Author's response to reviews

Title: Low-Concentration, Continuous Brachial Plexus Block In The Management Of Purple Glove Syndrome: A Case Report

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Author's response to reviews: see over
We thank the reviewers for their positive remarks and comments. The answers are as below.

1. Why was the infraclavicular approach not considered? This approach renders itself better for catheter placement, acceptance for a catheter secured in this area is better than in the neck especially for a duration as long as 8 days and lastly anatomically the affected areas (hand and forearm) are covered better with infraclavicular block than interscalene approach. Of course I do appreciate the fact that the patient’s pain was significantly relieved in this case.

   a. We agree with the reviewer that infraclavicular approach with a catheter placement might have been another option. We preferred supraclavicular posterior approach because of easy accessibility of the cords of brachial plexus using a cannula. Furthermore, in the infraclavicular approach, if the needle point is distal to the coracoid, which is frequently observed, most of the solution will move distally and the musculocutaneous and axillary nerves can be missed. (Brown DL, Bridenbaugh D. The upper Extremity Somatic Block in Neural Blockade in Clinical Anesthesia and management of Pain. Cousins MJ and Bridenbaugh PO, 3rd Edn. Pages: 345 – 371.) The manuscript has been modified to incorporate the possibility of infraclavicular approach using a catheter.

   b. We used a 20 G cannula since it is inexpensive, easy to secure as it lies comfortably in the groove and easy to secure. It reaches a depth of 2.5 cms which is adequate and there is no fear of migration. It lies within the neural sheath delivering the drug right at the site of action, reducing the volume required.

2. The authors have inserted the catheter through IV cannula in the interscalene groove, any specific reason that they did not utilize peripheral nerve stimulator or ultrasound guidance?

   a. The arm was painful and even tactile stimuli were excruciating. Hence peripheral nerve stimulator was not used. As ultrasound guidance was not available, it was not used. The potential benefit of using these has been added in discussion.

3. What was the depth at which the cannula was fixed? Again, for longer duration it is more advisable to insert catheters and subcutaneously tunnel for better security and infection control. Why was this not considered? It is very likely for an IV cannula to get displaced.

   a. Catheter with subcutaneous tunneling might have been an option but we felt the risk of infection in an arm with extensive inflammation was lesser with a cannula.
We did not encounter any problem with displacement throughout the treatment. Additional reasons for preferring a cannula are mentioned in the first answer.

4. Could they specify which infusion pump was used?
   a. We thank the reviewer for pointing out this omission. BD Terumo infusion pump was used. **It has been modified in the manuscript.**

Reviewer II

1. It does not become apparent until the last sentence of the discussion where the authors state that the use of low dose bupivacaine for the treatment of “purple glove syndrome” has not been described before. If this is the case, then the authors should state this early in the manuscript and specifically discuss the mechanism of action and pharmacodynamics of a low dose bupivacaine infusion. What other agents have been used? What are the advantages and disadvantages of bupivacaine? Has ropivacaine been used? Are there safer alternatives?

   a. We thank the reviewer for the comments. **As suggested, modifications have been made in the introduction and discussion to highlight the utilization of low concentration bupivacaine and the mechanisms involved. Other points mentioned by the referee have also been incorporated in the modified draft.**

   b. **Ropivacaine has been used for brachial plexus blockade. It was not used because of non-availability. The degree of motor blockade produced by ropivacaine is less than that of bupivacaine. So it is possible to produce a more selective sensory blockade with ropivacaine. Furthermore, if required, higher concentration of ropivacaine may be used with lesser risk of cardiotoxicity than with bupivacaine. This has been added in the discussion.**

2. In the last sentence of the introduction, the authors state that the added advantage of low dose bupivacaine is the fact that it preserves motor function to facilitate physiotherapy. Is this its main advantage or is it the sympathectomy it has created? Or is it the sympathectomy the main advantage and the pain relief to facilitate physiotherapy an added benefit? With a stellate block it is the sympathectomy that is sought after. A few words on how a sympathectomy provides benefit should be discussed.

   a. The main advantage is by the sympathectomy. Preservation of motor function is only an added advantage. However, it was vital in this case to begin physiotherapy. This sentence in introduction has been modified to improve
clarity. As described in the text, stellate block was initially performed to confirm the relief of symptoms with sympathectomy and it was maintained using the block. **Mechanism of sympathectomy has been added as suggested.**

3. I would like to know how and where this 20G catheter is placed. The authors state in the interscalene grove, but where? Is it placed high in the neck or in the supraclavicular region. If placed high in the neck as we do interscalene blocks for shoulder surgery, it is unlikely that the C8T1 nerve roots will be adequately covered especially with an infusion going at 1 – 2 ml/hour. The C8T1 nerve roots are especially important because it provided much of the innervations to the hand and to the analgesic benefits that the authors suggest for physiotherapy.

   a. It was placed at 2.5 centimeters above the clavicle in the supraclavicular region. **This has been modified in the manuscript.** As the analgesia and sympathetic blockade in C8T1 distribution was observed to be adequate, the infusion was continued as planned.

4. Supraclavicular blocks (which are also interscalene) are utilized in anesthesia practices for arm, forearm, and hand surgery. However, at 1 – 2 ml/hr I remain skeptical that this rate will provide adequate analgesia to the C8T1 distribution.

   a. We agree that there is a possibility of inadequate analgesia at this dose. But in our patient, the analgesia and sympathetic blockade were found to be adequate at this dose. It was evident by the fact that she could co-operate with the physiotherapists and perform the exercises. Hence we did not increase the dose of infusion.

5. What is the benefit of fentanyl? Peripheral opioid receptors have not been described. Therefore I question the peripheral action of fentanyl. If anything, fentanyl is probably being absorbed and acting systemically. Why not use clonidine?

   a. Though the peripheral action of fentanyl is not commonly discussed, it is well described. It improves analgesia without producing motor blockade. Fentanyl acts directly on the peripheral neuronal cells. Dorsal roots also contain opioid binding sites. Because of the presence of bidirectional axonal transport of opioid binding protein, fentanyl penetrates the nerve membrane and also acts at the dorsal horn. Fentanyl diffuses from the brachial plexus sheath to epidural and subarachnoid spaces and then binds with the opioid receptor of the dorsal horn. Also fentanyl potentiates local anaesthetic action via central opioid receptor
mediated analgesia by peripheral uptake of fentanyl to systemic circulation.
Fentanyl improves analgesia but prolongs the onset of axial brachial plexus
block by peripheral mechanism (Anaesthesia Analgesia 3000;91:384 – 387).

b. As we routinely add opioids with local anaesthetics for peripheral nerve blocks in
our department, addition of another adjuvant such as clonidine was not
considered. (Klein SM, Nielsen KC. Brachial plexus blocks: infusions and other
mechanisms to provide prolonged analgesia. Curr Opin Anaesthesiol. 2003
Aug;16(4):393-9). The possibility of adding an adjuvant like clonidine has
been added in the discussion.