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LETTERS TO THE EDITOR

Intrathecal Medications in Post-Herpetic Neuralgia

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Dear Editor:

We write to report on a series of patients with medication-refractory post-herpetic neuralgia (PHN) treated by continuous intrathecal opioid administration.

PHN is the persistence of pain for more than 1 month following the onset of a herpes zoster rash [1]. This condition occurs in 15% of patients with shingles and may last for years [2]. It is a notoriously difficult to treat, and multiple medications from a variety of medication classes have been used. Oral and transdermal opioids are used for treatment but are often overly sedating, particularly in the geriatric population. Intrathecal opioid administration has successfully treated certain chronic pain conditions [3]. Drug delivery directly to the central nervous system allows for smaller opioid doses and less systemic side effects and may provide a useful therapy for PHN.

A retrospective review was performed of the clinical records of five consecutive patients treated at Buffalo General Hospital for medication-refractory PHN by surgical implantation of a pump–catheter drug-delivery system (SynchroMed I, Medtronic, Inc., Minneapolis, MN, USA) for intrathecal opioid administration. The initial opioid agent administered was morphine, with sufentanyl used for those patients experiencing a morphine side effect. Doses of the primary opioid were escalated; and, if the patient's pain was still not controlled, a second agent was added. Medication selection and management were performed in accordance with current consensus guidelines [4].

All patients were treated for PHN by intrathecal opioid administration over an 11-year period between May 1997 and August 2008. Each patient had clinically diagnosed herpes zoster. Average patient age at the time of pump placement was 73 years; two patients were women. The average duration of clinical follow-up was 5.8 years (range 2.0–8.3 years).

Conventional medical therapy was a failure in all patients due to inadequate pain control or intolerable medication side effects. Failed conventional therapies included oral morphine, hydrocodone, and tramadol, transdermal fentanyl, epidural steroid injections, and transcutaneous electrical nerve stimulation. Four patients had pain rated 10/10 on a 10-point pain scale (0 = no pain; 10 = excruciating pain) while taking conventional oral and transdermal pain medications. The fifth patient's pain was controlled with oral morphine and hydrocodone and transdermal fentanyl, but this patient slept for 18 hours each day while on this pain management regimen.

Before pump implantation, two patients underwent an intrathecal morphine trial, two patients underwent an epidural morphine trial, and one patient (with a history of morphine intolerance) underwent an epidural sufentanyl trial. In each case, the patient's pain improved significantly during the trial. Trials were considered successful if patients had more than 50% reduction in pain score on the visual analog scale and an improved ability to sleep and/or perform activities as a result of pain reduction. This method of trial and the use of both intrathecal and epidural injections is in concordance with the methods described in the prospective, randomized trial by Anderson et al. [5] for the selection of patients for continuous intrathecal opioid infusion.

Following pump implantation and intrathecal drug delivery, all patients had more than 50% improvement in the pain score as measured by the visual analog scale [6]. Patient pain improved by an average of 6.8 points on the 10-point pain scale. There were no complications related to the pump or catheter drug-delivery systems.

Patients were assessed by a neurosurgeon (RJP) regularly, and the time between appointments ranged from 1 to 12 weeks. Each patient's pain remained controlled by intrathecal medications, without intolerable side effects for

Table 1 Demographics for consecutive series of patients receiving intrathecal opioids for post-herpetic neuralgia

Patient Number	Sex, Age at Time of Pump Placement (years)	Intrathecal Medications	Follow-up Duration
1	M, 77	Morphine, bupivacaine	8 years, 6 months
2	F, 83	Morphine	8 years
3	M, 67	Sufentanyl, bupivacaine, clonidine	5 years, 3 months
4	F, 76	Sufentanyl, bupivacaine	4 years, 7 months
5	M, 61	Sufentanyl	2 years

M = male; F = female.

the entire follow-up period. Medication tolerance occurred; however, four of five patients required escalating medication doses and/or additional medications to achieve long-term pain control. The medications used were morphine alone; sufentanyl alone; morphine and bupivacaine; sufentanyl and bupivacaine; and sufentanyl, bupivacaine, and clonidine (Table 1).

Neuropathic pain is difficult to treat, and its response to oral or transdermal opioids is variable. Large opioid doses are often required to control neuropathic pain. In the present study, even on large doses of oral and/or transdermal opioids, four of five patients still reported 10/10 pain, with the fifth patient over-sedated by the amount of opioid medication required to control his symptoms. Intrathecal opioid administration allows for direct drug delivery to the central nervous system, with minimal systemic side effects. In all five patients in the study, the neuropathic pain was well-controlled, without any significant systemic side effects.

The difficulty in controlling the pain of PHN has previously led to the treatment of this condition with invasive methods. Spinal alcohol neurolysis and sympathetic blocks have been performed with some success [7]. PHN has been treated previously by intrathecal medication administration. Intrathecal methylprednisolone has been given in bolus form and resulted in an improvement in neuropathic pain [8]. However, the utility of this treatment has been questioned because of the associated complications, including meningitis, arachnoiditis, and cauda equine syndrome [9]. A case has been reported in which baclofen was delivered continuously to the intrathecal space and was successful at controlling PHN [10]. Continuous drug administration was accomplished by a pump–catheter system, as was used in the present study. This method of drug delivery has a relatively low complication rate when used for other chronic pain conditions [3].

Herpes zoster and PHN are relatively common conditions. As the population ages and patients with acquired immunodeficiency syndrome live longer with their disease, the prevalence of PHN in the United States likely will increase. Even with more aggressive use of antiviral therapy, there is still likely to be a large group of patients with PHN [11]. The Varicella zoster virus vaccine is a live attenuated vaccine and, although it may reduce the risk of PHN, it is not protective against this condition, particularly in the immunocompromised [12]. The symptoms of PHN can be debilitating, severe, and chronic. Continuous intrathecal opioid administration may provide a treatment alternative in a select group of patients with refractory PHN. We recommend an intrathecal or epidural opioid trial prior to pump implantation, as was performed during this case series.

PHN is a chronic pain condition that can be difficult to treat. Patients with PHN refractory to medical management may benefit from intrathecal opioid administration. Further study is warranted, including a blinded, randomized-controlled trial, in order to make more definitive conclusions.

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