ECRONICON OPEN ACCESS

EC OPHTHALMOLOGY
Case Series

Evaluation of Intrastromal Autologous Blood Injection for Acute Cornea Hydrops

Júlia Teixeira Leite Pereira[1], Samara Barbara Marafon[1,2]*, Tiago Lansini[1], Sérgio Kwitko[1,3] and Diane Ruschel Marinho[1,3,4]

[1]*Hospital de Clínicas de Porto Alegre, RS, Brazil*

[2]*Neofocus Oftalmologia, Porto Alegre, Brazil*

[3]*Oftalmocentro, Porto Alegre, RS, Brazil*

[4]*Universidade Federal do Rio Grande do Sul, RS, Brazil*

***Corresponding Author:** Samara Barbara Marafon, Hospital de Clínicas de Porto Alegre, RS, Brazil.

Received: November 28, 2025; **Published:** December 08, 2025

Abstract

Purpose: To report the outcomes of corneal intrastromal injection of autologous blood to address clefts and stromal edema caused by hydrops, to expedite the resolution and reduce its complications.

Methods: This was a retrospective case series of corneal hydrops - due to keratoconus and marginal pellucid degeneration (MPD) - treated with intrastromal injections of autologous blood. The cases have all failed to respond to conservative traditional treatment. A 3.0-cc syringe filled with the patient's unprocessed, presently collected blood and attached to a 27-gauge needle was used to penetrate the cornea and fill the clefts and corneal edema. The follow-up ended with the resolution of the corneal hydrops. Pre- and postoperative evaluations were meticulously conducted, entailing photographic recording and corneal optical coherence tomography (OCT).

Result: The study evaluated the results of the treatment in 8 eyes, 7 patients. The mean pre-treatment corneal thickness was 1417.50 ± 432 µm (range 796 - 1920 µm). Following treatment, the cornea thickness was 1020 ± 328 µm (range 772 - 1652) at seven days and 762.50 ± 460.44 µm (range 384 - 1853) 30 days post intrastromal injection. There was a significant reduction from pre-op to thirty days after treatment in the cornea thickness of 655.00 ± 527.65 µm ($p = 0.010$). Six of the eight eyes exhibited a reduction in corneal thickness of over 50% within 30 days post-surgery. The median time to resolution was 4.2 weeks. No intraoperative or postoperative complications were associated with this procedure.

Conclusion: This case series demonstrates that intrastromal autologous blood is a promising and viable treatment option for managing corneal hydrops, particularly when traditional approaches have proven ineffective. The treatment is cost-effective and could be used as an alternative to reduce symptoms and improve quality of life while on the cornea waiting list. Furthermore, this series adds to the literature on OCT findings in corneal hydrops and the intrastromal application of autologous blood to address Descemet membrane (DM) rupture in acute corneal hydrops.

Keywords: *Keratoconus; Hydrops; Autologous Blood; Corneal Graft; Corneal Transplantation*

Abbreviations

DM: Descemet Membrane; OCT: Optical Coherence Tomography; KC: Keratoconus; PMD: Pellucid Marginal Degeneration; AC: Anterior Chamber; E-PRP: Eye-Platelet Rich Plasma; VA: Visual Acuity; CDVA: Corrected Distance Visual Acuity; HM: Hand Motion; CF: Counting Fingers; OD: Right Eye; OS: Left Eye

Introduction

Acute corneal hydrops is characterized by sudden corneal edema resulting from a rupture in the stretched Descemet membrane (DM) and endothelium, leading to the influx of aqueous humor from the anterior chamber into the corneal stroma and epithelium. In severe cases, the accumulation of fluid within the corneal stroma may lead to the formation of intrastromal clefts - single or multiple - that can be viewed with imaging techniques like optical coherence tomography (OCT). Ectatic corneal conditions, such as keratoconus (KC), keratoglobus, pellucid marginal degeneration (PMD), and post-refractive surgery ectasia have been linked to the occurrence of hydrops [1,2] and the incidence of hydrops in patients with keratoconus is about 2.8% [3-5] with a higher prevalence in males and individuals in their second and third decades of life [4]. Risk factors for corneal hydrops include advanced disease, eye rubbing, vernal keratoconjunctivitis, and Down syndrome [4-6].

Although corneal hydrops is a self-limiting condition, its signs and symptoms may take up to four months to resolve. Furthermore, chronicity increases the possibility of developing corneal perforation, scarring, infection, and neovascularization, which can raise the risk of graft rejection in future corneal transplantation [5,7,8]. Thus, it is crucial to shorten the duration of inflammation to improve the chances of future grafts. In addition, the COVID pandemic reduced transplantation rates and led to a longer waiting list, even years after the pandemic, and an available graft would take at least 12 months at our location.

Several treatment approaches have been proposed, including the medical, surgical, and expectant methods. Among the surgical treatments, techniques involving intracameral injection of air or expandable gases, with or without corneal suturing, have been extensively studied. However, these procedures are associated with the need for repeated interventions and complications such as pupillary block and increased intraocular pressure related to the gas and air, as well as foreign body sensation and infections from the sutures [2,3,9-11]. Furthermore, all these procedures incur additional costs for surgical materials.

Previous studies have explored the application of blood constituents in the treatment of corneal hydrops. Alio., *et al.* [12] described the use of eye-platelet rich plasma (E-PRP) in the anterior chamber (AC) to treat acute hydrops, proposing mechanisms that involve filling the posterior corneal surface with the blood derivative to create a mechanical barrier against aqueous humor influx, and to stimulate endothelial growth around the DM rupture. Conversely, Regis., *et al.* [13] presented the use of unprocessed blood corneal injections for hydrops treatment, suggesting that blood coagulation could act as a tamponade for the rupture and/or stimulate fibroblastic proliferation, thereby promoting case resolution. Based on these principles, we present a case series involving eyes treated with intrastromal autologous blood injection, without any formulations, as a cost-effective and low-risk procedure for managing DM rupture and corneal edema associated with hydrops.

Materials and Methods

The study was conducted in compliance with the tenets of the Declaration of Helsinki. All patients - or legal guardians in the case of minors - provided written informed consent before the procedure. This study was approved by the Health Research and Ethics Committee of the Hospital de Clinicas de Porto Alegre (CAAE 2023-0010).

This is a retrospective case series of eyes with hydrops due to ectatic corneal disease undergoing corneal intrastromal autologous blood injection. The study's inclusion criteria were patients presenting with acute corneal hydrops to a tertiary hospital, with documented failure of conventional treatment for at least 15 days, from January 2022 to December 2023.

Pre- and post-treatment assessment

All patients underwent slit lamp imaging, and corneal OCT (Cirrus, Carl Zeiss Meditec AG, Germany®). OCT corneal thickness measurements were taken from the epithelium surface to the endothelium through the central cornea. Patients were followed-up weekly for the first month and monthly thereafter.

The data were entered into Excel and exported into SPSS (version 21.0; IBM Corp., Armonk, NY, USA). Independent t-tests were used to compare pre- and post-procedure corneal thickness. The level of statistical significance was set at $p < 0.05$.

Surgical procedure

The injection was performed by an in-training surgeon (J.T.L.P.) supervised by an experienced corneal surgeon (D.M., S.M, or T.L.). Before the procedure, the nursing technician collected a 5 ml blood sample from the patient through peripheral venipuncture and transferred it to a sterile recipient on the surgical table.

The patients were prepared using a sterile technique in the supine position. Topical anesthesia with proxymetacaine hydrochloride eye drops (Anestalcon®, Alcon, Brazil) was used.

The patient's blood was aspirated into a 3-cc syringe attached to a 27-gauge needle. The area with the largest clefts in the cornea was identified under surgical microscope, and a small volume of blood was injected to fill all clefts and stromal edema. Clefts were accessed directly with the 27-gauge needle, and a difference in the stromal resistance indicated that the cleft was reached. There was no blood injection intentionally into the anterior chamber. All patients received a single treatment (Video 1).

Results and Discussion

A total of eight eyes of seven patients were included in this study: seven (87%) keratoconus and one (13%) pellucid marginal cornea degeneration, including two (29%) female and five (71%) male subjects. The mean age was 32 ± 19.89 years (range, 14 - 68 years) (Table 1). No complications were noted during or after intrastromal injection.

The time from onset of symptoms to injection and to resolution is also shown in table 1. The mean time from injection to resolution, including only the eyes that responded to the treatment was 4.71 weeks.

	Age	Sex	Ectatic disorder	Pre CDVA	Onset of symptoms to injection (weeks)	Injection to resolution (weeks)	Onset of symptoms to resolution	30 days Snellen CDVA
Case 1	22	M	KC	HM	2.8	2	4.8	20/50
Case 2	30	F	KC	CF	1.4	4.2	5.6	20/80
Case 3	44	F	KC	CF	2.7	6.4	9.1	20/400
Case 4	49	M	KC	HM	2.5	--	--	HM
Case 5	14	M	KC	CF	10.7	3	13.7	20/100
Case 6	14	M	KC	CF	82.14	4.2	86.3	20/80
Case 7	68	M	MPD	CF	8.5	-	-	CF
Case 8	15	M	KC	HM	2.1	5.8	7.9	20/80

Table 1: Baseline characteristics and timeline from symptom onset to treatment and resolution. *CDVA: Corrected Distance Visual Acuity; HM: Hand Motion; CF: Counting Fingers.*

The mean pre-treatment corneal thickness was 1417.50 ± 432 µm (range, 796 - 1920 µm). Following treatment, the cornea thickness was 1020 ± 328 µm (range 772 - 1652) at seven days and 762.50 ± 460.44 µm (range 384 - 1853) 30 days post intrastromal injection (Chart 1). A paired samples *t*-test was performed to evaluate whether there was a difference between the corneal thickness preoperatively and at different time points after the treatment. There was a significant difference of 325.71 ± 337.55 µm (p = 0.043) seven days after treatment; the difference from preop to fourteen days was 532.85 ± 557.65 µm (p = 0.045), and a significant reduction was observed from preop to thirty days after treatment in the cornea thickness of 655.00 ± 527.65 µm (p = 0.010).

Six of the eight cases demonstrated a substantial reduction of over 50% in corneal pachymetry, as measured by OCT within a 30-day timeframe. Excluding the two outlier cases that did not respond to the treatment (eyes 4 and 7), the mean cornea thickness before treatment was 1437.33 ± 364.75 µm and at 30 days after the injection it was 580.83 ± 140.72, with a significant difference of 856.50 ± 441.32 µm (p= 0.005). See chart 1.

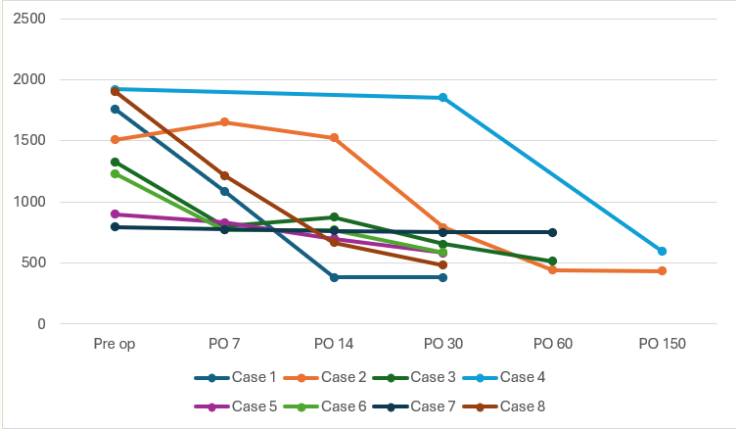


Chart 1: *OCT pachymetry measurement (in µm) before and after injection in eyes 1-8.*

Case 1

A 22-year-old male patient presented with ocular pain in the right eye (OD), reduced visual acuity (VA), photophobia, and tearing. He had a prior diagnosis of keratoconus and a history of hydrops in the contralateral eye. Corrected Distance Visual Acuity (CDVA) was defined as hand motion (HM) in both eyes. Slit lamp anterior segment examination revealed acute hydrops with corneal edema and intrastromal vacuoles in the OD (Figure 1a). Corneal OCT revealed stromal and epithelial edema associated with a large intrastromal cleft (Figure 1b). The patient exhibited resolution of corneal edema 14 days after the procedure (Figure 1c and 1d). The OD CDVA improved to Snellen 20/50 with a scleral contact lens.

Case 2

A 30-year-old female with keratoconus in the OD presented with sudden onset of pain, photophobia, and the presence of a white spot (Figure 2a). VA was measured by counting fingers (CF) at 6.5 feet distance. Anterior segment examination revealed central corneal edema (Figure 2b). Corneal OCT demonstrated stromal edema with clefts and epithelial edema, but evaluation of the DM anatomy was not possible. The patient exhibited resolution of the hydrops after 4 weeks (Figure 2c and 2d). CDVA 30 days after the injection was Snellen 20/80 before contact lens fitting.

Case 3

A 39-year-old female patient with KC and allergic conjunctivitis, presented with severe pain, photophobia, worsened VA (CF at 1-foot distance), and a white spot in the OD. Anterior segment examination revealed acute hydrops (Figure 3a), and OCT imaging revealed significant edema with intrastromal clefts (Figure 3b). Complete resolution of the hydrops was achieved within 45 days of blood injection (Figure 3c and 3d). The patient developed ocular hypertension in the postoperative period, which resolved upon discontinuation of the corticosteroid eye drops. Five months after the onset of hydrops, she underwent penetrating corneal transplantation, and histological analysis revealed revealed the presence of blood residues in the stroma and endothelial cells around the DM rupture (Figure 9). The histological evaluation illustrates the suggested mechanism: the blood is trapped in the clefts and plays a role in closing them. It may last for months.

Case 4

A 49-year-old male with morbid obesity, previously diagnosed with KC, floppy eyelid, and spastic entropion, sought medical attention because of sudden worsening of vision and pain in the OD. Anterior segment examination revealed acute hydrops throughout the cornea (Figure 4a), and OCT imaging revealed significant stromal edema without clefts (Figure 4b). Following the failure of the clinical treatment, an intrastromal injection was performed. However, the patient missed the follow-up visits for 30 days, and upon return, persistent severe corneal edema and entropion were observed. Eyelid surgery was performed to correct the entropion, and follow-up was lost again. Five months after the procedure, the patient showed resolution of the hydrops, but corneal neovascularization has developed (Figure 4c and 4d).

Cases 5 and 6

A 14-year-old male patient with KC in both eyes presented with intense photophobia and reduced visual acuity (CF at1-foot). The patient had been diagnosed with corneal hydrops in the OD 2 years ago and in the OS 3 months prior and remained with signs and signals. Slit-lamp biomicroscopic evaluation revealed edema and deep corneal neovascularization in both the eyes. Corneal OCT revealed stromal edema with a small stromal cleft in the OD and no clefts in the OS (Figure 5a and 5b). Progressive improvement in edema was observed in both eyes after injection (Figure 5c, 5d, 6c and 6d), with improvement in the symptoms throughout the period.

Case 7

A 68-year-old male patient, diagnosed with PMD presented with symptoms of redness, pain, and intolerance to contact lenses in the OS. Slit-lamp biomicroscopy revealed corneal edema in the inferior quadrant (Figure 7a). OCT imaging revealed corneal edema without clefts (Figure 7b). Sixty days after the procedure, there was a slight reduction in corneal thickness on OCT, improvement in epithelial edema (Figure 7c and 7d), and symptomatic relief. However, the stromal edema persisted. An inferior semilunar transplant was performed, and the patient is currently awaiting penetrating keratoplasty.

Case 8

A 15-year-old male patient with advanced keratoconus presented with acute hydrops in the OS (Figure 8a). Corneal OCT showed edema from the limbus to the limbus, with large clefts (Figure 8b). Following intrastromal autologous blood injection, the hydrops resolved 41 days after the procedure (Figure 8c).

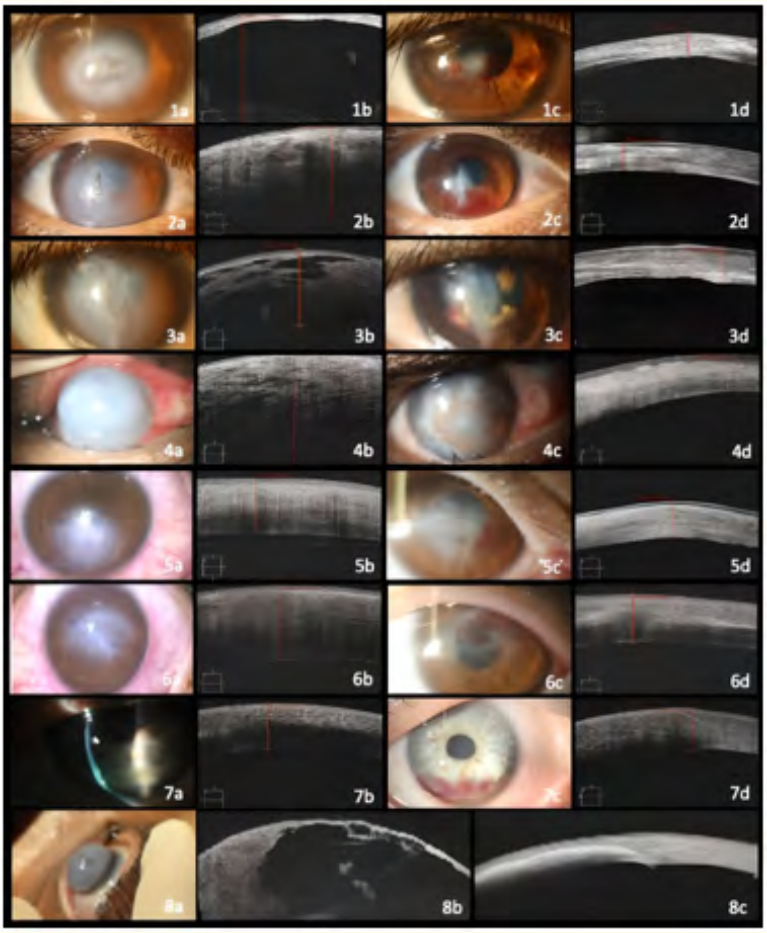


Figure 1-8: *a-b: pre injection slit-lamp biomicroscopy and cornea OCT; c-d: post injection biomicroscopy and cornea OCT. Red line in OCT imaging is measuring from corneal epithelium to corneal endothelium.*

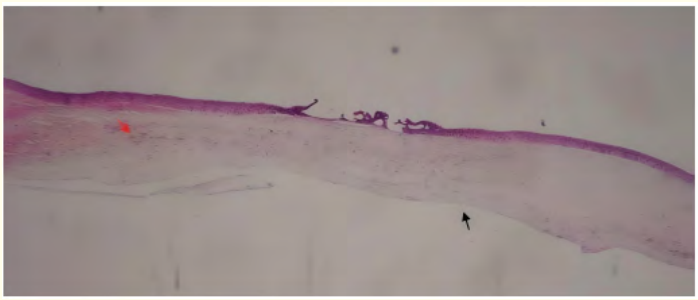
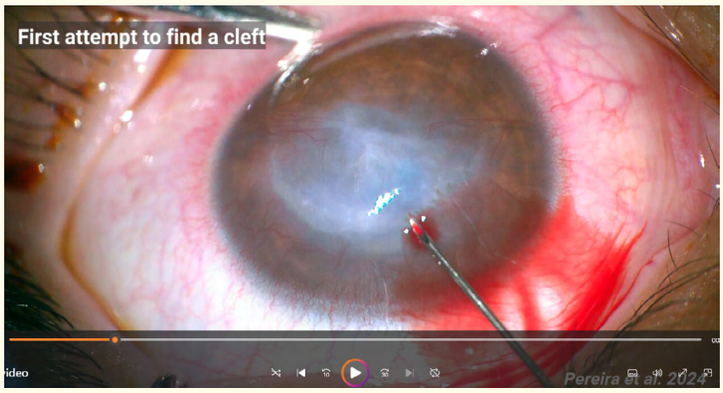


Figure 9: *Histological analysis showing stromal hematic content (red arrow) and endothelial cells at the site of Descemet's membrane rupture (black arrow).*



Acute hydrops is routinely managed with conservative treatment, which results in limited efficacy and an extended healing process. The absence of an effective approach affects patients' visual acuity and overall well-being and elevates the potential for severe complications, such as neovascularization, perforation, and infectious keratitis [5,7,8]. Our article presents a surgical technique involving the intrastromal injection of autologous blood to address the clefts and stromal edema caused by hydrops to expedite the resolution of hydrops in cases unresponsive to initial clinical treatments.

Basu., *et al*. [2] investigated the impact of intracameral octafluoropropane gas (C3F8) on the corneal edema in patients with acute corneal hydrops and found that intracameral C3F8 significantly reduced the duration of edema compared to conservative management (from 5 ± 31 weeks to 9.3 ± 4.5 weeks in the gas group). The researchers used anterior segment optical coherence tomography (AS-OCT) to analyze DM conditions and proposed a two-stage process for corneal hydrops resolution: DM reattachment to the corneal stroma and endothelial cell migration with the formation of a new basement membrane. Vajpayee., *et al.* [14] reported five eyes with large acute hydrops and DM detachment treated with intracameral gas and venting incisions. The rationale is to drain the intraestromal fluid from clefts through venting incisions and eliminate the continuous influx of aqueous humor though reattaching the DM. The shape of the DM detachment and rupture was not elucidated, and it might be an important factor when choosing the treatment. Regular tears on the DM might have better results with blood clot whereas DM scrolls may better respond to anterior chamber gas and active drainage. Nakagawa., *et al*. [4] used ultrasound biomicroscopy to study 13 eyes with acute corneal hydrops. They identified intrastromal clefts and DM breaks in all eyes, suggesting that intrastromal clefts may develop following or concurrently with DM rupture, potentially contributing to severe corneal edema by increasing the surface area exposed to the AC. Furthermore, the presence of a gap between the DM and corneal stroma caused by clefts might delay DM closure and corneal edema resolution.

Based on the proposed pathophysiology of corneal hydrops and its resolution, as well as the presence of growth factors and bioactive proteins in autologous blood [6], it is plausible that the application of fresh, unprocessed blood into stromal clefts may serve as a tamponade for the DM break and its communication with the anterior chamber, while also promoting endothelial cell migration. Therefore, corneas lacking significant stromal clefts may not respond as effectively to this treatment. This hypothesis may help explain the two outlier cases that showed suboptimal response to the blood injection. In Case 4, the eye exhibited diffuse corneal edema without identifiable clefts, and a similar presentation was observed in Case 7. We propose that the absence of stromal clefts may account for the lack of therapeutic response, as these clefts likely represent the primary site of action for blood components. Additionally, poor adherence to follow-up visits in Case 4 may have limited our ability to fully assess the outcome. For Case 7, no other specific explanation beyond the absence of clefts was identified, although it is possible that a baseline condition other than keratoconus contributed to the suboptimal response.

One limitation of the study is the absence of a comparison group. In addition, the study could not thoroughly investigate how the features of DM appear on corneal optical coherence tomography (OCT), which made it harder to understand its connection with the results.

Conclusion

As a final point, it is notable that our study elucidated a favorable outcome through the application of autologous blood, resulting in a significant reduction in the corneal hydrops resolution to an abbreviated span of 1 to 2 months. This procedural approach is underlined by

its inherent simplicity and financial viability, particularly when compared with costly blood preparations or expandable gases. Moreover, this intervention demonstrated the potential to mitigate symptoms and curb the incidence of complications concomitant with corneal hydrops.

We understand that further research with comparative groups is needed to confirm the results of this preliminary case series. Also, the use of intraoperative OCT could have facilitated a more effective approach and evaluation of the clefts.

Acknowledgements

We acknowledge the residents and fellows working in the Department at the time those patients were assessed, who certainly helped us accommodate the patients and surgical procedures. We also acknowledge Prof Lucia Maria Kliemann for the histopathological evaluation of the case 3.

Conflict of Interest

We declare no financial disclosure nor conflict of interest.

Bibliography

1. Fan Gaskin JC., *et al*. "Acute corneal hydrops in keratoconus - new perspectives". *American Journal of Ophthalmology* 157.5 (2014): 921-928.
2. Basu S., *et al*. "Anterior segment optical coherence tomography features of acute corneal hydrops". *Cornea* 31.5 (2012): 479-485.
3. Tuft SJ., *et al*. "Acute corneal hydrops in keratoconus". *Ophthalmology* 101.10 (1994): 1738-1744.
4. Nakagawa T., *et al*. "Ultrasound biomicroscopic examination of acute hydrops in patients with keratoconus". *American Journal of Ophthalmology* 141.6 (2006): 1134-1136.
5. Rubsamen PE and McLeish WM. "Keratoconus with acute hydrops and perforation. Brief case report". *Cornea* 10.1 (1991): 83-84.
6. Higuchi A. "Autologous serum and serum components". *Investigative Ophthalmology and Visual Science* 59.14 (2018): DES121-DES129.
7. Dantas PEC and Nishiwaki-Dantas MC. "Spontaneous bilateral corneal perforation of acute hydrops in keratoconus". *Eye and Contact Lens* 30.1 (2004): 40-41.
8. Donnenfeld ED., *et al*. "Infectious keratitis with corneal perforation associated with corneal hydrops and contact lens wear in keratoconus". *British Journal of Ophthalmology* 80.5 (1996): 409-412.
9. Basu S., *et al*. "Intracameral perfluoropropane gas in the treatment of acute corneal hydrops". *Ophthalmology* 118.5 (2011): 934-939.
10. Rajaraman R., *et al*. "Efficacy and safety of intracameral perfluoropropane (C3F8) tamponade and compression sutures for the management of acute corneal hydrops". *Cornea* 28.3 (2009): 317-320.
11. Daza J., *et al*. "Application of compression sutures with a modified technique for rapid resolution of large (Grade III) hydrops: A prospective interventional study". *Cornea* 44.1 (2024): 20-25.
12. Alio JL., *et al*. "Treatment of severe keratoconus hydrops with intracameral platelet-rich plasma injection". *Cornea* 38.12 (2019): 1595-1598.
13. Regis LM., *et al*. "Hidropsia corneana aguda gigante: relato de um caso tratado com injeção de sangue autólogo/Use of autologous blood as treatment of giant acute hydrops: A case report". *Revista Brasileira de Oftalmologia* (1998).
14. Vajpayee RB., *et al*. "Intrastromal fluid drainage with air tamponade: anterior segment optical coherence tomography guided technique for the management of acute corneal hydrops". *British Journal of Ophthalmology* 97.7 (2013): 834-836.

Volume 16 Issue 4 April 2025