

Dear Editors and Reviewers,

Thank you for your letter and comments on our manuscript titled “Apnea Caused by Retrobulbar Anesthesia: A Case Report” (**Manuscript NO.: 78959, Case Report**). We have addressed the editor’s and the reviewers’ comments to the best of our abilities (in red), and revised text to meet the style requirements. We hope this meets your requirements for a publication.

The main comments and our specific responses are detailed below:

Reviewer Comments:

Reviewer #1:

**Specific Comments to Authors:** It is an interesting case study on the apnea caused by retrobulbar anesthesia. It is a well described case report and may be of interest to medical stuff. Overall, I did not found any significant errors in this work.

**Response:** We are appreciated for your attention and careful reading of our manuscript.

Reviewer #2:

This is an interesting unique case report referred to apnea caused by retrobulbar anesthesia which is a rare but severe anesthetic complication. Here are my questions and suggestion.

Abstract - What is your suggestion for prevention and early identification of brainstem anesthesia such as anesthetic volume, size and length of needle tips, or practical point for observation period after the procedure?

**Response:** Thank you for your suggestions. In order to minimize the chance for brainstem anesthesia, we recommend low volume of anesthetic drug. According to our clinical observations, the anesthetic effect can be achieved when the dose of anesthetic is 2ml, with anesthetic precisely infiltrated the ciliary ganglion. The general anesthetic dose is 2-5ml, too much anesthesia may increase the orbital pressure, thereby increasing the probability of brainstem anesthesia. Early identification of brainstem anesthesia is important, especially during the first 20 minutes, so careful monitored of vital signs of the patient is important. Longer needles have deeper puncture, which may increase the risk of penetrating into the blood vessels or optic nerve sheaths, so maximum needle length recommended for retrobulbar block is 31 mm by Kostadinov et al.[8]. A

blunt needle is less likely to penetrate the optic nerve sheath, but its insertion may be painful and traumatic. For other practical points, we provided a trick of using cotton bud to assist the operation in the content (see **Figure 2**). It is recommended that the patient looking straight forward, rather than looking upwards, which help to avoid puncturing the blood vessels or the optic nerve. Due to the limitation of Word Counts in the **Abstract** section, we added the necessary description in our manuscript **Discussion** part:

1. “First, a low volume of anesthetic drug is recommended to reduce systematic side effect. According to our clinical observations, the dose of 2 mL (generally 2-5 mL) anesthetic is enough for a proper anesthetic effect, if the anesthetic infiltrates the ciliary ganglion. Second, longer needles have deeper puncture, which may increase the risk of penetrating the blood vessels or optic nerve sheaths, so the maximum needle length recommended for retrobulbar block is 31 mm according to Kostadinov et al[8]. A blunt needle is less likely to penetrate the optic nerve sheath, but its insertion may be painful and traumatic. Third, it is recommended that the patient look straight forward rather than upwards to avoid stabbing the blood vessels or the optic nerve.” (see **Discussion**, para 5.)
2. “Therefore, early detection of brainstem anesthesia is important, especially during the first 20 min after retrobulbar injection. Careful monitoring of vital signs of the patient during this period is important.” (see **Discussion**, para 3.)

Introduction - Consider describing the indication for retrobulbar anesthesia, comparing with topical, peribulbar, and blunt subtenons injections.

**Response:** Retrobulbar anesthesia is often used in eye surgeries, especially for posterior segment surgeries, including vitrectomy, external-route surgery, etc., which is characterized by blocking the motor and sensory branches of the ciliary ganglion, thereby avoiding eye movement. Topical anesthesia is often used for short-time or superficial anterior segment surgeries, such as corneal refractive surgery, cataract surgery, etc. For peribulbar anesthesia, since the injection site is on the side of the eyeball, the probability of penetrating the eyeball is low but the anesthesia effect is inferior compared with retrobulbar anesthesia. Therefore, peribulbar anesthesia is more suitable for long-time anterior segment surgery, such as cataract surgery with anterior angle dissection. Sub-Tenon capsule injection is suitable for anesthesia in posterior segment surgery and can reduce

complications, but need to first incise the conjunctival sac and blunt dissection into the sub-Tenon region, which is more complicated than retrobulbar anesthesia.

We added some content in our manuscript **Introduction** part:

“, especially for posterior segment surgeries, including vitrectomy, external-route surgery, etc. By injecting anesthetic drug into the posterior musculus cone of the eye to block the III, IV, and VI cranial nerves and the ciliary nerves, rapid analgesia can be achieved. Compared with topical anesthesia (often used for short-time or superficial anterior segment surgeries), peribulbar anesthesia (frequently used for long-time anterior segment surgery) or subtenon capsule injection (which requires conjunctival sac incision and subtenon region blunt dissection), retrobulbar anesthesia is a more effective and convenient anesthesia method for posterior segment surgeries.”(see **Introduction**, para 1.)

Case presentation - Has this patient ever received any anesthesia procedures before? Please consider describing in the history section.

- Prior to retrobulbar anesthesia, did this patient receive any narcotics or muscle relaxants?
- Please consider describing the actual order for 20% lipid emulsion in this patient. The recommended treatment regimen is an initial bolus of 20% lipid emulsification at a dose of 1mg/kg over 1 minute, followed by 15mL/kg/hr.

**Response:** Thank you for your advice. This patient has not experienced any anesthesia process before. Prior to retrobulbar anesthesia, no narcotics or muscle relaxants was used.

During our rescue process, we follow ASRA practice advisory on local anesthetic systemic toxicity by 1.5ml/kg 20% lipid emulsion bolus (over 1 minute), followed by 0.25ml/kg/min of infusion. After about 5 minutes, the patient regained consciousness. To stress these details, we have added some supplemented content in the corresponding part of the article:

1. “She reported that she had not previously experienced any procedure that necessitated anesthesia.” (see **Case Presentation, History of past illness**, para 1.)
2. “No narcotics or muscle relaxants was used prior to retrobulbar anesthesia” (see **Case Presentation, Treatment**, para 2.)
3. “Considering local anesthetic poisoning, an intravenous infusion of 250 mL of 20% lipid emulsion (1.5 mL/kg 20% lipid emulsion bolus over 1 min, followed by 0.25 mL/kg/min of

infusion) was given. After 5 min, the patient regained consciousness.” (see **Case Presentation, Treatment**, para 3.)

Discussion - An anomalous inferior ophthalmic artery can course near the optic nerve, increasing the risk for arterial injection.

- Intrathecal injection of the optic nerve can occur with upward deviation of the eyeball, which bends the optic nerve inferiorly and into contact with the advancing needle.
- The differentiating factor between intraarterial and intrathecal injection appears to be the speed of symptoms and the development of seizure activity in the former. Intraarterial injection usually causes symptoms seconds after injection, while BSA from a nerve sheath injection occurs over a matter of minutes (5–50 min, avg. 20.5 min, in the published literature)
- Please consider adding the discussion about the details of these 2 main mechanisms and how readers can differentiate between these 2 main mechanisms.

**Response:** Thank you for your advice. In our article, we mentioned the possibility of intra-arterial and intra-sheath injection. We strongly agree with your point that the identification of the first two mechanisms is based on the time of symptom onset. Therefore, we revised our manuscript by adding the details of these mechanisms and how readers can differentiate the mechanisms.

Here is what we added:

“For this patient, loss of consciousness and apnea occurred after retrobulbar anesthesia were found after her recovery from anesthesia. For the differentiation of mechanisms of intraarterial and intrathecal injection, if inadvertent intraarterial injection were achieved, the onset of symptoms such as loss of consciousness, apnea, and seizures would be expected within seconds, while brainstem anesthesia from a nerve sheath injection occurs over a matter of minutes, mostly 5–50 min[2]. For this case, the mechanism may be caused by accidental intrathecal injection, because the difficulty in breathing started about 6 min after the injection. The patient did not have any seizure or retrobulbar hemorrhage, and there was no return of blood during the puncture process; therefore respiratory arrest was unlikely to be caused by intravascular injection.” (see **Discussion**, para 2.)

## **EDITORIAL OFFICE'S COMMENTS:**

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, the author(s) must provide the Signed Consent for Treatment Form(s) or Document(s). Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

**Response:** Thank you for your comments, we have compliance with the requirement and revised our manuscript.

**Other revisions:**

(1) The Reference part of the article was revised accordingly.

We appreciate for Editors/Reviewers' warm work earnestly and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Sincerely,

Youxin Chen, MD, PhD

Professor of Department of Ophthalmology,

Peking Union Medical College Hospital