Epidural use for Neuropathic Pain Relief in a Guillain-Barré Syndrome Patient

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Abstract

Pain can be a challenging complication experienced by patients who have Guillain- Barré Syndrome(GBS). Managing pain can be difficult and may require the use of multiple agents and still may not treat pain. This case report describes the use of an epidural to manage pain in a patient with GBS.

Eudiet Trollip MD[1], Ken Hawkins MD, FRCP[1], Isabel Kwek BSPharm[2], Krista Dewart NP[2], Mehvash Qureshi NP[2], Janek Manoj Senaratne MD, MSc, FRCPC, FACC[2, 3, 4] Department of Anesthesiology and Pain Medicine, University of Alberta, Edmonton, Canada[1]; Department of Critical Care Medicine, Grey Nuns Hospital, Edmonton, Canada[2]; Department of Critical Care Medicine, University of Alberta, Edmonton, Canada[3]; Division of Cardiology, Department of Medicine, University of Alberta, Edmonton, Canada[4] Word count: 2284**Consent statement:**Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.**Conflict of interest:**All authors [1] through to [6], declare that there are no conflict of interest in the below case study. Address of correspondence: Eudiet Trollip, MD Telephone number: (780)830-8207 Email address:*eudiet@ualberta.ca*Summary: Severe pain is an uncommon but challenging complication experienced by some patients who have Guillain-Barré Syndrome (GBS). Managing pain can be difficult and may require the use of multiple agents that may have significant side effects and still may not satisfactorily treat pain. Contemporary data on the use of epidurals for refractory pain management in GBS is lacking. This case report describes the use of an epidural to manage severe refractory pain in a patient with GBS. Background: GBS is an immune-mediated disease of the peripheral nerves and nerve roots that is usually triggered by infection. It is characterized by acute progressive motor weakness and areflexia. Pain is a relatively common symptom in GBS. The reported frequency of pain is variable (55%-89%) and can range in intensity from very mild to severe.[1] Younger GBS patients are especially susceptible to pain, which can cause both prolonged hospital stay and recovery, as well as long term disability. Pain can be either neuralgic or myalgic in nature. There is little data on the optimum medical treatment of pain but pharmacologic agents that are typically used and studied include acetaminophen, non-steroidal anti- inflammatory drugs, gabapentin, opioids, ketamine, lidocaine, tricyclic antidepressants, and selective serotonin reuptake inhibitors.[2] In one study, pain was reported in 36% of patients in the two weeks preceding weakness, 66% during the acute phase, and 38% still reported pain after one year.[3] Severe refractory pain is relatively uncommon but does complicate the course of certain patients. Very little data is available on the treatment of pain refractory to traditional and adjunct oral/intravenous medications.[4] In the mid-1980' s, there were a few published case reports on the use of epidurals for GBS pain.[5] There have not been any published case reports or studies in the last 25 years. Given that refractory

pain in GBS is relatively rare, there are no randomized controlled trials on the pain management of this difficult to treat subset of patients with GBS. [6] In this case report, we describe the use of an epidural in a patient with GBS with refractory pain syndrome. An epidural infusion of morphine and bupivacaine was started at 10 ml/hr and after 6 hours the patient's pain went from a Critical Care Pain Observation Tool score (CPOT) of 8/10 to 2/10. Most adjunctive opiates were stopped within a day with the epidural being used for a pain break. No complications from the epidural trial were seen.

Case Presentation:

A previously healthy male in his twenties presented initially with symptoms of chills, night sweats, a sore throat, mild cough and upper back and abdominal pain. Over the next 10 days, symptoms progressed to painful paresthesia and weakness in the lower limbs, which ascended and progressed to complete lower extremity paralysis, constipation, and urinary retention. A lumbar puncture done on admission to hospital showed a protein level of 1.08 g/L with a white blood cell count of 0 cells/mm3. Nerve conduction studies were undertaken as per neurology consultation and were suggestive of an acute motor greater than sensory axonal and demyelinating polyneuropathy with conduction block. The studies also suggested prolonged F waves and distal motor latency prolongation in keeping with the diagnosis of GBS. At this time the patient was admitted to the intensive care unit and started on intravenous immunoglobulin immediately at 400 milligrams/kilogram for 5 days. Over the next 48 hours, his respiratory status deteriorated from room air to 4L of oxygen per minute with decreased lung volumes on chest x-rays. His negative inspiratory force was < 15 centimeters of water. He was electively intubated and mechanically ventilated due to risk of acute respiratory failure. Three days post-intubation (14 days since symptom onset), the patient's pain significantly worsened (localized mainly to the lower extremities and chest), and he was started on gabapentin 900 mg daily, ibuprofen 1600 mg daily, and intravenous hydromorphone 1 mg as needed, as suggested in single-centre, small randomized controlled trials.[7] His symptoms did not improve and his CPOT remained 8/10. Eighteen days after admission to hospital, a tracheostomy was performed. His pain further increased, and he was only able to sleep 1 hour per night with his CPOT score constantly ranging from 8/10-10/10. On Day 24, the patient was started on venlafaxine 75mg and zopiclone 7.5 mg. Exact drug dosages with timeline of escalation of therapy are provided in Table 1. On day 29, ketamine was started to a total of 40 mg daily via nasogastric tube followed by olanzapine 3 mg daily on day 31. Pain remained unchanged and sleep only slightly improved to 1-2 hours a night and on Day 34, nabilone 2 mg daily was started, and a fentanyl patch added at 25 mcg/hr. On day 35 due to continued poor pain control, a lidocaine infusion was started at 3.84 mg/hr with slight improvement in pain to a CPOT of 7/10. At this point, the patient was on total daily doses of acetaminophen 3900 mg, diclofenac gel 2.32%, fentanyl patch 37.5 mcg/hr, gabapentin 3600 mg, dilaudid 30 mg, ibuprofen 1600 mg, ketamine 40 mg, lidocaine infusion 3.84mg/hr, nabilone 6 mg, and olanzapine 2.5 mg and still had uncontrolled pain and could not tolerate weaning of any of the agents. Moreover, the patient's negative inspiratory force was essentially undetectable which was likely partially affected by all the sedation. On Day 37, a family conference with the patient and family regarding epidural use in GBS was held with the potential risks and benefits discussed. They were informed of the lack of existing data to support the use of an epidural for GBS pain. At this time the patient and his family provided informed consent to trial the epidural for a pain break. This was 39 days after initial symptom onset and 24 days after severe pain was reported by the patient. The patient agreed to a maximum of 5 days of epidural use to minimize the risk of local complications with a primary goal of a short pain break along with the psychological reassurance that his pain could be controlled. The weaning strategy post-epidural was also discussed with the patient. Table 1: Analgesia dosing before, during, and after epidural use. *CPOT: Critical Pain Observation Tool

Treatment:

A lumbar epidural was inserted by Anesthesia with a 9 cm Tuohy catheter which was inserted without complication. A continuous infusion was started with Morphine 10mg- Bupivacaine 250mg in normal saline 250ml running at 10ml/hr. One day before insertion of the epidural, the patient was on a total milligram morphine equivalent (MME) of 125 mg along with Lidocaine at 3.84mg/hr, and Gabapentin 1800 mg orally daily. Pain was still documented as 8/10 on the CPOT. A day after epidural insertion, the patient was able

to tolerate an opioid reduction to MME of 75mg along with lidocaine and ketamine discontinued with the epidural at 10ml/hour and a CPOT of 2/10 as shown in Table 2 and the graph in Figure 1. Two days after insertion, the epidural rate was decreased to 7.5 ml/hr and his total MME was further down by about 40% with hydromorphone being as low as 1 mg total daily and the fentanyl patch decreased to 12.5 mcg/hr with the CPOT scores maintaining at 2/10. On day 6, after slowly decreasing the epidural rate, the epidural catheter was removed, and pain eventually increased again resulting in subsequent increases in opiates to an MME of 150 mg with a CPOT score of 8/10.

Table 2: Pain score before, after and during epidural use.

Days since symptom onset	**CPOT* score**	**Total daily MME** (mg)**	**Total number daily analgesics**	**Epi**
34	8	17.92	9	-
35	8	17.92	9	-
36	6	12.17	10	-
37	6	17.17	9	-
38	7	17.17	9	-
39	7	17.17	8	-
40	8	16.67	8	-
41	8	16.92	8	-
42	7	10.67	9	10
43	2	5.5	8	10
44	2	5.75	8	7.5
45	7	6	8	6
46	8	17.42	9	5
47	8	18.17	8	4
48	8	17.92	7	-
49	8	18.42	7	-

*CPOT: Critical Pain Observation Tool

**MME: Morphine Milligram Equivalents

Outcome and Follow-up:

The patient reported a significant decrease in pain after insertion of the epidural. His CPOT score went from 8/10 the day before insertion to a score of 2/10. He also tolerated the discontinuation of the lidocaine infusion as well as a significant reduction in opioid use. As per the stated initial goals, after a pain break of a few days, the epidural was discontinued to reduce the risk of any complications with a subsequent increase in CPOT scores back to 8/10 and an increased need for opioids. The patient was subsequently decannulated on day 63 since onset of symptoms and by day 74 his pain was much improved with a CPOT of 2/10 daily. From day 77, the patient was discharged from ICU to a bed on the ward to continue rehabilitation. He was discharged from hospital to a rehabilitation center on day 115 needing only gabapentin 1200mg daily, venlafaxine 75 mg daily and nortriptyline 35 mg daily.

Discussion:

Pain is a common complicating factor in GBS. However, severe refractory pain is relatively uncommon but can complicate the course of some patients with GBS. There is limited data on how to best treat these patients. Data on the use of an epidural for refractory pain relief in GBS is even further limited. The potential benefit is a reduction in refractory pain which can have a psychological impact on patients (and families). Moreover, the use of an epidural could potentially spare the use of other medications such as opioids with their multitude of side effects and dependence as well as the use of other medications which may have varied effects such as QT prolongation, which in itself can increase mortality. Furthermore, most of these medications cause respiratory depression which may prolong the time that a GBS patient is

on a ventilator which has its own risks such as deconditioning, ventilator induced diaphragm dysfunction, ventilator induced lung injury, stress ulcers, decubitus ulcers, and ventilator associated pneumonia. This host of side effects to traditionally used pain management plans have prompted the development of safer therapeutic modalities.[8] The potential risks of an epidural include that of localized infection or bleeding which may go unnoticed especially in a patient that is already paralyzed and unable to sense. However, this risk is approximately 1/18,000 for epidural hematomas and an incidence of 0.2 to 2.8 cases per 10,000 for an epidural abscess and potentially could be reduced further with daily screening ultrasounds to look for localized fluid collections.[9][10] Furthermore, a tunneled epidural could further reduce the risk of infection though evidence is lacking in GBS patients.[11] Studies have supported the use of tunneled epidurals to provide not only timely, but extended analgesia for cancer patients.[12] In our case, the epidural produced a significant improvement in the refractory dysesthetic pain for our patient. The epidural was only kept in situ for five days to prevent infection. Most case studies documenting the use of epidural after failure of routine analgesics in GBS were documented in the late 80's and 90's. All used morphine sulphate epidurals in previously healthy adults. A short report from 1991 showed that 8/9 patients benefited from a morphine epidural to treat refractory pain with minimal side effects with the most common being urinary retention and pruritis.[13] Again, in 1992, a case study successfully reported the long-term use of a bupivacaine and fentanyl epidural, however, after day 24, opioid requirements increased suggesting development of tachyphylaxis.[14] Our case is novel in that more data has emerged since the 1990's in the use of adjunct therapies for pain control in GBS. In our case, our patient was already on what would be considered the contemporary management of pain in GBS with multiple adjunct agents. Even in the setting of being on all these drugs, the patient still had refractory pain. Despite this, the epidural was highly effective, which is in contrast to all previous studies from the 1980's where epidurals were used with very little adjunct medication on board. Further data is required on epidurals in GBS. Additionally, larger, well designed randomized control trials are required to further investigate the safety of potential interventions for patients with pain in GBS.[15] The present case report gives some observational evidence to the potential benefit of epidurals in GBS and may be a steppingstone to considering a trial of epidurals (or tunnelled epidurals) in patients with GBS and refractory pain.

Learning points:

Pain is common in the acute phase of Guillain-Barré Syndrome and rarely can be severe and refractory.

Pain in GBS may not always respond to contemporary pain and adjunct therapy.

An epidural can potentially be considered for the treatment of refractory pain after a careful patient-centered discussion with the patient about risks.

Authorship:

All authors, Eudiet Trollip MD[1], Ken Hawkins MD, FRCP[1], Isabel Kwek BSPharm[2], Krista Dewart NP[2], Mehvash Qureshi NP[2] and Janek Manoj Senaratne MD, MSc, FRCPC, FACC[2, 3, 4] have participated in:

* Conception and design, acquisition of data or analysis and interpretation of data

* Drafting the article or revising it critically for important intellectual content.

* Final approval of the version published.

* Agreement to be accountable for the article and to ensure that all questions regarding the accuracy or integrity of the article are investigated and resolved.

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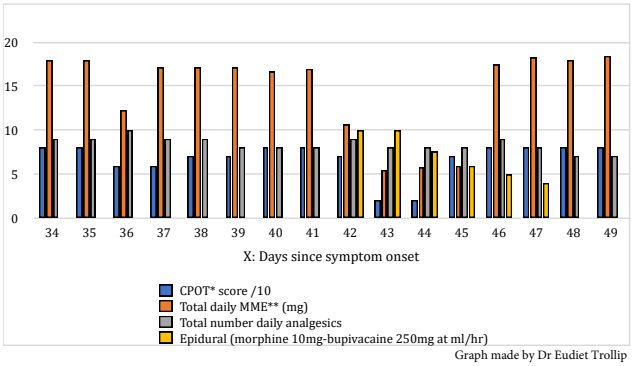
FIGURE/VIDEO CAPTIONS :

Figure 1: Graph showing change in pain scores and analgesic requirements based on epidural use.

Hosted file

`Pain drugs in GBS patient Table 1.docx` available at https://authorea.com/users/503202/articles/582983-epidural-use-for-neuropathic-pain-relief-in-a-guillain-barr%C3%A9-syndrome-patient

Figure 1: Graph



*CPOT: Critical Pain Observation Tool
**MME: Morphine Milligram Equivalents