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Abstract

Topical Ophthalmic preparation (cosmetics, apparel, and medications) can have adverse effects on the external eye by means of immunological reactions. The ocular adnexa is particularly vulnerable to allergies: This project is a literature review to assist the optometrist in identification, diagnosis and remediation of allergic reactions.

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ALLERGIC REACTIONS CAUSED BY TOPICAL
APPLICATIONS AFFECTING THE
OCULAR ADNEXA

By

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A thesis submitted to the faculty of the
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BIOGRAPHICAL INFORMATION

Sahera Dawoodjee graduated from the University of Zambia, with a Bachelors of Science in Psychology and Biology. She will be graduating from Pacific University College of Optometry in May 1990, and thereafter plans on joining a group practice in Canada.

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ABSTRACT

Topical Ophthalmic preparation (cosmetics, apparel, and medications) can have adverse effects on the external eye by means of immunological reactions. The ocular adnexa is particularly vulnerable to allergies: This project is a literature review to assist the optometrist in identification, diagnosis and remediation of allergic reactions.

INTRODUCTION

Contact dermatitis of the eyelids, conjunctiva and cornea is one of the most commonly encountered immunological conditions in the ophthalmic practice. With the increasing number of states introducing therapeutic drugs correctly diagnosing and remediating the effects of these allergens will become an important part of management in the optometric practice.

Contact allergies may be caused by a wide variety of substances. Iatrogenic contact dermatitis or drug induced dermatitis occurs frequently with the use of antibiotics, cycloplegics, anesthetics, and preservatives. Perfumes, cosmetics, clothing, jewelry, soaps, and even eyeglasses are as likely to cause these allergic irritations. Manifestations of the allergies in and around ocular adnexa may include a watery or mucus discharge with red, irritated, itchy eyes. The corneal signs are punctate keratitis, the conjunctiva becoming edematous and hyperemic, and the eyelids exhibit crusty, scaly, edematous tissue.

The two basic types of allergic mechanisms involved with contact dermatitis are Type I (immediate hypersensitivity, IGE mediated) or Type IV (delayed response cell mediated.) Type I occurs when an antigen (drug) is reintroduced in the person's eye. During the first exposure to the antigen IGE antibodies attach to mast cells causing the cells to rupture, at which point large quantities of pharmacologically active agents are released within minutes of exposure causing urticaria, angioedema, and anaphylaxis. Type IV reaction is caused by T lymphocytes interacting with the antigen and injuring the tissue by releasing lymphokines and other toxic chemicals. Lymphokines are associated with inflammatory responses.

Allergy of Conjunctiva

The frequency of allergic conjunctivitis is explained by the fact that direct contact to the allergen is fairly common site due to the proximity of cosmetic application and administration of drugs. Characteristics of conjunctival allergy consists of itching, papillary conjunctivitis, eczema of the eyelids and increase eosinophil count. (1,12,11,16)

Allergy of Cornea

The cornea may only show a mild punctate keratitis but symptoms such as pain, lacrimation and photophobia are exaggerated. Superficial infiltrates may also be present in the limbal area. (11,12,16)

Allergy of the Eyelid

Edemic reaction mechanism is usually immediate rather than delayed- this is marked and highly noticeable because of the extreme laxity of the skin and because fluid accumulation in the tissue is confined within the orbital structure. Histamines cause dilatation of the lymphatics and blood vessels exuding serum containing eosinophils and leukocytes into the tissue. Eczema of the eyelids is most often due to an allergic reaction in the epidermal area of the skin with symptoms of erythema, papulation, vesiculation, oozing, crusting, scaling, increased pigmentation and itching. Predisposing factors could be extreme dryness or greasiness as well as a fine texture and thinness of skin. There is a delayed period of 24-48 hours after exposure to the contagion before the eczema is noted. (11,12,16)

Allergic Reactions to Topically Applied Medication

ANESTHETICS

Few side effects are noted with anesthetics when instilled for short periods of time. Toxicity is generally uncommon since topical anesthetics are most often used in the office.

Anesthetics render the eye vulnerable to damage since the blink reflex is inhibited and abnormal drying of the cornea occurs. Vasodilation and stinging are frequently experienced but acute epithelial allergic reactions occur only 1/1000. (7). A diffuse necrotizing epithelial keratitis with filament formation and corneal edema may accompany. This reaction usually occurs within five minutes to half hour after exposure. Fluid accumulates in the corneal epithelium and stroma causing folds in descemet's membrane. Repeated application may lead to keratitis, pannus, decreased transparency, and ulceration with increased risk of infection. Allergies to anesthetics can be established in any person, however some people are more prone due to a genetic predisposition. All reactions require prior sensitization.

Tetracaine, buticaine sulphate, piperacaine, phenocaine, and dibucaine (16) are the least employed due to ocular irritation continuing even after wearing off of the anesthetic properties.

Proparacaine (Ophthaine) is usually the anesthetic of choice (half as toxic as tetracaine (7)) since it causes the least irritation. Cocaine, the first topical anesthetic to be used is also infrequently employed as an anesthetic since it causes erosion of the epithelium. Cocaine also causes fewer sensitivity reactions but can be used as an alternative when a patient is found to be allergic with to another anesthetic. Xylocaine, piperacaine, and cocaine do not cross-react since they are chemically unrelated. (16). If a reaction occurs due to one anesthetic another maybe substituted.

Antibiotics

Corneal side effects of antibiotics are seen more often from systemic use rather than topical. High concentrations of these drugs cause toxicity and irritation with severe inflammation and dermatitis. Neomycin is one of the most notorious drugs causing periorcular allergic dermatitis. (1,16,12,11,8). Neomycin is the most toxic to the corneal epithelium, it causes punctate keratitis, dermatconjunctivitis and papillary conjunctivitis.

Bacitracin, due to its high concentration is also known to cause epithelial keratitis and stromal edema but on a less frequent basis. Streptomycin use causes dermatitis of lids and conjunctiva in 6 to 8% of cases on reapplication. (16) Gentamycin, on rare occasion causes punctate keratitis and papillary conjunctivitis. Tetracycline use and exposure to U.V. light causes erythema and bullae, urticaria, rashes, and exfoliative dermatitis sometimes accompanied by punctate keratopathy and papillary conjunctivitis.

Sulfonamides

Numerous side effects are indicated with sulfur containing drugs, but by far of greatest importance is the Stephen Johnsons Syndrome. Sulfur ointment used as eyelid scrub causes the lids to become edematous and forms a distinct area of erythema resembling sunburn which is limited to the eyelid margin above the lash line. Clinical characteristics are variable; they include weals, delayed papular and eczematous eruption, urticaria, and mucous membrane. (16,1) Newer sulphonamides seem to cause fewer allergic reactions, eg: sodium sulphonamide rarely causes a sensitivity reaction but has been associated with spastic pain and pseudomembranous conjunctivitis. (5)

Antivirals

Reactions to antivirals such as Idoxuridine, Vidarabine, and Trifluridine are often mistaken for worsening of the disease and failure of the drug to respond. Idoxuridine causes many reactions on the ocular tissue such as punctate keratopathy, corneal epithelial dysplasia, superficial vascularization, dermatitis sicca and photophobia. (1,7,20) and formation of ulcers on the cornea. (20,16)

Vidarabine also causes punctate epithelial keratitis, corneal erosion and decreases the healing rate. Trifluridine causes similar reactions as well as diffuse punctate keratopathy, limbal pannus, conjunctival scarring and stromal edema, however, it is also the least likely of all to cause toxic effects thus it is usually the drug of choice for a viral infections. (12)

Metals

Mercury: All mercury containing agents cause allergic dermatitis and band keratopathy, particulate metallic opacities are often noticeable in the stroma. (1)

Silver: causes irritation with severe corneal opacification at higher concentrations. Silver nitrate can cause blindness (1,6) but in milder cases hyperemia, swelling and discharge have been experienced. Ten percent of infants receiving silver nitrate prophylaxis for ophthalmia neonatorum developed ocular reaction compared to only 4% who received erythromycin. The peak incidence of reaction occurred on the first day, suggests the probability of a chemical reaction rather than an infectious one. (6)

Glaucoma Drugs

Timolol prevalence of punctate epithelial keratopathy is higher in dry eyes. Long term pilocarpine use causes atypical band keratopathy with occasional haziness and neovascularization but is still one of the least toxic glaucoma drug.

Echothiopate is also implicated in band keratopathy: two cases of unilateral cicatricial pemphigoid have been cited by Rich (16). Carbachol is the most toxic of all antiglaucoma drugs.

Decongestants

Naphazoline and Tetrahydrozoline are both used in conjunctival allergies but paradoxically both cause epithelial keratitis with long term use.

Preservatives

Benzalkonium Chloride reaction include punctate gray epithelial opacities injuring both the epithelium and endothelium. Due to its high incidence of toxicity it is not used in contact lens solutions. Severe loss of microvilli disruption of plasma membranes and desquamation on the top two layers of the corneal cells are caused by BAK 0.01%. It is less frequently used as a preservative in ophthalmic drugs. Another study found that BAK produced excess mucous, corneal clouding and necrosis. (16)

Chlorobutanol produces an uncomfortable epithelial dermatitis but irritation is generally mild since its concentrations are very low in contact lens solutions. Thimerosal leads to cornea stromal opacities and hyperemia mimicking the signs of adenoviral dermatconjunctivitis. (1)

Corticosteroids

Severe superficial corneal infiltrate, corneal erosions, marginal keratitis, and activation of herpetic keratitis all indicate cautious use of corticosteroids. (1,16,13)

Antimetabolites

Used in treatment of herpes keratitis actually causes severe dermatitis characterized by vacoules and inclusions in the epithelium, sometimes resulting in corneal ulceration.

Non medical applications

It is a known fact that cosmetics, clothing, soaps, and adhesives have components that can cause irritations and allergies. Close to half of the cosmetic wearing women in America may develop some form of ocular allergy or inflammation related to their make-up. (21)

Many of these women are contact lens wearers, and often these irritative symptoms are blamed on the contact lenses instead of the allergens. (21,3) Contact lens use is given up due to red, irritated eyes and associated symptoms.

Cosmetics, after medications have been referred to as the largest group causing contact allergies. The obvious reason for this is the wide range and increasing propensity of its use. Cosmetic use dates back several centuries, especially in the embellishment of the eyes. Cosmetic caused allergies mainly affects the eyelids and to a lesser extent the conjunctiva. The most frequent offenders being perfume, oil bases or simply the deterioration of cosmetics due to age or improper storage. Hypoallergenic products are especially formulated for contact lens wearers. They contain fewer allergens and are water soluble, making removal easier.

Registration of cosmetics is voluntary and only about half of the cosmetic manufacturers file ingredient statements with the FDA. Fewer than 10% file experience reports detailing any possible adverse reactions. The FDA requires that all manufacturers list ingredients on the packaging but one fragrance out of the many is sufficient for that product. The FDA does not require that these manufacturers to state the cause or the result but only the experience of the allergy. This makes the identification of the particular allergen an almost impossible task for the optometrist. (21,22,3)

Some specific ingredients known to cause allergic problems are: Oils and creams; common ingredients in cosmetics are oils containing lanolin and mineral oils. Other offending agents in cream preparations are hydroquinone, mercurial salts, salicylic acid, perfumes, detergents, cocoa butter,

almond oil, and other oil based or emulsifying agents. Even hypoallergenic cream products have been found to cause allergies. Nail polish although applied far from the eyes can be considered among the common allergens. The offending agents are believed to be the synthetic resins such as methacrylates and dyes. Nail polish removers containing oils dissolved in ethyl acetate maybe the sensitizers too. Perfumes; most cosmetics and many medicines contain perfumes to make them more attractive. Perfumes may be a blend of various chemicals, both synthetic and natural, often causing eczema and scaling. A major cause of dermatitis regarding perfumes is oil of Bergamont (16) resulting in a prolonged photosensitivity reaction. Soaps normally cause irritation rather than a contact allergy due to its high alkalinity. True allergies from soaps maybe caused by fillers, fats, fatty acids, perfumes, antiseptics or dyes. Build-up of soap on contact lenses can cause significant irritation, blurry vision and tearing.

Eye lash/brow dyes containing coal tar chemicals like paraphenylenediamine (23) can be most toxic sometimes leading to blindness.

Kohl, commonly used in Asian cultures is usually made of carbon obtained by burning organic material or black oxide from manganese. Eyebrow pencils contain parafin to which pigments have been added. These pigments have simple composition and thus allergies are relatively rare. Eyeliners when not used properly can become a major source of irritation. If applied on the grey line of the lid margin the orifices of the meibomian glands can be blocked.

Mascara allergies are also relatively uncommon. The basic ingredients being trichanolamine sterate, beeswax and pigments (23). Mascara should be water soluble and not contain nylon/rayon lash brighteners that flake off and may become embedded in the conjunctiva as a foreign body causing an irritation. (3,21) Water proof mascaras are actually more popular since they remain on the lashes longer and do not smear. These have to be removed with oily or solvent type removers that may cause the irritation.

Eye shadow in ointment form consists mainly of petroleum and some lanolin, ceresin, beeswax, spermaceti, and pigments: (23,16) some brands

may also contain perfumes and preservatives. Allergies have been noted especially when the eye shadows are in an ointment base. Metallic glitter with mica and silica that become embedded in the tissue and causes irritation frequently.

Hair preparations such as lacquers, shampoos, tonics, lotion, gels, mousses, straighteners, and permanent wave preparation, although not directly applied to the ocular area, may cause allergies due to their close vicinity to the sensitive eye tissues. Hair mousse and sprays used by both males and females alike, can cause residual problems and allergic reactions on contact lenses. (24) Cosmetic aids, as harmless as they may seem, can be irritants. Powder puffs, lash curling wands, eyeliner/eyebrow brushes and cleansing pads should be taken into consideration when investigating an allergic reaction.

Spectacle Frames

Allergies due to frames are relatively rare but a few cases have been reported. Metallic frames containing nickel and even plastic (zyl) frames have been identified as causes. (23). The reaction is first apparent around the nose bridge area and temples behind the ears. The dermatitis often spreads to the eyelids and conjunctiva. Perspiration reacts with nickel forming allergenic nickel salts; in such cases solid gold or plastic frames may be beneficial. Zyl allergies are more complicated since this synthetic material is composed of many different substances and as many different processes are used to manufacture them.

With the introduction of therapeutic pharmaceutical agents (TPA's) the frequency of allergies presenting in the Optometrist's office will also increase. It is up to the optometrist to intervene and block the irritation in a manner that is safe and effective. The optometrist should be able to categorize the reaction according to the severity and to approach treatment from this angle.

Criteria for proving that a disease of the eye is an allergy can be done systematically.

1. Presence of antibody to antigen in higher quantities in ocular tissue than in serum.
2. Accumulation of plasma cells and lymphocytes at disease site.
3. Accumulation of immunoglobulin at disease site.
4. Inhibition of the disease with corticosteroid.
5. Induction time.
6. Association of the eye disease with disease elsewhere in the body for which an immune site has been proved or suggested. (21)

A careful history and physical exam with a slit lamp will reveal defects such as flaking of skin, loss of lashes, injected eyes, lesions, and thinning of the tissue are all tell-tale signs.

A skin patch test can be used to confirm the diagnosis. This is usually performed on a hairless area along the forearm. The drug/cosmetic/allergen is applied on the skin and covered by a impermeable membrane or band aid and kept on for 24-48 hours. This is however not without its problems. A false positive test maybe indicated if a very high concentration of the suspected allergen is applied, or a false negative test if the skin is very thick and impermeable. The history is probably the most important part of the diagnostic process.

DRUG THERAPY

Antihistamines are generally not effective in topical application and they have to be taken in large doses for the 'immediate response reaction'. Steroid reaction is both non-specific and non-curative but never the less of tremendous value. In cases of the exaggerated inflammatory process the blocking effect is most valuable especially when the condition is self limiting. (1,12,13,16,8).

Allergy of the conjunctiva, cornea, and eyelids are usually resolved with topical steroids, but the offending antigen have to be eliminated first. When the internal system such as the uvea are involved, systemic steroids either injections or parental maybe required. Steroids are contraindicated in viral disease or in cases where the steroid itself produces the irritative reaction.

Three available antihistamines for topical treatment of allergic reactions are pyrilamine maleate, pheniramine maleate and antazoline phosphate: Also available in combination with phenylephrine and naphazoline (vasoconstrictor). (12).

Non-prescription antihistamine available are Chlorphenamine maleate (Chlortrimetron), diphenylhydramine (Benadryl), methapyrilene (Histadyl), cyclizine (Merejilo) and promethazine (Pheneragan). These have side effects of their own of which the optometrist should be aware; (gastrointestinal disturbances, sedation, increased IOP, mydriases and anticholinergic effects.) For mild to moderate cases, phenylephrine and naphazoline may be quite valuable causing vasoconstriction: long term use is not recommended since rebound hyperemia may occur. Antihistamine are often more effective with concomitant use of oral agents. Contact allergy caused by antibiotics are typically cell mediated and antihistamines are of little help. Disodium Cromoglycate (Cromolyn Sodium) inhibits release of histamine from mast cells and effectively relieves symptoms. Two percent Cromolyn is more effective than antihistamines/vasoconstrictor preparation in treatment of vasoactive amine mediated forms of allergic conjunctivitis. (Severe cases may require employment of corticosteroids for relief of symptoms. Prednisolone acetate is used for relief for a maximum of 10 to 14 days but long term use is not recommended because of potential steroid toxicity. (12)). Management of cosmetic allergies are approached much the same way as those caused by drugs. Hypoallergenic products gives the patient an alternative since these products are especially formulated by elimination of impurities and the formulations are simplified thus reducing the chances of the allergies. (22) Sensitizers such as lanolin, cocoa butter, dyes, perfumes and preservatives are usually eliminated from the composition. Steroids are generally not required but may be used for severe reactions.

A less radical approach is the use of cold compress with aluminum acetate 1:16 concentration or Calcium Acetate for the wet, weepy stage. By far, the most important factor should be avoidance of the known allergens and those similar in composition.

This literature review has been presented in the hope that it will facilitate recognition, treatment, and prevention of iatrogenic and cosmetic allergies commonly presented in the optometrists' practice.

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