



OCULAR SIDE EFFECTS OF MISUSE OF PROPARACAINE HYDROCHLORIDE

Ophthalmology

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ABSTRACT

Public health is at risk because of the emerging trend of misuse and abuse of medications. With time there has been a trend of ophthalmic medication misuse. The difference between misuse and abuse is how they affect people's ability to feel good, unwind, have hallucinations, and have fewer symptoms of depression. Topical anaesthetic is commonly used by ophthalmologists in clinical practice, and in emergencies to remove corneal foreign bodies. In ophthalmology, proparacaine hydrochloride, also known as 2-(diethylamino) ethyl 3-amino-4-propoxybenzoate hydrochloride, is a common choice for topical anaesthesia. But these drugs are rarely prescribed to patients because of their easy availability their misuse is increasing tremendously leading to sight-threatening side effects. This article highlights the side effects and properties of proparacaine hydrochloride.

KEYWORDS

Proparacaine hydrochloride, ocular, side effects, anaesthesia, misuse.

INTRODUCTION:

There are many different medical and surgical specializations, including ophthalmology, which use topical anaesthetics extensively. Topical anaesthesia results in the temporary lack of sensation caused by the direct administration of local anaesthetic solutions, ointments, gels, or sprays to the skin, mucous membranes, or conjunctiva. Ocular surgeon Carl Koller proved in 1884 that general anaesthesia could be avoided for ophthalmic surgeries and cocaine could be used.¹

He was the initial user of local and topical anaesthesia in ophthalmology. He realized that if cocaine can cause numbness of his tongue, then it could make his eye numb also. He created an aqueous cocaine solution based on this concept, which he tested on an animal cornea before using it on himself and a companion.²

In ophthalmology, proparacaine hydrochloride, also known as 2-diethyl amino 3-amino-4-propoxy benzoate hydrochloride, is a common choice for topical anaesthesia.^{3,4} It acts by inhibiting Na⁺ channels on the neuronal membrane, it is assumed to have the main impact of preventing the creation and conduction of nerve impulses.^{5,6} Although it is questionable if topical ophthalmic anaesthetics are effective at reducing pain, they may only be needed for a brief time and may provide pain relief in some people.⁷⁻⁹ These drugs are sometimes used for these properties by patients leading to their abuse.

One of the most prevalent and harmful types of ocular damage is by abuse or misuse of topical anaesthetics. Given that these medications are occasionally prescribed by family doctors, emergency department doctors, optometrists, and ophthalmologists, it is rarely iatrogenic. It is in most cases self-induced ocular damage. Additionally, abusing topical anaesthetics can be a component of addictive behavior and can even take things so far as smearing cocaine powder directly into the eye. Additionally, some of these patients might have a connection to the medical field in some way, making it easier for them to acquire the agent and/or have a mental disorder at the time.

In previous studies, it has been seen that the common causes of abuse were personality disorder, chemical dependency, depression, bipolar psychosis, substance abuse, and suicidal tendencies. They usually present to the emergency unit complaining of severe pain, lacrimation, and photophobia with a wage history. The defects are discovered to be caused by corneal epithelial defects along with ring infiltrates in the corneal stroma and.¹⁰⁻¹²

In this study, we want to highlight the properties as well as side effects of proparacaine hydrochloride to prevent excessive misuse.

Method Of Literature Search:

A thorough literature review was conducted using EyeWiki, Medline, PubMed, Google Scholar, and Cochrane. The aforementioned keywords were utilized for the literature review; "Proparacaine hydrochloride," "ocular," "side effects," "anaesthesia," and "epithelium." All relevant articles, including review articles, original articles, case series, and case reports, were reviewed thoroughly. The search was conducted in August 2023. Mostly the publications listed in the review article were from the past 20 years but we did not exclude the older publications, which are commonly referenced.

Physical Properties:

The solution needs to be transparent to straw-colored. It is unsafe to use the solution if it turns darker.

Chemical Properties:

Benzoic acid, 3-amino-4-propoxy-,2-(diethylamino) ethyl ester, monohydrochloride.

Composition:

Active salt- Proparacaine hydrochloride 5 mg (0.5%).

Preservative: Benzalkonium chloride.

Inactive: Glycerine and Purified water

Duration Of Action:

The ocular solution of proparacaine hydrochloride is a quickly-acting anaesthetic agent. Its action lasts for 15-20 minutes.

Dosage:

For small procedures like Goldmann applanation tonometry, foreign body removal, Schirmer's- Single instillation of 1-2 drops per eye.

For long procedures like cataract surgery, corneal procedures, etc. – Repeated instillation is done after every 7-10 minutes.

Storage:

Protect from direct contact with sunlight. Temperature should be 2°-8° C (36°-46°F).

Mechanism Of Action:

It functions by lowering the input of sodium and inhibiting the sodium channels that are present inside the nerve cells. Due to the inability to attain the threshold potential, no action potential is produced, which prevents neuronal conduction along axons and dendrites.

Indications Of Use:

1. Removal of foreign body

2. Tonometry
3. Gonioscopy
4. Short conjunctival and corneal procedures
5. Intravitreal injections
6. Cataract surgery
7. Schirmer's test
8. Syringing procedure
9. For examination when the patient is unable to open their eye due to intense pain.

Indications For Repeated Use:

1. Patients of glaucoma for repeated Goldman applanation tonometry.
2. Patients of angle closure for repeated gonioscopy.

Probable Indications For Misuse:

1. When the patient is having severe pain following corneal abrasion and is unable to carry out daily work.
2. Patients with keratopathy with severe pain.
3. Recurrent filamentary keratitis.
4. Faulty contact lens-induced superficial punctate keratitis.

Risk Factors For Abuse:

1. Easy availability
2. Medical contacts
3. Addict
4. Mental illness
5. Misuse after prescription
6. Personality disorders
7. Depression

Reasons For Abuse:

1. To get pain relief
2. For getting a sense of numbness
3. To get a feeling of self-satisfaction
4. For self-pride

Side Effects Of Abuse:

1. Blurring of vision
2. Stinging
3. Burning
4. Conjunctival redness
5. Light sensitivity
6. Hyperallergic corneal reaction can occur leading to intense diffuse epithelial keratitis.
7. Sloughing of large areas of the Cornea can occur.
8. Conjunctival injection
9. Stromal oedema
10. Stromal infiltrates (classic ring infiltrates)
11. Folds in Descemet membrane
12. Damage of Endothelium
13. Ocular inflammation
14. Allergic contact dermatitis can cause the fingertips to crack and dry out.
15. Iritis can occur rarely.
16. Corneal melting and perforation in advanced cases.¹³⁻¹⁷

Mechanism Of Corneal Damage:

Proparacaine damages the vinculin and actin filament via a calmodulin-mediated mechanism and hence prevents epithelial cells from migrating and dividing.¹⁸ Ocular surface toxicity may also be a result of topical anaesthetic preservatives such as benzalkonium chloride.

Clinical Presentation Following Damage:

1. Diminution of vision
2. Lacrimation
3. Severe Pain
4. Photophobia
5. Glare
6. Redness
7. Foreign body sensation

How To Diagnose Damage:

Early diagnosis is better in such cases. These patients usually present with severe pain which is not appropriate with their slit lamp findings and usually give a wage history of past treatment. The clinical picture of the patient is usually epithelial defect with non-inflammatory stromal edema.¹⁹⁻²⁰

In some cases, the clinical picture is the same as in other cases like:

1. Acanthamoeba keratitis
2. Infectious keratitis

So, in these cases, corneal scrapings should be taken and sent for culture to rule out other causes.

Treatment of damage:

1. First of all, the most necessary thing is to stop topical anaesthetic use.
2. Hospitalize the patient in case of severe damage to ensure stoppage of anaesthesia and for better treatment.
3. Pain relieving therapy such as oral analgesics and/or regional anaesthesia is given.
4. Psychiatric consultation in case if needed.
5. Treat other causes if present.
6. Topical steroids are rarely prescribed as they can cause further corneal thinning.
7. In severe cases amniotic membrane transplant is needed.
8. Evisceration in some cases.

Cautious Use:

1. Pregnant females- foetal toxicity can occur.
2. Women trying to conceive- reproductive capacity can be affected.
3. Breastfeeding mother- can be excreted in milk.
4. Paediatric patients
5. Geriatric patients

REFERENCES:

1. Jackson T, McLure HA. Pharmacology of local anesthetics. *Ophthalmol Clin North Am.* 2006; 19:155-61.
2. Goerig M, Bacon D, Van ZA. Carl Koller, Cocaine, and Local Anesthesia. *RAPM.* 2012; 37:318-24.
3. Peng YY, Jin YX, Chen CF, Yu XP, Zheng JW. Reduced emergence agitation with proparacaine hydrochloride eye drops after general anesthesia for pediatric strabismus surgery. *Int J Nurs Sci.* 2015; 2:58-60.
4. Philip J, Bossart MD, Robert L, Stephen MD, Robert D, Herr MD, *et al.* Visual Acuity After Topical Application of Proparacaine. *Ann. Emerg. Med.* 1997; 29:158-60.
5. Daisy B, Whigan. Proparacaine hydrochloride. Elsevier. 1977; 6:423-56.
6. McGee H, Fraunfelder F. Toxicities of topical ophthalmic anesthetics. *Expert Opin Drug Safe.* 2007; 6:637-40.
7. Dass BA, Soong HK, Lee B. Effects of proparacaine on actin cytoskeleton of corneal epithelium. *J Ocul Pharmacol.* 1988; 2013:187-94.
8. Boljka M, Kolar G, Vidensek J. Toxic side effects of local anesthetics on the human cornea. *Br J Ophthalmol.* 1994; 2013:386-9.
9. Rocha G, Brunette I, Le François M. Severe toxic keratopathy secondary to topical anesthetic abuse. *Can J Ophthalmol.* 1995; 2013:198-202.
10. Erdem E, Undar IH, Esen E, Yar K, Yagmur M, Ersoz R. Topical anesthetic eye drops abuse: Are we aware of the danger? *Cutan Ocul Toxicol.* 2013; 32(3):189-93.
11. Tok, O. Y., Tok, L., Atay, I. M., Argun, T. C., Demirci, N., & Gunes, A. Toxic keratopathy associated with abuse of topical anesthetics and amniotic membrane transplantation for treatment. *Int J Ophthalmol.* 2015; 8(5):938.
12. Yagci A, Bozkurt B, Egrilmez S, Palamar M, Ozturk BT, Pekel H. Topical anesthetic abuse keratopathy: a commonly overlooked health care problem. *Cornea.* 2011; 30(5):571-5.
13. Harnisch JP, Hoffmann F, Dumitrescu L. Side-effects of local anesthetics on the corneal epithelium of the rabbit eye. *Albrecht Von Graefes Arch Klin Exp Ophthalmol.* 1975; 2013:71-81.
14. Moreira LB, Kasetsuwan N, Sanchez D, Shah SS, LaBree L, McDonnell PJ. Toxicity of topical anesthetic agents to human keratocytes in vivo. *J Cataract Refract Surg.* 1999; 2013:975-80.
15. Yeniad B, Canturk S, Ozdemir E. Toxic keratopathy due to abuse of topical anesthetic drugs. *Cutan Ocul Toxicol.* 2010; 2013:105-9.
16. Baykara M, Akova YA, Budak B. Our keratopathy cases associated with proparacaine. *Uludağ Üniversitesi Tıp Fakültesi Dergisi.* 2011; 2013:131-3.
17. Katsimpris JM, Sarantoulakou M, Kordelou A, Petkou D, Petropoulos IK. Clinical findings in patients with topical anesthetic abuse keratitis: a report of five cases. *Klin Monbl Augenheilkd.* 2007; 2013:303-8.
18. Rosenwasser GO, Holland S, Pflugfelder SC, Lugo M, Heidemann DG, Culbertson WW, *et al.* Topical anesthetic abuse. *Ophthalmology* 1990; 97: 967-975.
19. Pharmakakis NM, Katsimpris JM, Melachrinou MP, Koloipoulos JX. Corneal complications following abuse of topical anesthetics. *Eur J Ophthalmol.* 2002; 12:373-8.
20. Bunya VY, Moon C, Morales GO. Topical Anesthetic Abuse Keratopathy. *Am J Ophthalmol.* 2023.