

## Perioperative Hypersensitive Reaction to Hyaluronidase.

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### ABSTRACT

Hypersensitive reactions are one of the problems faced by Anaesthetist. In this case report we present a case who developed hypersensitive reaction following a peribulbar block with hyaluronidase. In this study we stress to perform test dose for hyaluronidase especially if non recombinant preparations are used.

**Keywords:** Hyaluronidase, lignocaine, peribulbar block.

### INTRODUCTION

The estimated incidence of immediate hypersensitivity reaction during Anaesthesia has been reported between 1/1000 and 1/25,0000 procedures [1]. Amongst the multiple agents used in perioperative period, neuromuscular blockers, latex and antibiotics represent the most frequently involved agents.

In this case report, we present a patient who developed hypersensitive reaction to hyaluronidase following a retrobulbar block.

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### CASE REPORT

A 67 year old man was posted for cataract surgery of the left eye. He had been previously operated for right eye cataract two years back at our institute under retrobulbar block uneventfully.

He is a known hypertensive and on Tab. Atenolol 50 mg once a day for the last 4 years. His blood pressure at the time of examination was well with in control (110/70 mmHg)

His perioperative investigations were within normal limits (Hb 12 gm %, Random blood sugar 112 mg%, urea 28 mg and serum creatinine 0.6 mg). He was scheduled for left small incision cataract surgery as a day care procedure under local anaesthesia.

On the morning of surgery intradermal sensitivity test was done with 1: 10 dilution of 2% Lignocaine (Zinocaine Laborate Pharmaceuticals) solution on volar side of left forearm. After confirming the negative test dose reaction, he was shifted to operating room.

After placing him on the table, an IV line was secured using 18G canula (Medicon iv catheter). Patient was connected to a multi parameter monitor and base line parameters (SpO<sub>2</sub>-99%, NIBP 126/84, Heart rate-84) were recorded.

Left retrobulbar block was then administered by the ophthalmologist using 4 ml of 2% lignocaine (Zinocaine-Laborate Pharmaceuticals) with 200 I.U of hyaluronidase (Facidase IP (ovine) -Sun Pharmaceutical Ind. Ltd).

Five minutes after the block, Ophthalmologist noted swelling of left eye and Anaesthesiologists were called in [Figure 1]. Suspecting the possibility of hyper-sensitivity reaction, resuscitating measures including Oxygenation through Hudson mask, rushing of Ringer lactate, Inj. Chlorpheniramine 10mg and Inj. Hydrocortisone 100 mg were administered intravenously at once. Meantime emergency cart was mobilised and kept ready. Continuous monitoring of hemodynamics showed stable vitals. (SpO<sub>2</sub>-99%, NIBP 136/76, Heart rate-88, Respiratory rate-14 )

Twenty minutes after the initial event, edema started spreading to forehead and also to opposite eye [Figure 2]. Ten minutes later patient had itching of chest wall and developed maculopapular rashes on right side of chest wall [Figure 3,4]. At this time, digital tonometry was done and retrobulbar haemorrhage was ruled out as intraocular pressure was normal.

The procedure was deferred because of presence of significant periorbital edema and the patient was shifted to postoperative ward where his vital parameters were continuously monitored. Periorbital edema had subsided on 2<sup>nd</sup> day, and subsequent ophthalmic examination was normal. After submitting the adverse drug reaction report to the institute, patient was discharged on third day with advice to come after 4 weeks for sensitivity testing as advised by dermatologist.



**Figure 1: Immediately after the block.**



**Figure 2: Edema spreading to forehead.**



**Figure 3: Maculopapular rash on the chest wall.**

## DISCUSSION

Critical incidents during cataract surgery may occur either secondary to pharmacological agents used or as complications of retro bulbar block.



**Figure 4: Periorbital edema to the spread to forehead and other eye.**

Retrobulbar block is usually administered using a local anaesthetic agent along with hyaluronidase. Hyaluronidase is an enzyme with spreading activity which is used to enhance the tissue spread of local anaesthetic agent.<sup>[2]</sup> Although hyaluronidase has been extensively used in ophthalmic procedures there are very few reported cases of hypersensitivity reaction.<sup>[3]</sup>

Hypersensitivity reaction refers to an excessive, undesirable (sometimes fatal) reactions produced by the normal immune system secondary to an offending agent. It requires a pre-sensitized state of the host.<sup>[4]</sup>

Hypersensitivity reactions are divided into four types, based on the mechanisms involved and time taken for the reaction with type I hypersensitivity reaction being the earliest to manifest. Immediate reactions depend on the release of mediators of inflammation by tissue mast cells or circulating basophilic leukocytes. These mediators include histamine, leukotrienes, prostaglandins, platelet-activating factor, enzymes, and proteoglycans. Drugs can trigger mediator release either directly ("anaphylactoid" reaction) or through IgE-specific antibodies.<sup>[4]</sup> The symptoms of type I hypersensitivity reaction takes only few minutes to manifest where as Type IV reaction will take few days to appear.

In this patient, immediate onset of symptom could represent a Type I hypersensitive reaction (IgE-mediated reaction).

During the procedure patient had received only two drugs (lignocaine and hyaluronidase) parenterally. Since the patient had not shown any reaction to lignocaine test dose one may assume that, the inciting agent is most probably hyaluronidase as he had already been sensitised to hyaluronidase during the previous surgery

Skin allergy tests are important for the confirming the diagnosis and further management of an allergic reaction. The tests, such as intradermal and skinprick test, are the most specific and common methods for determining the drug responsible for Type I (IgE-mediated) anaphylactic reactions.<sup>[5]</sup> In our case further confirmation with these tests could not be possible as the patient was reluctant to undergo the procedure.

Hyaluronidase has been extensively used in ophthalmology for improving the quality and efficacy of the block.<sup>[6]</sup>Animal derived Hyaluronidase has been associated with hypersensitive reactions and characterised by low purity and potency than recombinant preparations.<sup>[7,8]</sup> Though FDA has approved the use of recombinant human hyaluronidase *Hyalenex*® only<sup>[2]</sup> developing countries like India still use ovine preparations due to cost factor.

## CONCLUSION

To conclude, we would like to stress the importance of carrying out a test dose for Hyaluronidase especially when non recombinant preparations are being used. Though hypersensitive reaction to Hyaluronidase is rare<sup>[9]</sup>, it must be considered as one of the differential diagnosis in addition to orbital cellulitis, or retro bulbar haemorrhage during peribulbar/retrobulbar block.

This is of paramount importance, as hypersensitive reactions are one of the major causes of morbidity and mortality during perioperative period.

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