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Surgical Adhesives in Ophthalmology

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SUMMARY

Cyanoacrylate adhesives were tested for tissue tolerance in rabbit eyes. The monomers were applied on deepithelialized corneas, and the polymers were implanted intracorneally and in the anterior chamber. The following classification is made based on clinical and histological observations. Best tolerated: n-decyl, n-octyl, n-heptyl, n-hexyl, n-butyl, and isobutyl 2-cyanoacrylate; less well tolerated: β,β,β-trifluoroisopropyl 2-cyanoacrylate; and least tolerated: methyl 2-cyanoacrylate.

The clinical applications of cyanoacrylate adhesives in corneal and retinal surgery are reviewed, including, 1) sealing of traumatic perforations and ulcers in the cornea, 2) attaching artificial membranes to the anterior surface of the cornea (artificial epithelium) and to the posterior surface (artificial endothelium), 3) adhesives with penetrating corneal prostheses, 4) sealing choroidal perforations, and 5) sutureless scleral buckles.

1. OCULAR TOLERANCE OF CYANOACRYLATE ADHESIVES

The eyeball offers unique characteristics for testing the tolerance of artificial materials. The anterior wall of the organ, the cornea, is a transparent tissue through which the interior portion of the eye can be observed. Inside the eyeball, between the cornea and the lens, is the anterior chamber, filled

with approximately 0.2 ml of a transparent aqueous fluid. In the anterior chamber, in front of the lens, is the iris, a circular pigmented contractile membrane perforated centrally by the pupil. These parts of the eye, as well as deeper parts of the organ such as the vitreous body and the retina, and tissues external to the eye such as conjunctiva, can be directly observed during toxicity assays.

A. Experimental

Methyl, isobutyl, n-butyl, n-hexyl, n-heptyl, n-octyl, n-decyl, and β,β,β-trifluoroisopropyl 2-cyanoacrylate were investigated. n-Butyl and n-heptyl 2-cyanoacrylate were 99% pure and stabilized by approximately 50 ppm sulfur dioxide; both these adhesives were obtained from Dr. Fred Leonard, Walter Reed Army Medical Center, Washington, D. C. β,β,β-Trifluoroisopropyl 2-cyanoacrylate is an experimental biological adhesive obtained from the Medical Products Division of the 3M Company of Minnesota. The remainder of the adhesives used in this series were medical grade surgical adhesives from Ethicon, Inc., of Somerville, New Jersey.

Three types of test were carried out in rabbit eyes. In one type, the adhesives were polymerized in situ over deepithelialized cornea. In the second and third types of test, the adhesives were polymerized in vitro, and the polymers were then implanted intracorneally and in the anterior chamber of eyes.

In a preliminary series of experiments, adhesives were applied to the cornea over dried epithelium. One day after application, the adhesive was found to be detached from the tissue and the underlying epithelium had also separated from the stroma.

Tissue reaction to the adhesives was determined by frequent examination of the treated eyes. Observations were made of the degree and duration of perilimbal injection, conjunctivitis, corneal edema and vascularization, dilation of iris vessels, and amount of flare and number of cells in the anterior chamber. Particular attention was given to the duration of the reaction elicited by an implant. In deepithelialized corneal and intracorneal implants, reaction due to trauma should subside within a couple of days following the operation. In anterior chamber implants, the injury is more severe and traumatic reaction should be expected to last up to 2 weeks following the operation.

The eyes with implants were also examined histologically. This served only to confirm the degree of inflammation observed with the biomicroscope. In general, various degrees of infiltration of polymorphonuclear leucocytes and foreign body giant cells were found near every specimen examined.

B. Results and Comments

1. Adhesives on De-epithelialized Corneas. β,β,β-Trifluoroisopropyl and methyl 2-cyanoacrylate were released from the tissue within several hours to several days after being applied. Both elicited marked inflammation, persisting in several cases for many days after the adhesives had sloughed off. The other adhesives tested remained attached to the tissue for several weeks to several months and induced mild to moderate inflammation. With very few exceptions, all corneas became vascularized 3 to 4 weeks before the adhesive was released.

2. Adhesives Implanted Intracorneally. Intracorneal implants in rabbitt eyes are of relatively short duration, regardless of the inertness of the implant. Most implants will extrude early or late, depending on size, depth in the cornea, and permeability to water and metabolites. However, most polymers can be implanted in rabbit corneas and examined biomicroscopically and histologically before the process of extrusion begins, usually about 1 month postoperatively for thin discs (0.1 mm) of small diameter (4 mm).

Poly(methyl 2-cyanoacrylate) elicited marked inflammation and necrosis of surrounding tissues. Poly(β,β,β-trifluoroisopropyl 2-cyanoacrylate) induced severe reaction and necrosis, but to a lower degree than the methyl derivative. The remainder of the adhesives tested were much better tolerated, and they elicited moderate to mild reaction which usually subsided after a few days.

3. Adhesive in the Anterior Chamber. In general the tissue reaction to polymers implanted in the anterior chamber of the eye is less dramatic than the reaction to implants placed in more intimate contact with a tissue. The reaction elicited by any insoluble implant is to a large extent due to soluble impurities leaching from the implant, or to degradation products released from it. In the anterior chamber the impurities are released into a fluid which has a rate of exchange of approximately 50 μl/min (20% of the total volume per minute) [1]. The iris, cornea, and lens enclosing the anterior chamber respond sensitively to toxic substances in the chamber. Also, in the aqueous humor, inflammation can be observed by the Tyndall effect which is visible with the slit-lamp microscope and caused by proteins and cells in the aqueous.

Poly(methyl 2-cyanoacrylate) induced a severe reaction in the entire anterior portion of the eye; however, while the cornea and iris in close

proximity to the implant showed persistent reaction, that portion of these tissues further from the implant improved gradually. Poly(β,β,β-trifluoroisopropyl 2-cyanoacrylate) likewise elicited a marked reaction though obviously milder than that of the methyl derivative. The remainder of the polymerized adhesives implanted in the anterior chamber were remarkably well tolerated. The reaction ordinarily elicited by polymerized adhesives in the eye was localized to its close environs.

Even the best tolerated cyanoacrylate adhesive so far evaluated elicited some foreign body reaction. The degree of reaction, however, is dependent on the amount of adhesive applied: the smaller the amount of adhesive, the less the reaction in the tissue. Fortunately, the amount of adhesive required for ocular surgery is very small, ranging from about half a microliter to several microliters per application, depending on the procedure. In any procedure using a surgical device, a certain amount of reaction must be expected. To avoid major surgery, to save an eye, or to restore vision, the procedure of choice may very well justify the use of an adhesive.

In conclusion, the following classifications can be made, based on clinical and histological observations. Best tolerated: n-decyl, n-octyl, n-heptyl, n-hexyl, n-butyl, and isobutyl 2-cyanoacrylate; less well tolerated: β,β,β-trifluoroisopropyl 2-cyanoacrylate; and least tolerated: methyl 2-cyanoacrylate.

II. TENSILE STRENGTH OF ADHESIVE JOINTS

As has been indicated above, with the exception of the methyl and trifluoroisopropyl derivatives, all cyanoacrylates tested in this series are reasonably well tolerated by eye tissues. However, their power to adhere the substrates of interest to ophthalmology varies considerably. In ocular surgery adhesives will be used not only to adhere tissue to tissue but also to adhere artificial prostheses and devices, most of which are made of poly(methyl methacrylate) or silicone rubber, to the tissues. It was found that the tensile strength of corneal stroma-stroma, poly(methyl methacrylate)-corneal stroma, and silicone rubber-scleral adhesive joints are strongest with isobutyl cyanoacrylate adhesive, and decreased in strength as the homologous series increased from n-butyl to n-decyl cyanoacrylate [2]. The tensile strength required for clinical application of an adhesive is difficult to ascertain. But of several adhesives equally well tolerated by the tissues, the one which can make the strongest bond should always be employed.

From the point of view of tissue tolerance and bonding strength, isobutyl

2-cyanoacrylate is a reasonably good candidate for most foreseeable applications in ophthalmic surgery. However, other derivatives such as n-heptyl and n-octyl cyanoacrylate have proved very useful for some surgical procedures in the eye.

III. USES OF ADHESIVES IN OCULAR SURGERY

In general, the uses of adhesives in ophthalmic surgery can be classified under two main categories: temporary and permanent applications. In the first group the adhesive is used essentially external to the tissue as a temporary dressing over a wound, remaining in contact with the tissue for a certain amount of time after which the adhesive either sloughs or is removed. In the second group the adhesive remains in the tissue permanently or until it is absorbed by the body. Cyanoacrylate adhesives degrade in the body environment [3]; the higher alkyl derivatives, however, disappear extremely slowly from ocular tissues.

A. Adhesives in Corneal Perforations

A perforated corneal wound or ulcer which fails to seal naturally within a short period of time requires surgical intervention. There are several standard procedures to treat perforations, all necessitating major surgery. The prognosis is particularly poor in patients with infected ulcers and stromal melting. Furthermore, debilitated patients withstand major surgery poorly.

The technique of restoring the anterior chamber by applying an adhesive over a perforation is relatively simple and saves the patient a major operation [4]. The adhesive acts as a temporary tampon until scar tissue grows behind it. The adhesive is applied over the wound immediately after the area around the wound has been blotted of moisture. A polyethylene applicator [5] is used in order to obtain a smooth anterior surface of the polymerized adhesive covering the wound. A small drop (about 3 to 5 μl) of the adhesive is placed in the polyethylene applicator and the adhesive is then applied over the wound. Polymerization occurs rapidly, and the polyethylene applicator can be withdrawn, leaving the polymer over the wound.

B. Sealing Choroidal Perforations

Surgical and traumatic perforations through sclera, choroid, and retina were sealed with adhesives using two techniques [6]. One technique was similar to that previously mentioned for sealing corneal ulcers: a thin film of adhesive

covering the perforation was found useful for small perforations. The second technique, suitable for larger laceration, consisted of closing the perforation with a patch of silicone rubber bonded with adhesive. These techniques are useful in sealing accidental choroidal ruptures during retinal detachment surgery, sealing perforation sites subsequent to release of subretinal fluid, after vitreous injection or vitreous surgery, and for closing perforating traumatic wounds in the sclera.

C. Artificial Epithelium

It is possible to replace the corneal epithelium with an artificial membrane such as a poly(methyl methacrylate) contact lens attached to corneal tissue with an adhesive [5, 7, 8]. This procedure may be indicated for corneas with irregular and hazy epithelium, keratoconus, herpetic keratitis, chemical burns, dry eye, and normal aphakic cornea. The most significant complication is the regrowth of epithelium under the lens, which requires removal of the lens. If the visual result should be unsatisfactory, a penetrating keratoplasty can be performed later without jeopardizing the prognosis. It is reasonable to expect that the articifial epithelium procedure will at least postpone keratoplasty in many cases of edema and replace grafting altogether in some instances.

D. Artificial Endothelium

When a corneal graft fails it is usually because the endothelium in the donor cornea is damaged, either by trauma during surgery or by an immune reaction. If the endothelium has been damaged, the graft develops edema. Scar formation and graft opacification results if this edema persists. A transparent artificial membrane can be attached with sutures or with an adhesive [9] to the posterior surface of an edematous cornea or a corneal graft to regulate the amount of aqueous fluid entering the cornea. In cases of corneal or epithelial edema where the cornea is not yet opaque, the membrane can be placed in the patient's own cornea. Where the cornea is scarred or vascularized, the cornea can be replaced with a penetrating graft with the artificial membrane attached.

E. Through-and-Through Corneal Prostheses

One problem with the artificial endothelium has been the occasional development of epithelial defects in front of the membrane, resulting in corneal opacity. Since an artificial membrane can replace the corneal

epithelium, both procedures can be combined so that the grafted stroma is covered on both sides by artificial membranes. Because such a sandwiched stromal graft may become opaque, it might be desirable to have the anterior and posterior plates linked by a central optical stem [10].

Gluing the anterior plate of the prosthesis to the deepithelialized graft keeps the epithelium away from the penetrating portion of the implant. The epithelium appears to be the cause of the failure of most penetrating implants. The posterior plate is also glued to the cornea, assuring fixation of the prostheses and preventing aqueous leaks.

F. Sutureless Scleral Buckles

Age or disease may cause the vitreous gel to shrink. If, in the process of shrinking, the gel remains attached to the retina, it may cause retinal tears. A retinal tear or a traumatic blow to the eye may be causes of retinal detachment. Fluid will accumulate between the detached retina and the wall of the eye. The retina isolated from its blood supply will become insensitive to light, resulting in blindness.

A scleral buckling creates an indentation at the location of the retinal break, bringing the wall of the eye in contact with the detached retina. To make the sclera buckling permanent, silicone rubber implants and encircling bands are employed [11]. The implant which produces the buckle can be easily fixed to the tissue by means of adhesives. The ends of the encircling band can be glued together and also can be attached to the sclera in several spots to avoid displacement [12].

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