



## Case report

## Suspected systemic uptake of chlorpromazine after retrobulbar injection

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## ABSTRACT

**Purpose:** To present a case of suspected systemic uptake of chlorpromazine after a patient underwent retrobulbar injection for a blind painful eye.

**Observations:** The patient is a 63-year-old Hispanic female who presented to the surgery center with neovascular glaucoma and uncontrolled intraocular pressure of her right eye. Immediately following retrobulbar injection of chlorpromazine, the patient became very sedate and difficult to arouse and blood pressure recordings fell. After 4.5 hours, her symptoms improved, and the patient was discharged. There were no further systemic symptoms reported on follow up.

**Conclusion: and importance:** Systemic uptake of chlorpromazine following retrobulbar injection is a risk that should be considered when managing blind painful eyes. Ophthalmologists should practice caution with this technique and educate patients and staff on potential risks.

## 1. Introduction

Ocular pain in a non-seeing eye can have a significant negative impact on quality of life. Several treatment options exist with the definitive being enucleation; however, patients are often not psychologically ready for enucleation.<sup>1</sup> An alternative is retrobulbar injection of alcohol or chlorpromazine. Chlorpromazine is a low-potency neuroleptic that acts to block dopamine D<sub>2</sub> receptors, subsequently increasing cellular cyclic adenosine monophosphate (cAMP). Excess dopamine has been implicated in the positive symptoms of schizophrenia, and thus dopamine antagonists can be utilized systemically as antipsychotics in cases of schizophrenia, psychosis, bipolar disorder, and delirium. Therapeutic retrobulbar application of chlorpromazine acts to interrupt nervous impulses in the sensitive ciliary ganglion fibers thus resulting in post-synaptic membrane stabilization and analgesia.<sup>2,3</sup> Chlorpromazine injection has gained preference over alcohol since the 1980's, as studies have documented improved pain management with fewer side effects.<sup>1</sup> Potential adverse side effects of retrobulbar chlorpromazine include transient palpebral edema and chemosis, ptosis, neurotrophic ulcer, chronic orbital inflammation and sterile orbital cellulitis.<sup>3-9</sup> We report a case of suspected systemic uptake of chlorpromazine following retrobulbar injection.

## 2. Case report

A 63-year-old Hispanic woman, accompanied by her daughter, presented at our surgical center with uncontrolled intraocular pressure and neovascular glaucoma of her right eye. The patient was scheduled for diode laser and chlorpromazine injection of her right eye. She was pseudophakic with a visual acuity of no light perception (NLP) and an intraocular pressure of 48 mmHg.

Upon admission into the preoperative area the patient was extremely anxious and hypertensive; she was given 2 mg of midazolam for anxiolysis. Approximately thirteen minutes later she was given a combination of 2 mg of midazolam, 25 mcg of fentanyl and 10 mg of ketamine prior to administration of retrobulbar block for the transscleral diode cyclophotocoagulation (TSCPC) procedure. Using a 25 gauge retrobulbar needle, 6 mL of 50:50 mixture of 2% xylocaine and 0.75% bupivacaine with 50 units of hyaluronidase was injected without complications. A Honan cuff was placed over the eye. The patient began to exhibit decreased ocular pain shortly thereafter.

The patient was moved into the operating room where TSCPC laser was performed without incident. After completing the TSCPC, a second retrobulbar injection was carefully performed; 1 mL of 25 mg/mL chlorpromazine mixed with 1 mL of preservative-free 1% xylocaine was

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injected using a 25-gauge 1.25 inch retrobulbar needle. No complications were noted during the procedure and the patient was transferred to the Post Anesthesia Care Unit (PACU).

Approximately 10 minutes into the PACU admission, the patient became very drowsy and difficult to arouse. Anesthesia then administered a total of 0.4 mg flumazenil to reverse any effects of the midazolam. The patient's blood glucose level was measured 331 mg/dL, higher than the level of 229 mg/dL recorded during admission. The blood pressure recordings dropped precipitously and aggressive fluid hydration was initiated. Due to the patient's continued level of sedation, naloxone 0.08 mg was administered with no significant response in mentation noted. Vital signs normalized and the patient was placed into a recliner in the PACU area. Two hours after admission into the PACU, the patient was able to walk with assistance; however, she still exhibited unwarranted sedation. The anesthesia staff discussed transfer of the patient for monitoring, but the patient's daughter disagreed and requested that her mother remain at the surgery center where she could continue to be monitored. The patient remained in the PACU for a total of 4.5 hours and was finally discharged home with her daughter and followed up in our clinic the following day. The daughter reported no further systemic symptoms and her eye pain was resolved.

### 3. Discussion

Ophthalmologists frequently encounter blind and painful eyes due to a number of etiologies. Some causes include neovascular glaucoma, trauma, retinal detachment, intraocular inflammation, and corneal decompensation.<sup>3,10</sup> Treatment options are limited, each with unique considerations for the patient and physician. While enucleation is the most definitive treatment, some patients view this option as radical or traumatic. Thus, alternative treatments utilizing retrobulbar chlorpromazine or alcohol are often utilized. Side effects of retrobulbar chlorpromazine can be varied; symptoms have been known to include transient ptosis, palpebral edema, chemosis, neurotrophic corneal ulcers, sterile orbital cellulitis, and chronic orbital inflammation.<sup>3-9</sup> One prior case reports experiencing systemic uptake and notes it is a more serious potential side effect that can occur.<sup>2</sup> In the prior case, the patient developed dizziness and palpitations 1 hour following injection; serum phenothiazine panel 3 hours post-injection revealed elevated concentration of chlorpromazine. The hypothesized mechanism of action is through either arteriolar infiltration in the retrobulbar compartment or extravasation through the dural peri-optical sheath; the latter mechanism is more probable given previous radiologic studies on intracranial spread following peribulbar injection.<sup>2,3,11</sup> Inadvertent blockade of histamine receptors and alpha-1 receptors by chlorpromazine in systemic circulation causes the sedation and hypotension, respectively, that can be noted with this pharmacologic agent. This reiterates the importance of a protocol involving evaluation by anesthesia or cardiology prior to retrobulbar injection to grade risk in the event that systemic effects occur.<sup>3</sup> In the case of our patient, it is unlikely that another pharmacologic agent caused this episode. While she did receive fentanyl and midazolam, she exhibited no improvement in symptoms upon receiving naloxone and flumazenil, the respective reversal agents in case of overdose. She also received ketamine prior to her procedures. This is also an unlikely culprit as sedation begins shortly after injection; this patient's symptoms began about 20 minutes later, after both procedures and 10 minutes in PACU. Finally, xylocaine and bupivacaine were also administered in the retrobulbar block. Local anesthetic systemic toxicity (LAST) can potentially cause CNS depression. While the possibility of LAST cannot be excluded, it is commonly preceded by a CNS excitation phase and often presents with auditory and visual disturbances. Furthermore, toxic overdose with ophthalmic anesthesia is very rare due to the low doses administered. The quantity of chlorpromazine injected (25mg) is compatible with sedative symptoms when used intravenously. Resolution of its effects is documented to occur over 4-6 hours, consistent with our patient's symptom resolution over 4.5 hours.<sup>12</sup>

While the mechanism of the long-term effects of retrobulbar chlorpromazine is still not fully understood, it does raise the question regarding potential for prolonged CNS effects if systemic uptake occurs. Our case report and one other suggest that prolonged effect is unlikely and drug clearance occurs in a matter of hours, as with intentional systemic administration.<sup>2</sup> This potential risk of systemic uptake should be acknowledged and addressed with staff and patients to emphasize the importance of caution and follow up care. We propose this case as support for the potential risk of systemic uptake of chlorpromazine following retrobulbar injection; this knowledge is important as part of an informed decision in treatment plans for blind painful eyes.

### 4. Conclusion

Potential side effects of systemic chlorpromazine as an antipsychotic include anticholinergic, antihistamine, and alpha-1 blockade effects. Only one prior case report reports systemic uptake following retrobulbar chlorpromazine injection.<sup>4</sup> This presents an additional consideration in the management of blind and painful eyes. In conclusion, we reiterate the necessity to practice caution in injection and follow up care when utilizing retrobulbar chlorpromazine in the treatment of ocular pain.

### Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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### Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

### Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

### Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

### Declaration of competing interest

No conflict of interest exists.

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