5 μg/kg/hr naloxone is administered, and rapid tolerance occurs after 1–2 weeks

Conclusion: The most common drug-related side effect was difficulty urinating. Drug side effects recover within a few days after the ITM trial. In rare cases, complications related to the procedure may also occur, such as subdural hemorrhage or blocked IT catheter. An understanding of IT opioids, equipment, and meticulous procedural techniques is required to reduce complications associated with ITMT.

References

1. Pendi A, Acosta FL, Tuchman A, Movahedi R, Sivasundaram L, Arif I, et al. Intrathecal morphine in spine surgery: a meta-analysis of randomized controlled trials. Spine (Phila Pa 1976) 2017;42:E740–E747.
2. Ruan X. Drug-related side effects of long-term intrathecal morphine therapy. Pain Physician 2007;10:357–366
3. Webster LR. The relationship between the mechanisms of action and safety profiles of intrathecal morphine and ziconotide: a review of the literature. Pain Med 2015;16:1265–1277