Case Report

Priapism — A Rare Complication Following Continuous Epidural Morphine and Bupivacaine Infusion

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Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: None

Manuscript received: 07/06/2007
Revisions received: 08/01/07
Accepted for publication: 08/15/2007

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Background: Intraspinal drug delivery (IDD) therapy has been increasingly used in patients with intractable, nonmalignant pain who fail to respond to conventional treatment or can not tolerate systemic opioid therapy due to side effects. By infusing a small amount of analgesics directly into the cerebrospinal fluid (CSF) in close proximity to the receptor sites in the spinal cord, one is able to achieve the spinally mediated analgesia, sparing side effects ffrom systemic opioids. Prior to permanent intraspinal pump implantation, an intraspinal opioid screening trial is required to document the efficacy of intraspinal opioid for analgesia. Although there are a few approaches in conducting such screening trials, a patient-controlled continuous epidural morphine infusion trial, performed in an outpatient setting, is widely accepted by many interventional pain specialists. The major advantage of conducting an outpatient functional opioid infusion trial versus an inpatient trial is that it more closely mimics what the patient does in his or her usual activities of daily living, therefore minimizing the false positive rate of the inpatient screening trial.

Objective: To describe a rare complication, priapism, observed during an outpatient continuous epidural morphine and bupivacaine infusion trial.

Case Report: A 49-year-old male with intractable, chronic low back pain due to diffuse lumbar degenerative disc disease, lumbar spondylosis referred to our clinic for consideration of IDD therapy, after failing to respond to multi-modality pain management including medications, physical therapy with modality, transcutaneous nerve stimulation (TENS), and various interventional procedures. Following a pre-implant psychological evaluation, he was scheduled for the outpatient epidural morphine and bupivacaine infusion trial. A tunneled lumbar epidural a catheter was placed at L3-L4 with the catheter tip advanced to L1 under fluoroscopic guidance. The proximal tip of the catheter was then tunneled, subcutaneously, and connected to a Microject™ PCEA pump (Codman, Raynham, MA, USA) and reservoir bag containing preservative-free morphine 0.4 mg/mL and bupivacaine 0.016%. The pump was programmed to deliver a basal rate of 0.5 mL/h. The bolus dose was 0.2 mL with a 60-minute lock out interval. The patient was instructed how to use the pump properly before discharging home. Two hours following the initiation of infusion trial, the patient started to experience penile erection. It was initially painless, but became progressively painful and intensified. The unremitting priapism lasted 8 hours, finally resolving 2 to 3 hours after discontinuing the infusion. The patient recovered fully without any sequelae.

Conclusion: Priapism may occur as a rare complication following epidural morphine administration. This report represents the third case report thus far in the literature revealing priapism induced by epidural morphine administration, yet, it is the only report, to our knowledge, describing priapism occurring in a patient undergoing an outpatient epidural morphine and bupivacaine infusion trial. We believe that epidural morphine, rather than bupivacaine, is responsible for causing priapism in this patient, through a yet to be defined spinal mechanism.

Key words: Epidural morphine and bupivacaine infusion trial, intraspinal drug delivery pump, priapism

Pain Physician 2007; 10: 707-711

Intraspinal drug delivery pump therapy has been increasingly utilized in patients with intractable, nonmalignant pain (1-5). It is well accepted that a temporary trial of intraspinal analgesia be conducted to document efficacy prior to the implantation of a permanent intrathecal drug delivery pump (1). A patient-controlled continuous epidural opioid infusion trial, conducted on an outpatient basis, is one of the approaches chosen by many interventionists (6) including the authors. It consists of inserting a flexible lumbar epidural catheter under fluoroscopic guidance; tunneling the catheter subcutaneously and reconnecting it with Microject™ PCEA infusion pump (7,8). The pump is programmed by physicians to deliver selected analgesics mostly an opioid (e.g., morphine with or without local anesthetics, e.g., bupivacaine) in a continuous fashion with an on-demand bolus button accessible to the patient. The patient is discharged home to resume his or her usual activities of daily living. In our clinic, the outpatient infusion trial spans 1–2 weeks. The patient is usually weaned off oral opioids during the trial. More than 50% pain reduction together with an increased functional level during the trial is generally considered a "positive trial."

Priapism is a persistent painful erection that is usually not related to sexual activity. If untreated, priapism may result in impotence. The pathophysiology of priapism is not completely understood. Two types of priapism have been described: the low flow type and the high flow type (9). Priapism has been associated with spinal or epidural anesthesia especially in those urological procedures involving genital manipulations (10,11). However, priapism due to epidural opioid has been rarely seen. Indeed, there were only 2 previous reports describing the occurrence of sustained erection and inability to ejaculate following epidural morphine administration (12,13). Although our patient received an infusion mixture of morphine and bupivacaine, the bupivacaine dosage used in this epidural infusion trial was negligible in comparison to the multiple lumbar epidural blocks with bupivacaine he had received prior to the epidural infusion trial (see discussion). This is in sharp contrast to the previous reported case of priapism induced by an epidural local anesthetic (14) in which only epidural bupivacaine was used (see discussion). Our report, again, showed that priapism may occur as a rare complication in susceptible patients following epidural morphine administration.

Case Report

An otherwise healthy, 49-year-old male (100 kg) with severe, chronic low back pain, was referred to our clinic for pain management. He complained of having severe low back pain for over 7 years. He denied any significant extremity pain. The patient had MR evidence of multilevel displaced lumbar disc disease and spondylosis. He had failed to respond to multidisciplinary pain management including medications, physical therapies with modality, TENS, various interventional treatments under fluoroscopy including serial lumbar epidural blocks, lumbar facet blocks, and a sacroiliac joint block. He was on extended-release morphine 60mg bid with some efficacy, but with intractable nausea despite using a scopolamine patch and taking phenergan as needed. He was also on meloxicam 7.5mg daily, lidocaine patch 1–2 every other 12 hours, and hydrocodone/acetaminophen 10/500 tid as needed. He was without any history of psychiatric disorders and had been on no psychotropic medication. Intrethecal drug delivery was considered as a treatment option. Following a pre-implant psychological evaluation, he consented and underwent placement of a continuous epidural catheter for an outpatient analgesic infusion trial.

Under fluoroscopic guidance, the lumbar epidural catheter was placed at L3-L4 and advanced to L1. The proximal end of the catheter was tunneled subcutaneously and connected to a Microject™ PCEA pump. The pump was set to deliver preservative-free morphine (0.4 mg/mL) and bupivacaine (0.016%), at a basal rate of 0.5 mL/h. The patient could administer a bolus dose of 0.2 mL, with a lock-out interval of 60 minutes.

The patient was instructed how to operate the pump and discharged home. Two hours following the initiation of the infusion, the patient started to develop painless penile erection. About 30 minutes later, the erection became painful and sustained. The patient felt embarrassed and did not call the clinic for advice. Instead, he tried to "fix the problem himself." He first tried a distraction technique of watching his favorite TV shows without success. He then tried using an electric fan to blow air on it followed by applying an ice pack directly to the penis, still without much result. The erection remained forceful and painful. After about 8 hours, he finally contacted the clinic and was advised to turn off the infusion. The erection subsided

within 3 hours. Notably, the patient did not self-administer any boluses during the infusion. The patient was otherwise pain-free during the trial and suffered no adverse events, such as nausea, vomiting, or pruritus. He recovered completely.

Discussion

Priapism is an uncommon clinical entity with an incompletely understood pathophysiology. If not treated promptly, priapism may result in fibrosis of erectile tissues and subsequent permanent loss of erectile function (15). Priapism has 2 well-characterized types: low flow and high flow. Low flow or ischemic priapism, the most common type resulting from decreased penile venous outflow, is usually seen in patients with sickle cell disease or a tumor. It has also been seen in patients on antihypertensive medications or simply idiopathic. High flow priapism, the rare form resulting from the increased arterial inflow into the penile sinusoids, is generally seen in post-trauma settings or secondary to neuroaxial blockade (15). The pathophysiology of priapism can be considered simplistically as a dysfunctional hemodynamic process of the penis, where the genital organ excessively endures blood engorgement. Pelavski et al (14) believes that the autonomic imbalance between the sympathetic and parasympathetic nervous systems is responsible for creating this paradox: An erection appears if sympathetic vasoconstrictor action is blocked, whereas detumescence appears if the parasympathetic vasodilatory action is blocked. Therefore, epidural anesthesia could potentially block sympathetic impulses at L1-L2, causing a high flow status if the parasympathetic impulses originating from the sacral spinal cord is not simultaneously blocked.

Priapism has been reported as one of the complications of epidural analgesia (9,14). Pelavski et al (14) described a 6-year-old healthy boy (23.8 kg) who developed priapism one hour after the initiation of lumbar epidural infusion for post-op pain control, after a limb lengthening procedure. The epidural catheter was placed at L3-L4, delivering bupivacaine at 0.25 mg/kg/h. The priapism resolved within 45 minutes after the cessation of the epidural infusion. Interestingly, epidural anaesthesia was paradoxically used for the treatment of priapism that fails to respond to conventional treatment (15,16). Labat and Dubosset reported a case of priapism and abdominal vaso-occlusive crisis in a 9-year-old boy (35 kg) with sickle cell disease treated successfully by epidural bupivacaine and morphine (15). However, the infusion dosage included initial bolus of 17 mL of 0.25% bupivacaine with epinephrine (1/200,000), followed by the continuous infusion of 0.1% bupivacaine and morphine 40mcg/mL at a rate of 12 mL/h. The priapism resolved within 15 minutes after the initial epidural bupivacaine bolus. The patient subsequently developed urinary retention and motor blockade of the lower extremities. In the above case, we speculate that it was most likely the epidural bupivacaine that aborted the priapism. The immediate resolution of priapism contradicts other reports, where patients experienced priapism after epidural anesthesia with local anesthetics (9,14,17,18). It should also be remembered that priapism in patients with sickle cell disease belongs to the low flow type. It seems reasonable to speculate that the bupivacaine dosage used for the lumbar epidural block may have created this paradox. With varying the bupivacaine dosage and catheter position, one could block the lumbar sympathetic fiber or sacral parasympathetic fiber alone or both rendering a different penile flow status. Labat and Dubosset (15) advocated the usage of lumbar epidural anesthesia for the low flow type and cautioned about the likelihood of worsening priapism by using an epidural block in the high flow type.

In our case, however, we believe that it was not the epidural blockade by local anesthetic, i.e., bupivacaine, that precipitated priapism. This is because the bupivacaine used in our infusion is extremely minute [infusate consists of preservative-free (PF) morphine 0.4 mg /mL and PF bupivacaine 0.016%, infusion rate of 0.5 mL/h], [i.e.0.0008 mg/kg/h (body weight: 100 kg)]. The patient started to experience a sustained erection 2 hours (infused bupivacaine dose of 0.16 mg) after the continuous infusion. In our clinic, we intentionally add a small amount of bupivacaine for all our outpatient epidural opioid infusion trials in order to deter diversion of the infused opioid. It is inconceivable that such a tiny dosage of bupivacaine could cause any significant sympathetic block. Indeed, prior to the trial, the patient had received multiple lumbar epidural steroid injections with the epidural needle placed from L2-3 to L5-S1 on different occasions, confirmed under fluoroscopy, each with 4-5 mL 0.25% bupivacaine (administered average bupivacaine dose of 10–12.5 mg per injection) without ever experiencing

priapism. Therefore, we believe, it was the opioid, i.e. morphine, which was infused epidurally that caused the painful erection.

Previously, Rawal et al (12) and Torda et al (13) independently described epidural morphine causation of sustained erections and the inability to ejaculate in healthy male volunteers. Torda et al described the inability to ejaculate despite prolonged erection in 3 healthy males following epidural injections with 3–4 mg morphine in 10 mL normal saline delivered at L3-L4. Our patient, however, started to develop priapism after receiving 0.8 mg of epidural morphine infused in 1 mL normal saline, delivered via an epidural catheter at L1 over 2 hours duration. We suspect that the epidural catheter tip position might have a contributing role in inducing priapism. In our patient, the catheter tip (at L1) was in close proximity to the sacral spinal cord, usually at T12-L1.

Interestingly, Wiesenfeld-Hallin and Soderstern (19) demonstrated that intrathecal morphine increased while intrathecal naloxone decreased the number of intromissions prior to orgasm in male rats. Based on these properties, intrathecal or epidural opioids were once suggested to be viable treatment options for premature ejaculation (19,20). An erection is under the influence of this parasympathetic nervous system whereas ejaculation and termination of an erection are under the influence of the sympathetic nervous system (20). Pybus at al (20) believed that a sustained erection and the inability to ejaculate were secondary to the spinally mediated, opioid induced decrease in sympathetic nervous system response to sexual stimulation, as such phenomenon were not observed in males who received intravenous or intramuscular opioids (12,13,19).

The effects of opioids on sexual functioning are somewhat variable. It is known that by reducing the testosterone level, opioids affect sexual desire, erectile dysfunction, and delayed ejaculation (21,22). These are often seen in chronic opioid users (21,22). Recent literature on long-term intrathecal morphine therapy revealed that impotence and decreased libido occurred more frequently than previously recognized by physicians (23). To the best of our knowledge, there has been no report in the literature on systemic morphine causing priapism, although there was one report of 2 individuals experiencing priapism when taking dihydrocodeine and sildenafil together (24).

In our case, the patient had been on chronic opioid, i.e. extended-release morphine 60 mg bid for more than a year, and did experience a lack of sexual desire and erectile dysfunction prior to the epidural infusion trial, yet developed severe priapism following a small dose of epidural morphine, requiring termination of the infusion trial. We calculated the total dose of bupivacaine our patient received during the 10 hours of continuous epidural infusion to be roughly 0.8 mg (infusion solution of morphine 0.4 mg/mL and bupivacaine 0.016%, infusion rate 0.5 mL/h, bolus dose 0.2 mL, lockout interval 60 minutes, with no extra bolus dose attempted by patient). As mentioned previously, prior to the epidural infusion pump trial, the patient had received multiple lumbar epidural steroid injections with epidural needle placed between L2-3 and L5-S1, in which 4–5 mL of 0.25% bupivacaine was routinely used which correlated to an average bupivacaine dose of 10–12.5 mg per injection. Yet, none of the previous lumbar epidural blocks was complicated by the development of priapism, suggesting the insignificant role of the bupivacaine in our case.

We believe the epidural morphine the patient received during the infusion trial to be the cause of the priapism in our patient, through a spinally mediated mechanism resulting in the blockade of sympathetic outflow from the sacral spinal cord, although the exact mechanism needs further characterization. This conclusion is concordant with the previous hypothesis by Pybus at al (20). Nevertheless, priapism is of such rare occurrence that many interventionists, including the authors, frequently add a low dose of morphine to lumbar epidural steroid injections without encountering this complication. It is unclear what contributed to the susceptibility of the development of such a complication in our patient.

Conclusion

Priapism may occur as a rare complication following an epidural morphine infusion. A spinally mediated mechanism is speculated, which requires further investigation. This represents the third publication on priapism caused by epidural morphine administration, but the first case report of priapism observed in the patient on a continuous epidural morphine infusion. It confirms and adds to the body of literature of possible side effects of epidural morphine.

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