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Original Contribution

Considerations for Epidural Blood Patch and Other Postdural Puncture Headache Treatments in Patients with COVID-19

Pascal Scemama, MD[1], Fadi Farah, MD[2], Glen Mann, MD[2,3], Roman Margulis, MD[2], Karin Gritsenko, MD[2], and Naum Shaparin, MD[2,4]

From: [1]University of Massachusetts Medical School, Worcester, MA
[2] Albert Einstein College of Medicine
[3] Children's Hospital at Montefiore
[4]Montefiore Medical Center, The Bronx, NY

Address Correspondence:
Pascal Scemama, MD, MBA
Dept. of Anesthesiology & Perioperative Medicine
University of Massachusetts Medical School
UMass Memorial Medical Center
55 Lake Avenue North
Worcester, MA 01655
E-mail:
pascal.scemamadegialluly@umassmed.edu

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Background: A primary concern in the use of EBP in these patients is the possibility of seeding the virus in the CNS. Another important concern is related to the known hypercoagulable state in COVID-19 positive patients and associated organ dysfunction that may alter the metabolism of anticoagulants. The safety of the providers performing the EBP, the position of the patient and choices for image guidance (blind, fluoroscopic) are also key considerations to review. It is also important to explore the current state of knowledge about using allogenic instead of autologous blood as well as emerging techniques to eliminate the coronavirus from the blood.

Objectives: In this article we pose the questions of how to manage PDPH in the COVID-19 positive patient and more specifically, the use of epidural blood patch (EBP).

Methods: Literature review.

Results: EBP is usually considered after the failure of conservative and pharmacological treatments. Because of the additional risks of EBP in COVID-19 patients it is important to also consider less traditional pharmacological treatments such as theophylinnes and cosyntropin that may offer some additional benefit for COVID-19 patient. Finally, other interventions other than EBP should also be considered including occipital nerve blocks, sphenopalatine ganglion blocks (infratemporal or transnasal).

Limitations: A narrative review with paucity of literature.

Conclusion: Going forward, an effective treatment for COVID-19 or a safe vaccine and a deeper understanding of the pathophysiology of the virus will certainly change the risk calculus involved in performing an EBP in a COVID-19 patient.

Key words: COVID-19; PDPH; Epidural Blood Patch; Post-dural Puncture Headache

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In this new age of coronavirus disease 2019 (COVID-19) and during the early phase of the pandemic, much of the focus has been on the acute critical care of the COVID-19 patient. Going forward, the management of certain medical conditions in this patient population will also need to be addressed, as it presents several challenges. In this article, we discuss the treatment approach of postdural puncture headache in the COVID-19 patient and more specifically, the use of an epidural blood patch (EBP).

Postdural puncture headache (PDPH) is a rare but known complication after an epidural procedure or lumbar puncture. While in severe cases it can cause cerebral herniation and brain death if not treated promptly, in most cases it is not a life-threatening condition, but can be associated with severe and acute suffering as well as temporary but significant functional impairment. One of the most common and effective procedures in the treatment of PDPH is an EBP. The success rate for this procedure continues to be as high as 93% after the first attempt and 97% on the second attempt, with few complications (1).

COVID-19 is a novel coronavirus that has resulted in significant worldwide morbidity and mortality. It has

become increasingly common in the community, and yet can remain asymptomatic in as many as 80% of presenting patients. These patients are part of the general population that may also be receiving spinal procedures such as labor epidurals, surgical anesthesia, and procedures for pain management. In addition, patients may undergo lumbar punctures as a diagnostic tool to aid in treatment, planning, and administration of therapeutics such as chemotherapy or in the urgent diagnosis of increased intracranial pressure. Furthermore, there have been recommendations from multiple medical societies to maximize the use of regional and neuraxial anesthesia for COVID-19-positive patients in the perioperative period (2). This is hypothesized to reduce the risk of aerosolization of viral particles associated with the airway manipulation that occurs with general anesthesia (3). As a result, it is reasonable to expect a higher use of neuraxial anesthesia for COVID-19-positive patients in the months to come. Inevitably, a percentage of these patients may develop complications such as a PDPH – requiring the utilization of an EBP to manage their symptoms. When treating COVID-19 patients with an EBP for PDPH, a significant concern is the potential seeding of virus into the central nervous system (CNS). The sequelae of such seeding in the CNS, especially in patients who have no or mild COVID-related symptoms, could be devastating.

This article discusses the risks of transmission of the virus to the CNS while performing an EBP on COVID-19-positive patients, leading to possible neurological sequelae as well as options to process the blood to decrease this risk of transmission. Other considerations specific to COVID-19 patients, such as coagulation status and protection of the care team performing an EBP, will also be highlighted. Finally, we will review both pharmacological and interventional alternatives to an EBP for the treatment of PDPH and their use in the treatment of PDPH in COVID-19 patients.

COVID-19 and the Central Nervous System

While literature on COVID-19 is evolving daily, the spread of this virus within the CNS, including cerebrospinal fluid (CSF) and the epidural space, has yet to be fully understood. There are known CNS-related COVID-19 manifestations such as anosmia, ageusia, confusion, altered mental status, encephalitis, and meningitis. These may be attributable to factors including direct infection, injury, neuronal pathway disruption, acute cerebrovascular disease, vascular changes affecting the blood brain barrier via ACE2 receptors, and the sequelae of acute thromboembolic events (4-6). It also remains unclear whether CNS symptoms are a reflection of CSF viral load. There have been cases of COVID-positive patients with Guillain-Barre syndrome and CSF-negative SARS-CoV-2 polymerase chain reaction (PCR) assays, as well as patients with symptoms of meningitis found to have CSF-positive SARS-CoV-2 PCR assays and negative nasopharyngeal swabs (5-7).

These concerns lead us to question the appropriateness of our current practice of injecting autologous blood in COVID-19 patients who may or may not have CNS manifestations. Should we be assaying CSF involvement for the presence of SARS-CoV-2 prior to an EBP and potential introduction of virus into the CNS? Answers to these questions may become clear as we learn more about the COVID-19 virus and its pathophysiology. It is worthwhile to note that there have been numerous articles reviewing specific patient populations and implying that the risk of a new CNS infection related to a neuraxial procedure or intervention, while possible, is extremely low, ranging from 0.007% to 0.6% with ongoing bacteremia (8,9). In patients with documented bacteremia, such as chorioamnionitis, there were no patients who developed CNS infection after neuraxial procedures (10-12). Review of patients with known or highly suspected orthopedic localized joint infections and neuraxial anesthesia likewise did not report any new neuraxial infectious process (8,9). In patients with HIV, a blood patch after dural tap does not predispose for neurological disease progression (13). Similarly, active herpetic lesions did not lead to infectious complications following neuraxial anesthetic techniques in the obstetric population (14,15). So, in general, these findings suggest an extremely low risk of transferring a blood-borne pathogen in the CNS when performing an EBP using autologous blood for a patient with an ongoing infection. Others have suggested that central neuraxial blocks should not be performed in patients with untreated systemic infections, but that patients may safely undergo spinal anesthesia if prior antibiotic therapy has been initiated (16). Since there is no gold standard treatment for COVID-19 at this time and since there are still many unknowns about this virus, these findings may not be applicable to COVID-19-positive patients.

Can Allogenic Blood be Used for Blood Patch?

To alleviate the concern of injecting autologous blood during active infection that likely contains viral

particles, it may be worthwhile to examine the use of allogenic blood from appropriately matched donors. In one case report (17), a woman with intractable PDPH and fever received an EBP with crossmatched blood that was screened for infectious diseases. The patient went on to have complete resolution of her headache and remained symptom-free after a one-month follow-up. Although no studies have demonstrated a direct causal relationship between meningitis and dural puncture in the presence of infection, the authors concluded that it is appropriate to use crossmatched and tested blood, as long as it is conducted under aseptic conditions (17). While this approach certainly requires further investigation and should only be reserved for patients who exhibit no response to conventional therapy, it does address the concern of directly introducing COVID-19 into the CNS.

Can Blood Be Disinfected?

Another consideration for novel and nonconventional therapy is the use of ultraviolet light for disinfection of blood prior to injection into the epidural space. The idea of using ultraviolet radiation in the treatment of bacterial and viral infection was introduced more than a century ago (18). Ultraviolet blood irradiation (UVBI) works by enhancing the body's natural immune response as well as being directly lethal to viral and bacterial pathogens. During this process, a needle is inserted into a vein and 60 or more milliliters of blood are passed through tubing where it is exposed to an ultraviolet light. The treated blood is then directly returned to the patient's bloodstream. In a study looking at the treatment of patients with hepatitis C infection, UVBI was both safe and effective in reduction of viral load and improvement of symptoms (18). If there is a similar effect on COVID-19-infected blood, this therapy may prove to be a reasonable and safe option in cases of active infection and debilitating PDPH. However, at this time, there is little data to support its use and further investigation is certainly needed.

One future consideration for safe blood administration in patients might be the ExThera Seraph®100 Microbind® Affinity Blood Filter - a hemoperfusion device for the reduction of pathogens and reduction of viral load in filtered blood. Although used in Europe, it has not yet been approved in the United States (19).

Coagulation Considerations

Another significant concern relates to the known hypercoagulable state in patients with COVID-19, leading to thrombosis, venous and pulmonary thromboembolism, stroke, and acute coronary syndromes. This is especially prevalent in patients with early elevation of d-dimers, c-reactive protein, and precalcitonin (20). These patients will often be treated with anticoagulants such as unfractionated heparin, low-molecular weight heparin or direct oral anticoagulants. Prior to performing a blood patch in this population, the lab work and last dose of anticoagulation will need to be reviewed with greater vigilance. The risks of suspending anticoagulation for an EBP should be carefully weighed against the risks associated with a hypercoagulable state and when necessary, discussed with a hematologist. As with any patient exhibiting changes in their coagulation cascade, any procedure must be carefully considered with active hematologic changes in mind as a dynamic variable.

Perhaps most important, prior to beginning the procedure, is determining the correct timing of the intervention. There are many articles that explore the best timing to perform spinal procedures safely, especially in challenging populations such as patients with coagulation issues (i.e., low platelets) or those who exhibit symptoms of a PDPH shortly after an epidural steroid injection (21,22). Anticoagulation guidelines for neuraxial anesthesia provide a possible easy road map assuming all anticoagulants work as expected in this new disease state. Possible concurrent organ dysfunction (kidneys in particular) should be considered while deciding on the timing of an EBP after discontinuation of anticoagulation.

Has there been an Adequate Trial of Conservative Treatments?

It is important to keep in mind that PDPH is rarely an emergency unless intractable or associated with a severe CSF leak that causes traction on the epidural bridging veins. The most conservative approach for treating PDPH in COVID-19 patients is to wait for the resolution of active infection. As the sensitivity, specificity, and availability of COVID-19 testing continues to improve, this time period may be reduced. Since PDPH can result in significant morbidity, considering alternative treatments in COVID-19 patients may also be of great importance. Below is a review of the non-interventional treatment options that are utilized with some success.

Noninterventional Treatment Options

In most cases of PDPH, there is a strong emphasis on conservative measures. The majority of cases resolve on

their own within days or weeks with minimal intervention. However, episodes that are refractory to treatment can persist for months (23). In patients who do require an escalation of care, simple medications and treatment options are usually effective. Bedrest, caffeine, hydration, as well as acetaminophen and nonsteroidal anti-inflammatory drugs are all useful in improving symptoms in many patients (24). Caffeine specifically has also shown benefit with breathing as it enhances inspiratory muscle endurance and reduces the workload on inspiratory muscles during respiration (25). Barbiturates such as butalbital and opioids can help with pain, but their use in patients with an active compromised respiratory status carries significant risk (25). Other options include theophyllines and adrenocorticotriopic hormone (ACTH) analogs, such as cosyntropin, as both have shown some efficacy in small studies (24). Theophylline has also shown some anti-inflammatory effect on the lungs and thus may be appropriate for COVID-19 patients (26). There is also evidence that part of the pathophysiology of the COVID-19 virus is to reduce the host's cortisol response. This may occur due to viral production of amino acids that mimic ACTH, resulting in antibodies that attack ACTH (27). Clinical trials are underway examining the use of cortisol and ACTH in the treatment of COVID-19 patients (28). To that effect, cosyntropin may offer some benefit in treating PDPH in this population.

Interventional Options Other Than Blood Patch

Several other interventions have been considered for the treatment of PDPH. One alternative investigated the use of epidural administration of various fluids or substances other than autologous blood. However, currently there is insufficient evidence to recommend the use of epidural crystalloids or other substances such as dextran, hydroethyl starch, or fibrin glue (24).

Additional interventions that have been studied include bilateral greater occipital nerve blocks (GON) and sphenopalatine ganglion blocks (SPG). Both have shown some efficacy in small studies, although there is a concern of aerosolization during transnasal sphenopalatine ganglion block as the procedure may induce cough (24). For COVID-19 patients, a possible alternative is to use an ultrasound-guided infratemporal approach (29).

Risks to Treatment Team

Substantial consideration must also be given to how a blood patch can be performed with the greatest safety to the patient and care team. For instance, what should be the setup of the room? Where should everyone stand in relation to the patient to mitigate viral spread? What is the best patient position, prone or sitting, for the procedure and for the practitioner? There is evidence to support that patients with COVID-19 improve respiratory mechanics in the prone position (30). Furthermore, a fluoroscopic approach may be preferable as it has been shown to be more precise and associated with a higher success rate than a blind technique (31). Prone positioning may also offer greater distance for the care team from the patient's face and may be more comfortable for the patient. A lateral recumbent position may also be an option to consider. Of course, complete personal protection including an N95 mask, face shield, gown, head cover, and sterile gloves need to be available and utilized. The patient should remain masked throughout the procedure.

Clinical Recommendations

In the decision-making algorithm to pursue interventional treatment for PDPH, an assessment of the risks and benefits must be considered by the patient and the care team with consideration of the patient's clinical state and potential for complications. Although evidence for the EBP's effectiveness remains the strongest for the treatment of PDPH, initially a conservative approach using therapies such as hydration, bed rest, supine posture, caffeine, analgesics, theophylline, and cosyntropin is warranted for patients with an ongoing COVID-19 infection given the multitude of unknown implications for this patient population (26).

If traditional pharmacological treatments have failed, are not available, or not indicated, consider bilateral occipital nerve blocks (GON) or sphenopalatine ganglion blocks (SPG) using local anesthetics only. GON nerve blocks can be easily performed blindly or using ultrasound guidance and carry little risk of complications even for a patient on anticoagulation. While some of the authors have performed many transnasal sphenopalatine ganglion blocks without inducing cough, it should be considered an aerosolization procedure and requires appropriate PPE. Alternatively, an infratemporal ultrasound-guided approach could be used but is more technically challenging. If peripheral nerve blocks as listed above have failed, an EBP should be considered. Depending on the patient's presentation and clinical condition, risk of viral contamination of the CSF or epidural space should be weighed against the benefit of the EBP and the severity and impairment from

the PDPH. The prone position and use of fluoroscopic guidance may be beneficial both in terms of accuracy, speed of the procedure, patient comfort, and safety of the procedural team.

Limitations

One limitation of this review is that it is based on preliminary knowledge of COVID-19. There is little conclusive literature at this time on the rate, progression, and specific complications of COVID-19 spread in the CNS. Furthermore, the use of alternatives to EBP is based on small studies and often difficult to extrapolate to the general population. This topic also addresses a patient population that is difficult to study and in which it may be unethical to withhold treatment that is considered standard of care.

Conclusion

The treatment of PDPH in COVID-19 patients presents added risks and considerations. Specifically, the performance of an EBP in a COVID-19 patient may invite seeding of the COVID-19 virus into the CNS, increase the CNS viral load, or both, the clinical implications of which, at this time, remain unknown. Previous studies of CNS infections after neuraxial procedures in patients with ongoing bacterial or viral infections point to an extremely low risk of seeding the CNS. Because of the paucity of information surrounding COVID-19 and its pathophysiology in the CNS, at this time we must rely on this evidence to guide our decision-making. We recommend caution before performing an EBP in a COVID-19 patient with PDPH. Initial treatment strategies should consist of nonpharmacologic and pharmacologic treatment including the use of theophyllines and cosyntropin, although evidence for these remains insufficient. When appropriate, peripheral nerve blocks (GON or SPG) should also be considered before performing an EBP. The evidence for the efficacy of these blocks is still limited but they generally present a very low risk (32). Going forward, an effective treatment for COVID-19 or a safe vaccine and a deeper understanding of the pathophysiology of the virus will certainly change the risk calculus involved in performing an EBP in a COVID-19 patient.

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Conflict of interest:

Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

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