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Combined Topical Application of a Regenerative Agent With a Bandage Contact Lens for the Treatment of Persistent Epithelial Defects

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Purpose: The aim of this study was to report 3 cases of persistent epithelial defects (PEDs) successfully treated with the combined topical application of a regenerative agent (RGTA; Cacicol20, OTR3, Paris, France) with a bandage contact lens (BCL).

Methods: This is a case series.

Results: Three patients suffering from a PED for 4–8 weeks and unresponsive to conventional therapy were treated with the combined application of an RGTA (Cacicol20) and a silicon hydrogel BCL. The PED healed in all patients after 4–21 days, and no side effects were noted.

Conclusions: The combination of an RGTA (Cacicol20) with a BCL seems to be an effective treatment for PED.

Key Words: regenerative agent (RGTA), Cacicol, bandage contact lens (BCL), persistent epithelial defect (PED)

CASE SERIES

Three patients (3 eyes) with a PED for 4–8 weeks and unresponsive to conventional therapy were enrolled in our case series. All the patients received a combined treatment of RGTA (Cacicol20) with a silicon hydrogel BCL (PremiO, OTR3, Paris, France). Cacicol20 is an RGTA that binds to matrix proteins and protects them from proteolysis; this allows the extracellular matrix microenvironment to get restored to its original architecture.

In this article, we present 3 patients with PEDs who were successfully treated with an RGTA (Cacicol20) combined with BCL.

CASE 1

A 53-year-old woman was referred to our department for the management of a PED in her left eye, which was...
caused by neurotrophic keratopathy. The PED was resistant to conventional treatment for 8 weeks. Conventional therapy during the 8-week period included the use of BCL, pressure patch, short-acting absorbable punctal plugs, serum eye drops, and several topical eye drops (eg, tobramycin, fluorometholone, dexamethazone, and moxifloxacin). At the time of referral, slit-lamp examination showed a central corneal epithelial defect [1.6 mm (height) × 2.4 mm (width)] with underlying and surrounding stromal opacification (Figs. 1A, B). Mild conjunctival hyperemia was noticed.

No improvement in the epithelial defect occurred during the washout period (7 days with BCL and artificial tears used 4 times daily). One week after the combined treatment commenced, the dimensions of the epithelial defect decreased to 1.0 mm (height) × 1.3 mm (width) (Figs. 1C, D). Two weeks later (3 weeks after the treatment commenced), slit-lamp examination showed a complete corneal epithelial healing (Figs. 1E, F), and the combined treatment was discontinued. There was no event of recurrence during the 4-month follow-up.

Case 2

A 62-year-old woman referred to our department for the management of a PED in her left eye. The PED arose immediately after her cataract surgery and was resistant to the conventional treatment for 4 weeks. The patient’s regimen over the 4-week period included BCL, pressure patch, topical antibiotic/steroid eye drops (chloramphenicol/dexamethasone; Dispersadron C, Laboratories Thea, Clermont-Ferrand, France), systemic medication (Acyclovir), short-acting absorbable punctal plugs, and artificial tears. At presentation, slit-lamp examination showed an extended epithelial defect [8.2 mm (height) × 6.4 mm (width)] and corneal edema withDescemet folds (Figs. 2A, B). Intense conjunctival hyperemia and mild blepharitis were noticed while the pupil was in semidilation.

The epithelial defect did not improve during the washout period. Four days after the introduction of the combined treatment, complete corneal epithelial healing was achieved (Figs. 2C, D). Corneal stromal edema and Descemet folds were diminished, and dexamethasone 0.1% eye drops (Maxidex; Alcon Lab Inc) were prescribed. Two weeks later, the corneal stromal pathology was restored; the slit-lamp examination revealed map dot dystrophy, a disease implicated for 50% of epithelial defects.6 During the 3-month follow-up, no recurrence was observed.

Case 3

A 36-year-old man was monitored in our department for 6 weeks because a PED had appeared in his left eye 4

FIGURE 1. Slit-lamp images of the left eye (case 1) at initiation (A, B), 1 week (C, D), and 3 weeks (complete epithelial healing; E, F) after the combined treatment of an RGTA (Cacic20) with BCL.
months after he had undergone a penetrating keratoplasty. The graft PED was treated unsuccessfully over the 6-week period with conventional treatment, including lubricants, BCL, short-acting absorbable punctal plugs, antibiotics, and pressure patch. The application of a new therapeutic agent was decided because the PED was unresponsive to conventional therapy during this period.

On the first day of the washout period, the slit-lamp examination showed a peripheral epithelial defect [2.2 mm (height) × 1.0 mm (width)] (Fig. 3A). There was no conjunctival or palpebral abnormality. Intraocular pressure measured values were within normal limits. The epithelial defect did not improve during the washout period. Five days after the combined treatment commenced, the dimensions of the epithelial defect decreased (Fig. 3B). Nine days after the combined treatment started, the slit-lamp examination showed complete corneal epithelial healing (Fig. 3C). During the 3-month follow-up, no recurrence was observed.

**DISCUSSION**

Several treatments have been proposed for the treatment of PEDs such as artificial tears, eye patching, tarsorrhaphy, fibronectin, autologous serum eye drops, nerve growth factor, amniotic membrane, and topical application of autologous limbal stem cells. BCL has been successfully used in the reepithelialization process and enhancement of corneal healing However, in some cases, these treatments have poor therapeutic outcomes. Additionally, a combination of BCL with serum eye drops or epidermal growth factor has been reported to be an effective approach for the treatment of PEDs. Nevertheless, treatment failure for PEDs may occur even after these combined treatments are given.

RGTAs compose a family of biodegradable glucose-based polymers engineered to replace heparan sulfates. RGTAs mimic the action of destroyed heparan sulfate molecules, break the negative repair–destruction cycle occurring in chronic lesions and inhibit proteolytic enzymes in vitro. Experimental studies have already reported the efficacy of RGTAs. In a corneal alkali-burn model, RGTAs treatment seemed to be effective in reducing the clinical signs of inflammation, enhancing reepithelialization, and improving histological patterns such as edema, fibrosis, neovascularization, and inflammation. In a recent experimental study, RGTAs facilitated the healing of alkali-injured rabbit corneas via the reduction of proteolytic, oxidative, and nitrosative damage.

An RGTA (Cacicol20) matrix therapy agent has already been used as a monotherapy for the treatment of ocular surface disorders such as neurotrophic ulcers and keratitis and has provided encouraging results. Aifa et al reported corneal healing in 8 of 11 patients treated with an RGTA (Cacicol20) as a monotherapy at a dosage of a single drop every 2 days, with 1 case of recurrence. In another study, Chebbi et al treated 11 eyes (6 with keratitis and 5 with corneal ulcers) with 1 drop of an RGTA (OTR4120) weekly, and reported a moderate efficacy on keratitis and a favorable effect on the healing of corneal ulcers. This topical RGTA replaces the destroyed heparan sulfates and binds to matrix proteins to protect them from proteolysis; the extracellular matrix microenvironment protection improves the production of signals and growth factors needed for tissue healing.
In our article, we report a new treatment approach of combined RGTA (Cacicol20) with a BCL for treatment of PEDs. In particular, we describe our experience of this combined treatment in 3 patients who presented with a PED for 4–8 weeks. All patients after topical daily instillation of an RGTA (Cacicol20) combined with a silicon hydrogel BCL improved their clinical condition (complete corneal epithelial healing at 4–21 days). No deposits on the BCL surfaces were observed in any of the patients during the treatment period.

We decided to combine this novel agent (RGTA; Cacicol20) with BCL because the BCL protects the cornea from additional mechanical injury, whereas the RGTA (Cacicol20) enhances epithelial healing. RGTA (Cacicol20) improves the reepithelialization process and enhances extracellular matrix remodeling, optimizing wound healing. The combined therapeutic approach of an RGTA (Cacicol20) with BCL was successfully used in all 3 patients to achieve tissue reconstruction and homeostasis restoration. Despite the limitation of the small number of patients included, all patients, who were unresponsive to the usual approaches, were treated successfully after they had received the combined therapy.

In conclusion, the combination of RGTA (Cacicol20) with a BCL seems to be an effective alternative therapeutic approach for the treatment of PEDs, which takes the pharmaceutical boundaries outside the already known and established treatment regimens, because now the target is the extracellular matrix of the cornea. However, further studies with a larger number of patients are needed to evaluate treatment potential.

REFERENCES


FIGURE 3. Slit-lamp images of the left eye (case 3), at initiation (A), 5 days (B), and 9 days (complete epithelial healing; C) after the combined treatment of an RGTA (Cacicol20) with BCL.

