

Hypersensitivity reaction following peribulbar block containing hyaluronidase in a patient posted for cataract surgery – A Case Report

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Abstract

Hyaluronidase (HA) is a common additive to local anaesthetic eye blocks because it catalyzes the hydrolysis of hyaluronic acid, a major component of connective tissue. This increases tissue permeability, thereby increasing the dispersion and efficacy of local anaesthetics. Adverse reactions to HA are rare with an incidence of 1 per 2000. Though reactions after peribulbar, retrobulbar and subtenon's blocks are rare and mostly benign, allergy to HA should be included in the differential diagnosis when chemosis, proptosis and restriction of eye movements occur after these blocks.

The reactions can be divided into local and systemic reactions, although both can occur simultaneously. They also can be classified according to the speed of onset of symptoms. Immediate-type hypersensitivity reactions

tend to be mediated by immunoglobulin E, whereas delayed-type hypersensitivity reactions tend to be mediated by immunoglobulin G.

We present here a case of hypersensitivity after peribulbar block for small incision cataract surgery. Patient presented with local as well as systemic symptoms in the form of periorbital oedema, angioedema and respiratory depression requiring immediate resuscitation. In such patients who show both local reactions and severe respiratory depression, a fatal outcome is possible if careful rapid treatment is not administered. Therefore, anaesthesiologists should consider the possibility of allergic reactions to hyaluronidase whenever it is added as an adjuvant in ophthalmic blocks. Animal-derived products have been associated with low purity, variable potency, and uncertain safety. Hence use of recombinant human hyaluronidase merits consideration to help improve the safety and quality of these blocks.

Keywords : Hyaluronidase, Hypersensitivity, Peribulbar block, Cataract Surgery.

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Article History

Received: 25th Nov 2022

Revision: 1st Dec 2022

Accepted: 26th Dec 2022

Published: 28th Jan 2023

How to cite this article: Suman Shree R, Sudha G, Md Mashooque Ali. Hypersensitivity reaction following peribulbar block containing hyaluronidase in a patient posted for cataract surgery – A Case Report. *Ind J Ophthal Anaesth* 2022;3(1):20-4

Introduction

Hyaluronidase enzyme modifies the permeability of connective tissue through the hydrolysis of hyaluronic acid, a polysaccharide found in the intercellular ground substance of connective tissue, and of certain specialized tissues. It provides rapid penetration of anaesthetic agents by reducing the viscosity of cellular matrix, particularly to difficult locations. It has been used to facilitate the dispersion and/or absorption of fluids or medication for many years.¹ Hyaluronidase products approved by the USFDA, has been derived from the bovine, ovine, and recombinant human product.

Hyaluronidase is most frequently used in combination with local anesthetics for ophthalmic surgery (e.g, retrobulbar block, peribulbar block, sub-Tenon's block, and van Lint block). The combination is being used for various reasons which includes smaller increases in intraocular pressure (IOP),² less distortion of the surgical site, reduced incidence of postoperative strabismus and limiting potential myotoxicity of local anesthetics due to quicker spread. It also reduces the dosage of local anaesthetic agent used in the block. It has also been seen in certain studies that addition of hyaluronidase increases globe and lid akinesia, which may improve the safety of the procedure.

Animal-derived hyaluronidase (bovine or ovine testes) is purified through a series of

multiple precipitation, fractionation and filtration steps. The final extract is often contaminated with proteases, immunoglobulin, and other elements, which may potentially cause IgE-mediated hypersensitivity reactions. Hyaluronidase allergy, presenting as both type I and type IV hypersensitivity reactions, has been widely reported by several authors.³ Here we present a case report of a patient who presented with hypersensitivity after peribulbar block posted for small incision cataract surgery.

Case History

Sixty-five year old female patient with no known co-morbidities, was posted for cataract surgery. After application of topical drops, peribulbar block with 2% xylocaine 3ml and 0.5% bupivacaine 2ml with Inj hyaluronidase 15 IU/ml was administered. The intra-operative period was uneventful. In the postoperative ward, bilateral periorbital edema with erythema was noticed which was more on the side of surgery. Patient was not able to vocalize. Immediately oxygen 2-3 litres / minute was supplemented through nasal cannula. Intravenous access was secured and the vitals were checked. (Blood pressure – 160/80 mm of Hg, pulse rate- 82 bpm, SpO₂- 96% in room air). Injection Adrenaline 1ml of 1/10000 dilution, Injection Hydrocortisone 100mg and Injection Avil (Chlorpheniramine) 2ml were administered intravenously slowly. Around two minutes later, patient became apneic and unconscious.

Her Pulse rate was 90 beats/min, SpO₂ was around 90%, and blood sugar level was 80mg/dl. Rescue breaths with Ambu bag was given. Meanwhile 100ml of 25% Dextrose and Injection Dexamethasone 8mg were administered. Around two minutes later, spontaneous breathing attempts resumed and patient started responding to oral commands. On auscultation of chest, normal breath sounds was heard without any added sounds.

Vitals were stable with pulse rate around 70 bpm, blood pressure – 130/70 mm of Hg, SpO₂- 98%. The patient was shifted to multispeciality hospital for further evaluation and observation. After around 4 hours, patient's periorbital edema gradually reduced and she was shifted back to our hospital where she was monitored throughout the remaining day. Next day, patient was examined and discharged with oral steroids and antihistamines.

Discussion

Peribulbar block has been commonly used to achieve akinesia and anaesthesia for intraocular surgeries. Hyaluronidase has been frequently used as an adjunct with local anaesthetic agents for better penetration of local anaesthetic agents. Though few cases of reaction due to local anaesthetics like lignocaine or bupivacaine have been reported, the incidence is very low. Reactions due to hyaluronidase have been reported previously.^{4,5,6,7,9} The incidence of reactions due to hyaluronidase is approximately 1:2000.

Patients have shown acute, early, intermediate and delayed reactions after peribulbar block for ophthalmic surgery. Hypersensitivity reactions have occurred at various doses of hyaluronidase.

Hypersensitivity reactions are divided into four types, based on the mechanisms involved and time taken for the reaction, with the 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. The symptoms of type I hypersensitivity reaction takes only few minutes to manifest whereas Type IV reaction may take a few hours to days in order to appear.¹⁰

In this patient, immediate onset of symptom could represent a Type I hypersensitive reaction (IgE mediated reaction). Patient had received peribulbar block with three drugs (lignocaine, bupivacaine and hyaluronidase). Since the incidence of hypersensitivity to local anaesthetics is rare, the reaction is most probably due to hyaluronidase. Mostly it presents with local symptoms, systemic reactions like pruritis, generalized rash, diffuse bilateral wheeze, anaphylaxis have also been reported. Most commonly axial proptosis,

periorbital erythema and edema, rapid rise in orbital pressure leading to vitreous loss, reaction of extraocular muscles, restriction of extraocular muscles movement, periorbital pain and chemosis have occurred. These can lead to expulsive choroidal hemorrhage, retrobulbar hemorrhage or orbital cellulitis. Delayed onset may simulate pseudotumour. The reaction and proptosis may mimic peribulbar hemorrhage and orbital cellulitis also. Systemic effects may be mild to severe. There has been a case report of patient going into hypotension, tachycardia, hypoxia requiring immediate intubation and ICU care. Allergic reactions have also been reported with retrobulbar⁷ and, sub-Tenon's blocks.

Kirby et. al⁴ reported type 1 hypersensitivity with periorbital edema and chemosis in few minutes. Quick hill⁶ reported delayed reaction, after 36 hours of peribulbar block.

Bowman and Newman conducted a study to investigate whether Hyaluronidase improved the efficacy of peribulbar block.⁸ It was found that there was no statistically significant difference between the 2 groups receiving peribulbar block with and without Hyaluronidase. Hence addition of Hyaluronidase as an adjuvant in ophthalmic blocks can be avoided if possible; especially in patients with tendency to develop allergic reactions to drugs.

Conclusion

Anaphylaxis to hyaluronidase is a rare complication of peribulbar anesthesia.

It can cause both Systemic type I anaphylactic reaction as well as delayed local type IV reactions. They may occur even without prior sensitization as in the above case. In this case, the local reaction in the form of periorbital edema, systemic effects like angioedema and respiratory depression occurred. The reaction required administration of antihistamines, systemic steroids and required CPR to assist respiratory depression. Although rare, the possibility of hyaluronidase allergy should be considered even in patients with no known previous exposure.

Conflict of interest:

None

Financial Disclosure:

No financial interest



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