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Lacrimal Duct Occlusion for the Treatment of Dry Eye

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ABSTRACT The most widespread treatment for dry eyes in clinical practice is an instillation containing artificial tear fluid. When an instillation does not ameliorate dry eye, we use punctal plugs. The insertion of punctal plugs is an eminent curative that positively improves the corneal and conjunctival epithelial disorders and the amount of lacrimal fluid accumulated in the conjunctival sac. We shall introduce the lacrimal duct occlusion utilizing atelocollagen solutions, which solves many of the issues induced by conventional methods.

KEYWORDS atelocollagen, dry eye, fluorecein staining, lacrimal duct occlusion, phenol red thread test, punctal plug, rose bengal staining

INTRODUCTION

Many new therapeutic methods and curative medicines for dry eyes are under development. The most widespread method in clinical practice is an instillation containing artificial tear fluid. When an instillation does not ameliorate dry eye, lacrimal duct occlusion is carried out. This report explains mostly the punctal plug, which is the most typical method used, as well as a new method for lacrimal duct occlusion utilizing atelocollagen.

PUNCTAL PLUGS

Characteristics

The most well used method these days is the insertion of punctal plugs. Those with various materials have already been developed while most of them are made of silicone. However, the hardness of the silicone varies depending on each product. The basic figuration is of a cone-shaped head with which it is inserted from the lacrimal punctum, the shaft in the middle, and the brim (caudal area) to prevent the plug from getting lost in the lacrimal passage. The sizes of plugs are called differently depending on each product, and the range of sizes provided also varies; generally those with a diameter of 0.5–1.0 mm are used. In Japan, Bernard-Fayet Plug (FCI Ophthalmics, Inc., Paris, France) (Figure 1a), Eagle Flex Plug (Figure 1b) and Eagle Plug (Eagle Vision, Inc., Memphis, TN) are being used in clinical practices.

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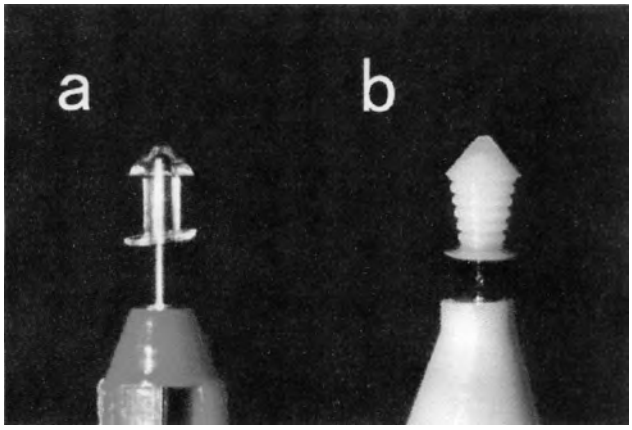

FIGURE 1 Plugs clinically used in Japan. a. Bernard-Fayet Plug; b. Eagle Flex Plug.

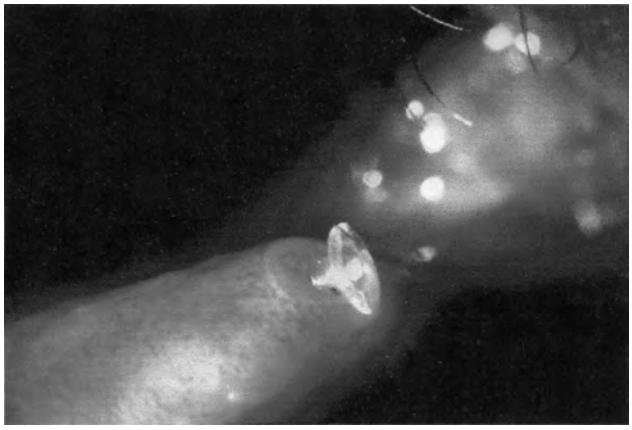

FIGURE 2 Punctal plug extrusion because of granulation formed inside the canaliculus.

Methods of Insertion

Methods of insertion vary slightly depending on each individual product while they are roughly the same. First of all, you measure the size of the lacrimal punctum using the special gauge and select the size of the plug in accordance with it. The selection of the plug size is the most crucial point. If a bad choice is made, the effects of the treatment cannot be obtained, and it can be the cause of after-mentioned complications. When the preparations for plugs of the appropriate size are completed, you should slightly extend the lacrimal punctum with the needle for lacrimal punctum extension, and then insert the punctal plug. At this time, you should pay attention so as not to tuck the plug into the lacrimal passage.

Effects of Treatment

We indicate the effects of treatment using punctal plugs with the score of rose bengal staining[1] ranging from 0 to 9, which is commonly used as an index mark of corneal and conjunctival epithelial disorders, and phenol red thread tear test,[2,3] which reflect the tear volume accumulated in the inferior conjunctival sac. The mean value of the score of rose bengal staining of 38 dry eyes decreased from 5.2 to 2.1 ($n = 26, P < 0.01$) and the mean value of phenol red thread tear test increased from 8.7 mm to 15.7 mm ($n = 31, P < 0.01$), as a result of inserting punctal plugs.[4] In the group of another 40 dry eyes, the score decreased from 5.8 to 2.4 ($n = 30, P < 0.01$) and the mean value of phenol red thread tear test increased from 6.6 mm to 15.6 mm ($n = 38, P < 0.01$).[5] Paired t test was employed for these statistical analyses.

As shown above, the insertion of a punctal plug is an eminent curative that positively improves the corneal and conjunctival epithelial disorders and the amount of lacrimal fluid accumulated in the conjunctival sac.

Complications

Although the insertion of punctal plugs is an eminent curative for dry eyes, some issues have been pointed out.

Granulation[6–8] is the most frequently observed complication of punctal plugs (Figure 2). The cause of this is considered to be the local stimulation by the plug. Generally, plugs made of hard materials tend to trigger complications. Even if the material is soft, complications tend to occur if the finishing of the edge is not satisfactory or the figuration tends to stimulate tissues. As a countermeasure for granulation you should, first of all, remove the punctal plug and wait for it to disappear (Figure 3). When inserting a plug once again, use one that causes least stimulation.

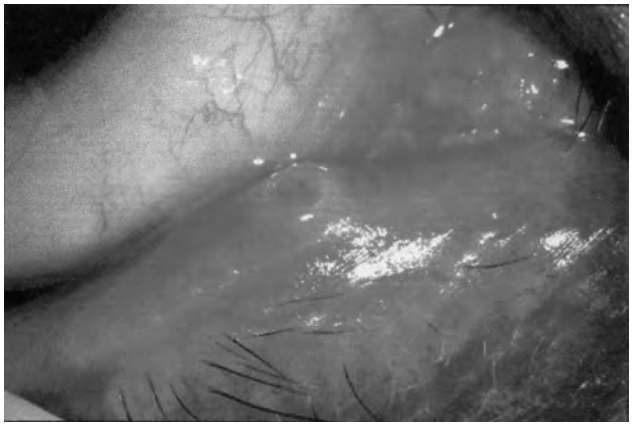

FIGURE 3 Granulation after the punctal plug was removed.

The issue of a plug migration tends to rise when the plug is pushed in to the point that is deeper than the lacrimal punctum. Some cases have been reported in which the plug migration inside the lacrimal passage caused peripheral inflammations and infections.[6,9] In order to prevent this from happening, due care must be taken so as not to let the plug become lost and in case this has happened, follow-ups must be made without fail.

Although the design of the plug has been improved, epithelial disorders caused by the caudal part of the plug coming into contact with the cornea and conjunctiva are still frequently observed. In these cases, patients do not experience discomfort in frontal vision while they do in lateral vision. Removing the causal plug, and inserting another plug of a different figuration, or a plug into a different lacrimal punctum, must deal with this.

Punctal plug extrusion[10] is another issue, which has not yet been solved. The plug is supported structurally by the lacrimal punctum while its elasticity has an individual difference. Therefore, even if the size of the punctal plug inserted was appropriate, there is an individual difference in the frequency of plug extrusion. As a countermeasure, you should insert a plug the size of which is larger by one scale compared to the one used previously.

What is expected of punctal plugs as products now is that they are easy to insert, tend not to migrate in the lacrimal passage, and tend not to bring about epithelial disorders of cornea and conjunctiva.

LACRIMAL DUCT OCCLUSION USING ATELOCOLLAGEN

At the present time, insoluble lacrimal canaliculus plugs and soluble lacrimal canaliculus collagen plugs are used as a substitute for punctal plugs. However, insoluble lacrimal canaliculus plugs are reported to be associated with complications such as infections and inflammations.[11,12] No serious complications are reported to be associated with lacrimal canaliculus collagen plugs; however, it is difficult to select the collagen plugs with an appropriate size. When the diameter of the plug is too small, there would be no effects of closure of the lacrimal duct, and when it is too large, the insertion would be difficult. In order to solve such problems, using a material that is in a liquid form at the time of insertion and is later solidified in the lacrimal canaliculus,[13,14] has been attempted.

Next, we shall introduce lacrimal duct occlusion using atelocollagen solution.[15]

Characteristics

The substance that is generally called atelocollagen[14] is a type I collagen in which the telopeptide with a high antigenicity is excised by pepsinating it. Therefore, the antigenicity of it is significantly low compared to other collagens. At 4°C and under, atelocollagen dissolves in a neutral phosphate buffer solution. When heated up to 37°C, the atelocollagen forms a core, and the entire solution turns into a white-colored gel, and obtains enough intensity to be retained with forceps.[15]

It has been confirmed in experiments using rabbits[15] and dogs[16] that atelocollagen solution becomes gel after being filled in the lacrimal canaliculus from the lacrimal punctum using a lacrimal irrigation needle, and controls the excretion of lacrimal fluid. Furthermore, clinical application of it for human eyes has already been attempted.[17]

Method of Injection

The technique of lacrimal duct occlusion using atelocollagen is the same procedure as for a diagnostic test of the lacrimal duct using saline and easier than the insertion of punctal plugs. Atelocollagen solutions are packed in the cartridge syringe for exclusive use, and are injected in the lacrimal duct of patients' eyes using the lacrimal duct irrigation needle. After being filled, the patients should not blink and keep their eyes closed for approximately 15 minutes. This is to prevent the filled solution from leaking out of lacrimal duct by means of its pumping behavior. After several minutes, the lacrimal duct is filled with gelated atelocollagen and lacrimal duct occlusion is completed. Figure 4 shows the lower lacrimal punctum that have been occluded with gelated atelocollagen. The amount of atelocollagen to be used is approximately 170 μl per eye.[18]

Effects of Treatment

Clinical tests of this atelocollagen used for 136 dry eyes (69 cases) showed that the score of rose bengal staining was reduced compared to before the treatment ($p < 0.0001$ for the first, the fourth, and the eighth week). In addition, the score of fluorescein staining decreased ($p < 0.0001$ for the first, the fourth, and the eighth week) and tear volume measured by phenol red

FIGURE 4 **Inferior lacrimal punctum occluded with gelated atelocollagen.**

thread increased ($p < 0.005$ for the first week, $P < 0.05$ for the fourth and the eights week). Wilcoxon signed-ranks test was employed for these statistical analyses. Eight weeks after the treatment, physicians made 4-scale objective evaluations ("Significantly improved," "Improved," "Unchanged," and "Worsened") of the score of rose bengal staining, the score of fluorescein staining, and tear volume measured by phenol red thread. At the same time, subjects made 4-scale subjective evaluations ("Significantly improved," "Improved," "Unchanged," and "Worsened"). Objective evaluations of "Significantly improved" or "Improved" were obtained in 57 cases and subjective evaluations of "Significantly improved" or "Improved" in 60 cases. In both objective and subjective evaluations, effects confirmed in 56 cases. Moreover, no physicians or subjects were evaluated as "Worsened."

Experimentally, the intensity of gelation atelocollagen reaches a maximum in approximately 70 hours and attains equilibrium. On the other hand, the duration of the effectiveness of the gelation atelocollagen in inhibiting tear drainage is considered to vary from individual to individual depending on the tear volume, frequency of blinking, and functions of the nasolacrimal duct; the effectiveness is expected to last for about 8 weeks in human eyes, judging from the results of our clinical tests.

Lacrimal duct occlusion using atelocollagen solutions has not been reported to cause such serious complications as those caused by insoluble plugs.

As shown above, lacrimal duct occlusion using atelocollagen solutions solves many of the issues induced by conventional methods. Moreover, as it is a cure that can be carried out safely and easily, our expectations for it to be one of the most widespread methods for lacrimal duct occlusion are high for the future.

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