



# Topical insulin to treat a conjunctival defect after glaucoma surgery: A case report

Barbara Burgos-Blasco<sup>a,\*</sup>, Sonia N. Yeung<sup>a</sup>, Gavin Docherty<sup>b</sup>, Alfonso Iovieno<sup>a</sup>

<sup>a</sup> Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, Canada

<sup>b</sup> Department of Surgery, Ophthalmology, Kelowna General Hospital, Kelowna, Canada

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## ABSTRACT

**Purpose:** Insulin has been postulated as a novel and effective treatment for re-epithelialization of the ocular surface and different pathologies have been suggested as possible indications.

**Observations:** A 69-year-old diabetic male was referred for a left non-healing conjunctival epithelial defect over the superotemporal scleral patch used in the placement of the Ahmed ClearPath. In the left eye, he was on latanoprost/timolol once daily, prednisolone 1 % once daily and tobramycin/dexamethasone ointment at night. Best-corrected visual acuity was 20/20 in the right eye and 20/25 in the left eye. Slit lamp examination of the left eye showed patches of avascular scleral tissue nasally and superiorly, conjunctival and Tenon defect over a thin avascular scleral patch graft. The patient was started on Humulin insulin 1UI/mL 6 times a day and the defect healed after 3 months of treatment.

**Conclusions and importance:** Insulin eye drops may be used in the treatment of chronic conjunctival epithelial defects following implantation of glaucoma drainage devices.

## 1. Introduction

Insulin has been postulated as a novel and effective treatment for re-epithelialization of the ocular surface. Recent works have highlighted a potential role for topical insulin in the treatment of persistent corneal epithelial defects, suggesting better re-epithelialization results than autologous serum.<sup>1</sup>

The mechanisms by which insulin improves epithelialization of the ocular surface are not completely known, but may be similar to the mechanism of action of the closely related insulin-like growth factor (IGF). IGF plays a central role in the growth, differentiation and proliferation of corneal epithelial cells. Known extracellular ligands for the insulin and IGF-1 receptors include insulin, IGF-1, and IGF-2. Rocha et al. demonstrated the presence of insulin in the human tear film, and insulin and IGF-1 receptors on the human ocular surface, including conjunctival epithelial cells, which suggests that insulin could play a metabolic and/or mitogenic role in conjunctival cells.<sup>2</sup>

Based on the mechanisms of action, different pathologies of the ocular surface have been postulated as possible indications for insulin eye drops. We present a persistent conjunctival and Tenon defect overlying a glaucoma drainage device in a diabetic patient that healed after

initiating treatment with topical insulin.

## 2. Case report

A 69-year-old male was referred due to a nonhealing conjunctival defect in the left eye for 11 months. The patient complained of pain and numbness around the left eye. Past medical history was significant for well-controlled type 2 diabetes mellitus.

Past ocular history was significant for left glaucoma secondary to a traumatic injury in 1999 while playing baseball, selective laser trabeculoplasty, trabeculectomy in 2014, ab interno revision in July 2021, needling in October 2021 and Ahmed ClearPath (New World Medical) implantation in December 2021. After Ahmed ClearPath surgery, the patient developed a necrotizing scleritis that required systemic immunosuppression with methotrexate and oral prednisone.

The patient was referred to our attention for a non-healing conjunctival epithelial defect over the scleral patch used in the placement of the Ahmed ClearPath. He was on latanoprost/timolol once daily in both eyes, prednisolone 1 % once daily in the left eye and tobramycin/dexamethasone ointment at night in the left eye. Systemic treatment was prednisone 5mg daily, methotrexate 25 mg/weekly, folic acid and

\* Corresponding author. Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, Canada.

E-mail address: [bburgos171@hotmail.com](mailto:bburgos171@hotmail.com) (B. Burgos-Blasco).

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metformin 1g daily.

Best-corrected visual acuity was 20/20 in the right eye and 20/25 in the left eye. Intraocular pressure was 14 mmHg in both eyes. Slit lamp examination of the left eye showed a quiet eye, patches of avascular scleral tissue nasally and superiorly,  $3.5 \times 2.5$ mm conjunctival and Tenon defect over a thin avascular superotemporal scleral patch graft, clear cornea, and a deep and quiet anterior chamber (Fig. 1). Fundus examination showed disc cupping (cup-to-disc ratio 0.5 in the right eye and 0.7 in the left eye).

The patient was started on Humulin insulin 1UI/mL 6 times a day in the left eye for one month and then four times a day for 4 months. The patient responded well to topical insulin, reducing to  $2 \times 2$ mm after one month and  $1.5 \times 1$ mm after two months of treatment. The defect healed 3 months after initiation of treatment (Fig. 2). The patient was able to taper off his methotrexate and oral prednisone during this time. Visual acuity and intraocular pressure remained stable.

### 3. Discussion

Glaucoma drainage devices represent an effective option for management of refractory glaucoma, although conjunctival epithelial defects are not uncommon post-surgically (1–5%). Erosion and tissue melts post glaucoma surgery are not infrequent, but this one was resistant to traditional treatments. In eyes with multiple previous ocular surface surgeries or chronic ocular surface diseases, successful closure of the conjunctiva can be very difficult to obtain because of the fragile nature of the tissue, the use of antifibrotic agents and in cases of thin or avascular blebs.

Conjunctival epithelial cells help maintain the health of the ocular surface and are involved in mucin secretion and ion transport. In the rabbit conjunctiva, IGF-I receptors have been found on the apical surface and are capable of binding IGF-II and insulin. IGF-binding protein 3 (IGFBP-3) is also abundant in the human conjunctiva and modulates IGF action. These receptors may have an important role in conjunctival epithelial cell proliferation.<sup>3</sup>

In our case, the conjunctival epithelial defect developed post-surgically as a consequence of diabetic neuropathy or may be

secondary to the presence of large areas of avascular conjunctiva/sclera, or a combination of both. IGF-1 promotes epithelialization by improving cell proliferation and inducing the activation and differentiation of limbal stem cells. In the current case, these mechanisms could have helped to heal the conjunctival and Tenon's defect.<sup>4</sup> Furthermore, the history of a necrotizing scleritis and the use of systemic and topical steroids could have played an additional role in the persistence of the conjunctival defect. Although, methotrexate and prednisone were decreased after topical insulin was started, this was only after an decrease in the conjunctival defect was noted, hence being a result of this improvement and less likely the cause of the impaired epithelialization. Nonetheless, several changing factors could have affected the outcome of the case.

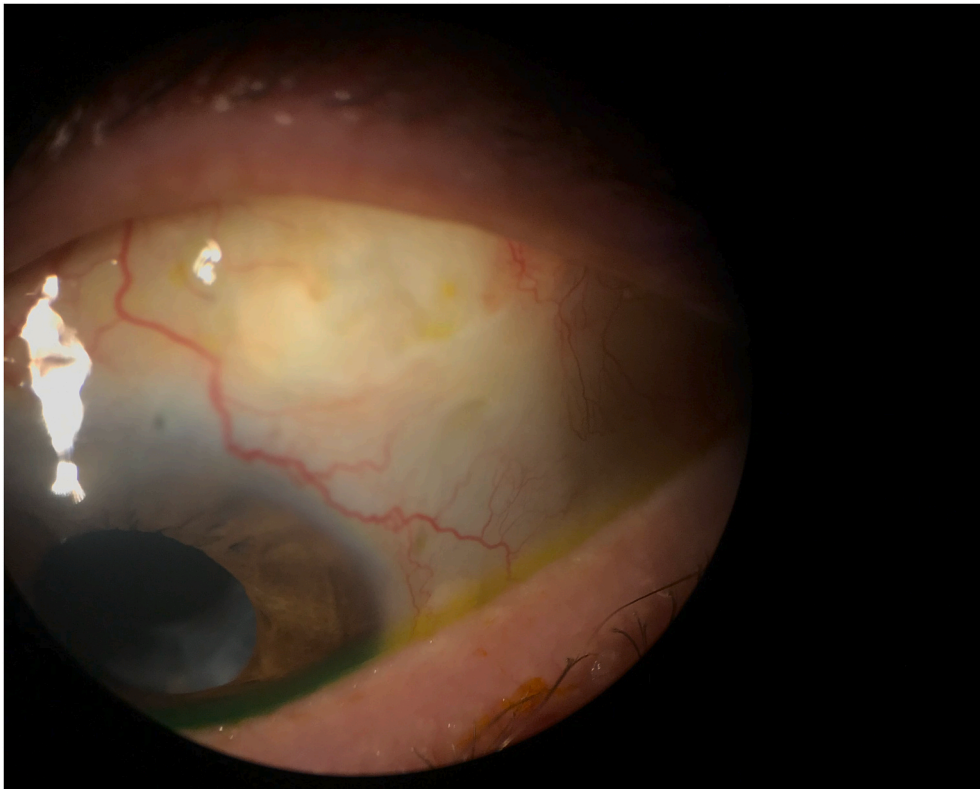
Although first suggested by TR Aynsley in 1945, it was not until 2013 that Bastion and Ling evaluated the use of topical insulin after surgical corneal de-epithelialization to improve visualization during retinal surgery in diabetic patients. Diabetic patients treated with insulin presented a significantly smaller epithelial defect compared to diabetic eyes with standard treatment. Similar results were described by Fai et al. in a controlled, randomized, double-blind study that included diabetic patients with corneal epithelial defects after vitreoretinal surgery. Although diabetic patients were initially thought to respond better, further investigations have also yielded excellent results in non-diabetic patients.<sup>5</sup>

Diaz-Valle et al. compared the use of 1UI/ml topical insulin in persistent epithelial defects to autologous serum.<sup>1</sup> Epithelialization was achieved in 84 % with insulin and 48 % with autologous serum. The time to re-epithelialization was  $32.6 \pm 28.3$  days with insulin and  $82.6 \pm 82.4$  days with autologous serum. No differences were found in the epithelialization rate between diabetics and non-diabetics. The need for amniotic membrane transplantation was significantly lower with insulin. These series, along with others, have demonstrated the efficacy of 1UI/ml topical insulin in persistent corneal epithelial defects. Our case herein adds conjunctival defects as another possible indication for topical treatment.

In conclusion, our case shows a potential novel use of insulin eye drops in the treatment of chronic conjunctival epithelial defects



Fig. 1. Slit-lamp image of the patient before topical insulin was started. A conjunctival defect in the superotemporal conjunctiva is observed.



**Fig. 2.** Slit-lamp image of the patient 3 months after topical insulin was started, which shows a healed superotemporal conjunctiva.

following implantation of glaucoma drainage devices. Multiple clinical trials are currently underway to investigate the use of topical insulin in different ocular surface pathologies and compare their efficacy to those of other available treatments.

#### Patient consent

Consent to publish this case report has been obtained from the patient.

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#### Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

#### CRediT authorship contribution statement

**Barbara Burgos-Blasco:** Writing – original draft, Methodology.  
**Sonia N. Yeung:** Writing – review & editing, Methodology,

Conceptualization. **Gavin Docherty:** Writing – review & editing, Validation, Conceptualization. **Alfonso Iovieno:** Writing – original draft, Supervision, Investigation, Formal analysis, Conceptualization.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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