Ophthalmol Ther (2023) 12:377–388
https://doi.org/10.1007/s40123-022-00613-9

ORIGINAL RESEARCH

Intravitreal Fluocinolone Acetonide Implant (FAc, 0.19 mg, ILUVIEN®) in the Treatment of Patients with Recurrent Cystoid Macular Edema After Pars Plana Vitrectomy

Mário Lima-Fontes · Mariana Leuzinger-Dias · Ricardo Barros-Pereira · Vítor Fernandes · Manuel Falcão · Fernando Falcão-Reis · Amândio Rocha-Sousa · Pedro Alves-Faria

Received: September 21, 2022 / Accepted: November 2, 2022 / Published online: November 21, 2022

ABSTRACT

Introduction: Postoperative cystoid macular edema (PCME) is a complication of several ocular procedures, including pars plana vitrectomy (PPV), due to the activation of the inflammatory cascade. The purpose of this case series is to evaluate the effectiveness and safety of fluocinolone acetonide intravitreal implant (FAc, 0.2 μg/day; ILUVIEN®) in the treatment of refractory PCME after successful PPV.

Methods: This retrospective observational case series includes consecutive eyes of patients with recurrent PCME after PPV and treated with a single FAc implant at Centro Hospitalar Universitário de São João, Porto, Portugal. Previous treatments, best-corrected visual acuity (BCVA, ETDRS letters), central macular thickness (CMT, μm), intraocular pressure (IOP, mmHg), and IOP-lowering medication needed were recorded at baseline and during follow-up. Total macular edema resolution was defined as CMT less than 300 μm or a reduction of greater than 20%, and partial macular edema resolution was defined as a reduction of greater than 10%.

Results: Nine eyes from nine patients were included. Before FAc implant, all eyes received intravitreal short-action corticosteroids (triamcinolone and dexamethasone implant), with a good response but relapse 1–5 months later. At baseline, BCVA was 55.0 ± 10.6 letters, CMT was 514.9 ± 165.6 μm, and IOP was 15.4 ± 2.4 mmHg with four eyes under IOP-lowering medication. After FAc implant, all eyes achieved edema resolution (eight total and one partial) with a peak gain of 17.2 letters and a maximum decrease of 208.2 μm in CMT. During follow-up (44.0 ± 14.8 months), 66.7% of the eyes kept their macula dry and three showed recurrence after 11, 14, and 28 months, respectively. The maximum IOP registered was 17.0 ± 6.0 mmHg. IOP-lowering regimen was increased in one eye and two additional eyes started hypotensive drops.

Conclusion: FAc implant can be considered a therapeutic alternative in PCME refractory to other therapies in vitrectomized eyes, reducing the need for repeated treatments.

M. Lima-Fontes (✉) · M. Leuzinger-Dias · R. Barros-Pereira · V. Fernandes · M. Falcão · F. Falcão-Reis · A. Rocha-Sousa · P. Alves-Faria
Department of Ophthalmology, Centro Hospitalar Universitário São João, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal
e-mail: marioruifontes@gmail.com

M. Lima-Fontes
Department of Biomedicine, Faculty of Medicine, University of Porto, Porto, Portugal

M. Falcão · F. Falcão-Reis · A. Rocha-Sousa · P. Alves-Faria
Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Keywords: Fluocinolone acetonide implant; Recurrent cystoid macular edema; Pars plana vitrectomy

Key Summary Points

PCME is a well-known macular complication and a primary cause of reduced vision after several ocular procedures, including PPV.

Persisting cases of PCME present a therapeutic challenge and increase the burden on healthcare systems.

PCME usually responds well to short-acting steroids. However, some eyes show frequent recurrence after treatment.

FAc implant is an effective strategy in refractory PCME, with longer recurrence-free periods after a single injection.

INTRODUCTION

Cystoid macular edema (CME) is a well-known postoperative macular complication and a primary cause of reduced vision after several ocular procedures, including successful cataract and vitreoretinal surgeries [1–3]. Although mostly self-limited, persisting cases present a therapeutic challenge to ophthalmologists and are associated with substantial costs for the healthcare system [4].

The incidence of postoperative CME (PCME) after pars plana vitrectomy (PPV) is not well established and its pathogenesis also remains unclear [5]. It is thought to result from multifactorial changes in the retinal microenvironment, secondary to inflammation, vitreous traction, and light damage [6]. Inflammation plays a key role in the development of PCME, conveyed by increased levels of intraocular prostaglandins, cytokines, and other vasopermeability factors released during surgical trauma. These mediators disrupt the blood-retinal barrier, increasing permeability of the capillaries, and ultimately resulting in perifoveal intraretinal and/or subfoveal fluid accumulation [7–9].

Several risk factors influence the development of PCME. Regarding systemic conditions, diabetes mellitus (DM) and systemic hypertension (HTN) promote the development of PCME even in the absence of previous retinopathy [10, 11].

Preexisting ocular conditions also compromise the integrity of the blood-retinal barrier and boost inflammatory activity, increasing the risk of PCME, such as in patients with a history of uveitis, diabetic retinopathy, retinal vein occlusion, epiretinal membrane (ERM), previous retinal detachment (RD) repair, and topical use of prostaglandin analogues [6]. Vitreomacular traction syndrome (VMT) and ERM can independently contribute to CME formation because of the anteroposterior and tangential tractions on the fovea. Even after surgery to relieve these tractions, CME can persist [12, 13]. Risk factors associated with persistent CME after vitrectomy include the presence of preoperative CME and concurrent or subsequent cataract surgery [13–15].

The introduction of phacoemulsification has led to a significant decrease in pseudophakic CME. Still, surgical complications raise the risk for CME, including posterior capsule rupture, secondary capsulotomy, vitreous loss, vitreous prolapse to the wound, iris incarceration, aphakia, and implantation of an anterior chamber intraocular lens (IOL) [6, 16].

Recurrent PCME is difficult to treat, and several strategies have been employed with varying degrees of success [17]. First-line therapy for PCME typically consists of topical corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs). Second-line therapies typically include intravitreal (IV) anti-vascular endothelial growth factor (VEGF) injections and IV or periocular corticosteroid injections [18]. Intravitreal triamcinolone acetonide (IVTA) and dexamethasone (DEX) implants (Ozurdex, Allergan Inc, Irvine, CA) typically exhibit a 3- to 6-month duration of action [6, 19]. The 0.19-mg fluocinolone acetonide (FAc) IV implant (ILUVIEN; Alimera

Science, Alpharetta, GA) can last up to 3 years [18, 20].

Scarce reports with samples of 1–4 patients described the use of FAc implant in the treatment of PCME in vitrectomized eyes [5, 18, 21, 22].

The purpose of this case series is to evaluate the effectiveness and safety of FAc IV implant in the treatment of refractory CME after successful PPV in our center.

METHODS

This retrospective observational case series evaluates the effectiveness and safety of FAc implant in patients with recurrent PCME after isolated PPV or PPV combined with phacoemulsification, at Centro Hospitalar Universitário São João, Porto, Portugal.

Consecutive eyes of patients with recurrent CME after PPV and treated with an implant of FAc were included.

Demographics, laterality (right eye—OD; left eye—OS), systemic and ocular (pseudoexfolation—PEX; proliferative diabetic retinopathy—PDR; vitreous hemorrhage—VH) comorbidities, surgery characteristics (inner limiting membrane—ILM; C_3F_8—perfluoropropane; SF_6—sulfur hexafluoride), previous treatments, best-corrected visual acuity (BCVA, ETDRS letters), central macular thickness (CMT, μm), intraocular pressure (IOP, mmHg), and IOP-lowering medication needed before FAc implant were recorded at baseline.

The highest BCVA and IOP values and the lowest CMT values registered throughout the study were recorded as well as time to edema recurrence and the need for hypotensive drops.

Baseline and post-FAc implant BCVA, CMT, and IOP were compared.

Total macular edema resolution was defined as CMT less than 300 μm or a reduction of greater than 20%, and partial macular edema resolution was defined as a reduction of greater than 10%.

Statistical analysis was performed using the IBM® SPSS® Statistics software (version 27.0 for Windows; SPSS Inc., Chicago, IL, USA). Variables' normal distribution was verified by skewness, kurtosis, and Kolmogorov–Smirnov test. Parametric or non-parametric tests were used for comparison of variables, according to the data distribution. The level of significance was established at a P value of less than 0.05.

This case series complies with the guidelines for human studies and was conducted ethically in accordance with the tenets of the Declaration of Helsinki. Moreover, it was approved by the local Ethics Committee (project no. 225-22, CHSJ/FMUP). Informed consent was waived because of the retrospective nature of the study and the absence of reported data that can identify individual patients.

RESULTS

Nine eyes from nine patients were included. The mean age was 68.7 ± 10.8 years, and eight patients (88.89%) were female.

The most frequent systemic comorbidities were dyslipidemia (77.89%, n = 7) and diabetes and hypertension (55.56%, n = 5 each). Other systemic conditions are listed in Table 1.

Five eyes (55.56%) had previous phacoemulsification and IOL implantation. There was also history of proliferative diabetic retinopathy treated with laser, retinal detachment submitted to PPV, pseudoexfoliative glaucoma, and iridotomy due to acute angle-closure glaucoma in one eye each.

The causes for PPV in this sample were ERM in six eyes (66.67%), retinal detachment, vitreous hemorrhage with a retinal tear, and dislocated intraocular lens in one eye in the remaining three eyes, respectively (11.11% each).

Four eyes underwent phacoemulsification simultaneously with PPV, while the remaining were already pseudophakic. Table 1 includes a succinct description of each surgery. No intra- or postoperative complications were identified, except for PCME.

Previously to FAc implant, all eyes received IV short-action corticosteroids (IVTA and DEX implant) with CME resolution but with relapse 1–5 months later. Mean IVTA and DEX implants were 1.11 ± 0.60 and 3.11 ± 2.76, respectively.

Table 1 Baseline characteristics of patients treated with FAc implant

Patient	Age (years)	Sex	Eye	Systemic history	Ocular history	Surgical diagnosis	Surgical procedure	Prior IVTA	Prior IV DEX implant	Recurrence of CME after
1	65	F	OD	T2DM; HTN; dyslipidemia; breast cancer	RD (phaco + PPV)	ERM	PPV + ERM and ILM peeling + laser + SF_6 18%	1	3	IVTA 1 month DEX 5 months
2	65	F	OS	–	–	ERM	Phaco + PPV + ERM and ILM peeling + SF_6 25%	1	10	IVTA 3 months DEX 3–6 months
3	58	F	OS	T2DM; coronary disease; asthma; meningioma	PDR (treated with laser); acute angle-closure glaucoma (iridotomy)	ERM	Phaco + PPV + ERM and ILM peeling + SF_6 22%	0	2	DEX 3–5 months
4	67	F	OS	T2DM; HTN; dyslipidemia	–	ERM	Phaco + PPV + ERM and ILM peeling + laser + SF_6 22%	2	2	IVTA 4 months DEX 3 months
5	51	F	OS	T2DM; HTN; dyslipidemia	Phaco	DR	PPV + laser + C_3F_8 14%	1	4	IVTA and DEX 2–3 months
6	72	M	OD	T2DM; asthma; dyslipidemia	–	VH with tear	Phaco + PPV + ERM and ILM peeling + laser + SF_6 26%	1	3	IVTA 1 month DEX 2–3 months
7	74	F	OS	T2DM; HTN; dyslipidemia	Phaco	ERM	PPV + ERM and ILM peeling + laser + SF_6 18%	2	2	IVTA and DEX 3 months

Table 1 continued

Patient	Age (years)	Sex	Eye	Systemic history	Ocular history	Surgical diagnosis	Surgical procedure	Prior IVTA	Prior IV DEX implant	Recurrence of CME after
8	87	F	OD	T2DM; HTN; dyslipidemia	Phaco; PEX glaucoma	Dislocated IOL	PPV + ERM and ILM peeling + angle-supported IOL	1	1	IVTA and DEX 3 months
9	79	F	OS	T2DM; dyslipidemia; CKD	Phaco	ERM	PPV + ERM and ILM peeling + laser + SF_6 22%	1	1	IVTA and DEX 3 months

CKD chronic kidney disease, *CME* cystoid macular edema, *DEX* dexamethasone, *ERM* epiretinal membrane, *F* female, *HTN* systemic hypertension, *ILM* inner limiting membrane, *IOL* intraocular lens, *IVTA* Intravitreal triamcinolone acetonide implant, *M* male, *OD* right eye, *OS* left eye, *PDR* proliferative diabetic retinopathy, *PEX* pseudoexfolation, *PPV* pars plana vitrectomy, *RD* retinal detachment, *T2DM* type 2 diabetes mellitus, *VH* vitreous hemorrhage

At baseline, BCVA was 55.0 ± 10.6 letters and CMT was 514.9 ± 165.6 µm. Table 2 describes individual patient data.

Mean IOP was 15.4 ± 2.4 mmHg with four eyes under IOP-lowering medication (Table 3).

After FAc implant, all eyes achieved edema resolution (eight total and one partial resolution) with a peak gain of 17.2 ± 10.0 letters ($p = 0.001$) and a maximum decrease of 208.2 ± 180.4 µm ($p = 0.009$) in CMT. Figures 1 and 2 illustrate the variation in BCVA and CMT. Detailed data for each patient is represented in Table 2.

During follow-up (44.0 ± 14.8 months), 66.7% of the eyes kept their macula dry and three showed CME recurrence after 11, 14, and 28 months post-FAc implant (patients 9, 1, and 8, respectively).

Maximum IOP registered was 17.0 ± 6.0 mmHg at 9.0 ± 11.2 months after FAc implant ($p = 0.089$, versus baseline). From the four eyes under hypotensive drops at baseline, the IOP-lowering strategy was increased in one and maintained in the remaining during follow-up. The other two eyes started IOP-lowering medication, and three remained without the need for IOP-lowering drops. IOP variation and associated medication can be found in detail in Table 3.

Since all patients were pseudophakic prior to FAc implant, the risk of cataract formation could not be assessed.

Mean follow-up after FAc implant was 44.0 ± 14.8 months.

DISCUSSION

While most cases of PCME resolve spontaneously, an important portion can be difficult to manage and significatively affect visual outcomes of PPV and other ocular procedures. The following sequential management strategy was proposed [6]:

1. Topical NSAIDs × 3–4/day + topical corticosteroids × 4/day
2. Sub-Tenon triamcinolone
3. IV corticosteroids (possibly IV anti-VEGF agents)

Table 2 Functional and anatomical results of patients treated with FAc implant

Patient	OD/OS	Functional results			Anatomical results				Follow-up
		BCVA pre-FAc 0.2 µg/day implant, ETDRS letters	BCVA post-FAc 0.2 µg/day implant, ETDRS letters	Δ BCVA versus baseline, ETDRS letters	CMT pre-FAc 0.2 µg/day implant, µm	CMT post-FAc 0.2 µg/day implant, µm	Δ CMT versus baseline, µm	CME recurrence (months)	Months
1	OD	65	70	5	487	417	− 70	14	34
2	OS	70	80	10	393	290	− 103	NA	22
3	OS	65	70	5	529	264	− 265	NA	62
4	OS	55	70	15	372	243	− 129	NA	60
5	OS	55	70	15	332	254	− 78	NA	56
6	OD	50	85	35	881	241	− 640	NA	52
7	OS	50	70	20	634	332	− 302	NA	30
8	OD	50	75	25	480	333	− 147	28	49
9	OS	35	60	25	526	386	− 140	11	31
Mean ± standard deviation versus baseline		55.0 ± 10.6 letters	72.2 ± 7.1 letters	17.2 ± 10.0 letters	514.9 ± 165.6 µm	306.7 ± 64.3 µm	208.2 ± 180.4 µm	–	44.0 ± 14.8 months

BCVA best-corrected visual acuity, *CME* cystoid macular edema, *CMT* central macular thickness, *ETDRS* Early Treatment Diabetic Retinopathy Study, *FAc* fluocinolone acetonide intravitreal implant, *OD* right eye, *OS* left eye

Table 3 IOP variation and control strategy at baseline and after FAc implant

Patient	OD/OS	Prior IOP medication	Safety results				Follow-up
			IOP pre-FAc 0.2 µg/day implant, mmHg	IOP post-FAc 0.2 µg/day implant, mmHg	Δ IOP versus baseline, mmHg	Need for IOP-lowering medication	Months
1	OD	No	17	25	8	Timolol	34
2	OS	Brinzolamide + brimonidine and timolol + latanoprost	10	10	0	No	22
3	OS	Dorzolamide	14	14	0	No	62
4	OS	No	12	25	13	Timolol	60
5	OS	Timolol + dorzolamide	13	22	9	Timolol and dorzolamide + brimonidine	56
6	OD	No	18	18	0	No	52
7	OS	No	14	14	0	No	30
8	OD	Brinzolamide + brimonidine and timolol	9	9	0	No	49
9	OS	No	16	16	0	No	31
Mean ± standard deviation versus baseline			15.4 ± 2.4 mmHg	17.0 ± 6.0 mmHg	3.3 ± 5.2 mmHg	–	44.0 ± 14.8 months

FAc fluocinolone acetonide intravitreal implant, *IOP* intraocular pressure, *OD* right eye, *OS* left eye

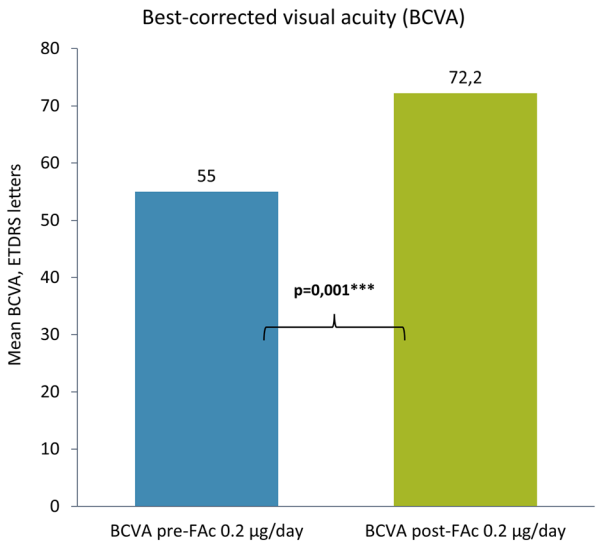

Fig. 1 Mean BCVA at baseline and after intravitreal fluocinolone acetonide (FAc) implant

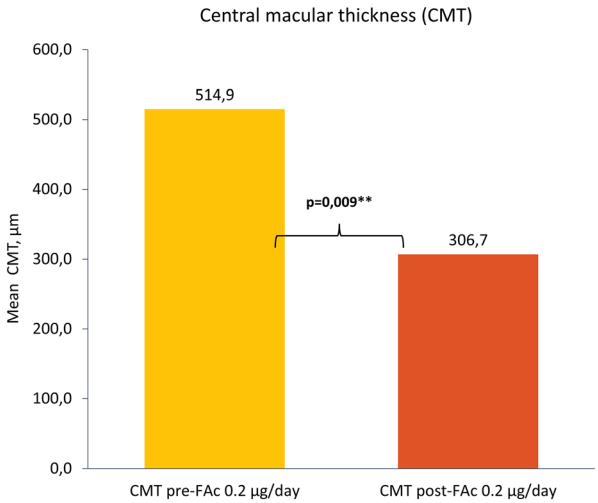

Fig. 2 Mean CMT at baseline and after intravitreal fluocinolone acetonide (FAc) implant

4. Vitreous incarceration → consider surgery
5. Persistent inflammatory reaction → consider IOL removal or vitrectomy

However, drug clearance of topical treatment and IV anti-VEGF agents is faster in vitrectomized eyes, resulting in lower concentrations and limited efficacy [5, 23].

Since inflammation plays a key role in the pathophysiology of PCME, steroids are an important ally in its treatment.

IVTA has been used successfully to treat CME secondary to other conditions, such as retinal vein occlusion, uveitis, and diabetic maculopathy [6]. Small case series have shown high efficacy of IVTA for refractory PCME [24–27].

Dexamethasone is a more potent corticosteroid available as a biocompatible IV implant (Ozurdex®), slowly releasing 0.7 mg over up to 6 months. Small case series and case reports showed good efficacy in the treatment of PCME [28–30].

The use of sustained-release IV implants offers the advantage of a longer-term delivery of the drug. When comparing both IVTA and DEX implants in PCME, their efficacy in improving visual acuity and reducing macular thickness seems to be similar. However, 40% of the eyes treated with IVTA usually need a repeated injection within 6 months and there is usually a more frequent, pronounced, and prolonged rise in IOP after IVTA [31].

Even though DEX implant has a prolonged duration of action when compared to IVTA, 63% of the patients require more than one injection to treat PCME, as reported by the EPISODIC-2 study [32]. In this sense, the FAc IV implant may represent a reasonable option, especially in recurrent CME after IVTA and DEX implant, since its effect may last up to 3 years. FAc implant is currently approved for the treatment of diabetic macular edema and recurrent non-infectious uveitis [20, 33]. The vitreoretinal pharmacokinetic profiles of both DEX and FAc implants do not show significant differences between vitrectomized and non-vitrectomized eyes [34].

In this study, we report nine cases of PCME after isolated PPV combined with phacoemulsification. In two-thirds of the sample, the indication for surgery was the formation of an ERM, which is a known risk factor for the development of PCME [13].

All eyes had been previously treated with IVTA and/or DEX implant with good anatomical responses but with CME relapse after 1–-5 months. A single FAc implant achieved a significant improvement in anatomical and functional outcomes, with a mean maximum decrease of 208 µm in CMT and a mean peak gain of 17.2 letters in BCVA, respectively.

During the follow-up period (44.0 ± 14.8 months), only three eyes showed CME recurrence after 11, 14, and 28 months post-FAc implant (patients 9, 1, and 8, respectively). While these eyes did not reach the ideal 3-year period without CME recurrence, resolution was approximately three to nine times longer than with previous DEX implant (Table 1).

To our knowledge, eight cases of PCME in vitrectomized eyes treated with FAc have been published in the literature [5, 18, 21, 22].

Alfaqawi et al. and Ong et al. published single case reports of patients who developed after PPV to treat vitreomacular interface diseases [18, 21]. CME recurred in both patients after treatment with IVTA and/or DEX implant. FAc implant controlled CME during 20 and 13 months of follow-up, respectively.

In a published case series of 37 patients with postoperative CME following surgical removal of ERM, two of these patients (three eyes) received FAc after multiple DEX implantations. An improvement in CRT and BCVA was observed, with good tolerance and prolonged efficacy over a follow-up period of more than 12 and 24 months, respectively [22].

Miguel-Escuder et al. reported four cases of PCME treated with FAc implant. Only one patient showed a suboptimal response to the treatment [5]. However, this patient underwent ERM peeling and intraocular lens fixation surgery 1 month after FAc implantation, probably causing an increase in inflammation. In this case, CME was managed with additional treatment with DEX implants.

When compared to these isolated case reports, our case series demonstrates longer periods of CME control with a single FAc implant, with only two eyes showing recurrence in the first 2 years.

The most common complications after treatment with steroids are cataract formation and IOP increase. In the FAME studies for the treatment of diabetic macular edema, cataract surgery was performed in 74.9% of patients who were phakic at baseline and incisional glaucoma surgery was performed in 3.7% of 375 patients who received 0.19 mg FAc at 2 years [20]. As in the previously reported cases of CME after PPV [5, 18, 21, 22], all treated eyes in our series were pseudophakic prior to FAc implant, so the risk of cataract formation could not be assessed. Regarding IOP, four eyes were under topical treatment at baseline because of hypertensive response to previous steroid treatment. After the FAc implant, the IOP treatment strategy was increased in one of these patients and two additional patients started treatment with hypotensive drops. IOP remained under control with these regimens and no additional measures were necessary. Maximum IOP measured after FAc implant did not significantly differ from the baseline levels. In the four-case series reported by Miguel-Escuder et al., two patients showed an increase in IOP to 25–26 mmHg after receiving FAc implant and required topical treatment [5].

Our work does present some limitations, namely its retrospective nature, which resulted in varying degrees of patient follow-up and possibly some loss of information. Second, this is a single-center study, invariably limiting the sample size. Third, we included both isolated and combined PPV with phacoemulsification, which may affect the results of the implant. Fourth, IOP was not determined by a single examiner, which can add some variability to the measurement, and the decision to add hypotensive drops was at the discretion of the attending physician. Fifth, the addition of visual fields and retinal fiber layer thickness information would be interesting to understand the effect of the implant and its induced increase in IOP in the optic nerve.

CONCLUSIONS

IV corticosteroid injections are an effective treatment option for recurrent CME after PPV. This case series showed that a single FAc implant not only maintained an anatomical dry macula but also provided visual improvement for longer periods than the previous steroid treatments. These results demonstrate that the FAc implant can be considered a therapeutic alternative in cases of PCME refractory to other therapies in vitrectomized eyes, reducing the burden of repeated treatments with longer

recurrence-free periods after a single injection. Significant IOP increase was observed in one-third of the patients, and it was effectively managed with topical treatment.

ACKNOWLEDGEMENTS

The authors would like to thank the patients involved in this case series.

Funding. The Rapid Service Fees were funded by Alimera Sciences Ltd. No other funding or sponsorship was received for this study or publication of this article.

Authorship Contributions. All authors contributed to the study conception and design. Study design, material preparation, data collection and analysis were performed by Mário Lima-Fontes, Mariana Leuzinger-Dias and Pedro Alves-Faria. The first draft of the manuscript was written by Mário Lima-Fontes, and all authors (Mário Lima-Fontes, Mariana Leuzinger-Dias, Ricardo Barros-Pereira, Vítor Fernandes, Manuel Falcão, Fernando Falcão-Reis, Amândio Rocha-Sousa, Pedro Alves-Faria) commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Disclosures. All authors (Mário Lima-Fontes, Mariana Leuzinger-Dias, Ricardo Barros-Pereira, Vítor Fernandes, Manuel Falcão, Fernando Falcão-Reis, Amândio Rocha-Sousa, Pedro Alves-Faria) declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Compliance with Ethics Guidelines. This case series complies with the guidelines for human studies and was conducted ethically in accordance with the tenets of the Declaration of Helsinki. Moreover, it was approved by the local Ethics Committee of CHUSJ. Informed consent was waived because of the retrospective nature of the study and the absence of reported data that can identify individual patients.

Data Availability. All data generated or analyzed during this study are included in this published article/as supplementary information files.

REFERENCES

1. Gass JD, Norton EW. Fluorescein studies of patients with macular edema and papilledema following cataract extraction. Trans Am Ophthalmol Soc. 1966;64:232–49.

2. Irvine AR. Cystoid maculopathy. Surv Ophthalmol. 1976;21(1):1–17.

3. Shimura M, Yasuda K, Nakazawa T, et al. Panretinal photocoagulation induces pro-inflammatory cytokines and macular thickening in high-risk proliferative diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol. 2009;247(12):1617–24.

4. Schmier JK, Halpern MT, Covert DW, Matthews GP. Evaluation of costs for cystoid macular edema among patients after cataract surgery. Retina. 2007;27(5):621–8.

5. Miguel-Escuder L, Olate-Pérez Á, Sala-Puigdoners A, et al. Intravitreal fluocinolone acetonide implant for the treatment of persistent post-surgical cystoid macular edema in vitrectomized eyes. Eur J Ophthalmol. 2021:11206721211046718.

6. Zur D, Loewenstein A. Postsurgical cystoid macular edema. Dev Ophthalmol. 2017;58:178–90.

7. Miyake K, Ibaraki N. Prostaglandins and cystoid macular edema. Surv Ophthalmol. 2002;47(Suppl 1):S203–18.

8. Rossetti L, Autelitano A. Cystoid macular edema following cataract surgery. Curr Opin Ophthalmol. 2000;11(1):65–72.

9. Ersoy L, Caramoy A, Ristau T, Kirchhof B, Fauser S. Aqueous flare is increased in patients with clinically significant cystoid macular oedema after cataract surgery. Br J Ophthalmol. 2013;97(7):862–5.

10. Pollack A, Leiba H, Bukelman A, Oliver M. Cystoid macular oedema following cataract extraction in patients with diabetes. Br J Ophthalmol. 1992;76(4):221–4.

11. Flach AJ. The incidence, pathogenesis and treatment of cystoid macular edema following cataract surgery. Trans Am Ophthalmol Soc. 1998;96: 557–634.

12. Bottós J, Elizalde J, Arevalo JF, Rodrigues EB, Maia M. Vitreomacular traction syndrome. J Ophthalmic Vis Res. 2012;7(2):148–61.

13. Frisina R, Pinackatt SJ, Sartore M, et al. Cystoid macular edema after pars plana vitrectomy for idiopathic epiretinal membrane. Graefes Arch Clin Exp Ophthalmol. 2015;253(1):47–56.

14. Staudt S, Miller DW, Unnebrink K, Holz FG. Incidence and extent of postoperative macular edema following vitreoretinal surgery with and without combined cataract operation. Ophthalmologe. 2003;100(9):702–7.

15. Mylonas G, Sacu S, Deák G, et al. Macular edema following cataract surgery in eyes with previous 23-gauge vitrectomy and peeling of the internal limiting membrane. Am J Ophthalmol. 2013;155(2):253-9.e2.

16. Cohen SM, Davis A, Cukrowski C. Cystoid macular edema after pars plana vitrectomy for retained lens fragments. J Cataract Refract Surg. 2006;32(9): 1521–6.

17. Daruich A, Matet A, Moulin A, et al. Mechanisms of macular edema: beyond the surface. Prog Retin Eye Res. 2018;63:20–68.

18. Ong SS, Walter SD, Chen X, Thomas AS, Finn AP, Fekrat S. Bilateral intravitreal 0.19-mg fluocinolone acetonide implant for persistent nondiabetic cystoid macular edema after vitrectomy. Retin Cases Brief Rep. 2021;15(3):261–5.

19. Kim SJ, Martin DF, Hubbard GB 3rd, et al. Incidence of postvitrectomy macular edema using optical coherence tomography. Ophthalmology. 2009;116(8):1531–7.

20. Campochiaro PA, Brown DM, Pearson A, et al. Sustained delivery fluocinolone acetonide vitreous inserts provide benefit for at least 3 years in patients with diabetic macular edema. Ophthalmology. 2012;119(10):2125–32.

21. Alfaqawi F, Sarmad A, Ayesh K, Mitra A, Sharma A. Intravitreal fluocinolone acetonide (ILUVIEN) implant for the treatment of refractory cystoid macular oedema after retinal detachment repair. Turk J Ophthalmol. 2018;48(3):155–7.

22. Hattenbach LO, Springer-Wanner C, Hoerauf H, et al. Intravitreal sustained-release steroid implants for the treatment of macular edema following surgical removal of epiretinal membranes. Ophthalmologica. 2017;237(4):232–7.

23. Edington M, Connolly J, Chong NV. Pharmacokinetics of intravitreal anti-VEGF drugs in vitrectomized versus non-vitrectomized eyes. Expert Opin Drug Metab Toxicol. 2017;13(12):1217–24.

24. Conway MD, Canakis C, Livir-Rallatos C, Peyman GA. Intravitreal triamcinolone acetonide for refractory chronic pseudophakic cystoid macular edema. J Cataract Refract Surg. 2003;29(1):27–33.

25. Benhamou N, Massin P, Haouchine B, Audren F, Tadayoni R, Gaudric A. Intravitreal triamcinolone for refractory pseudophakic macular edema. Am J Ophthalmol. 2003;135(2):246–9.

26. Boscia F, Furino C, Dammacco R, Ferreri P, Sborgia L, Sborgia C. Intravitreal triamcinolone acetonide in refractory pseudophakic cystoid macular edema: functional and anatomic results. Eur J Ophthalmol. 2005;15(1):89–95.

27. Koutsandrea C, Moschos MM, Brouzas D, Loukianou E, Apostolopoulos M, Moschos M. Intraocular triamcinolone acetonide for pseudophakic cystoid macular edema: optical coherence tomography and multifocal electroretinography study. Retina. 2007;27(2):159–64.

28. Khurana RN, Palmer JD, Porco TC, Wieland MR. Dexamethasone intravitreal implant for pseudophakic cystoid macular edema in patients with diabetes. Ophthalmic Surg Lasers Imaging Retina. 2015;46(1):56–61.

29. Brynskov T, Laugesen CS, Halborg J, Kemp H, Sørensen TL. Longstanding refractory pseudophakic cystoid macular edema resolved using intravitreal 0.7 mg dexamethasone implants. Clin Ophthalmol. 2013;7:1171–4.

30. Meyer LM, Schönfeld CL. Cystoid macular edema after complicated cataract surgery resolved by an intravitreal dexamethasone 0.7-mg implant. Case Rep Ophthalmol. 2011;2(3):319–22.

31. Dang Y, Mu Y, Li L, et al. Comparison of dexamethasone intravitreal implant and intravitreal triamcinolone acetonide for the treatment of pseudophakic cystoid macular edema in diabetic patients. Drug Des Devel Ther. 2014;8:1441–9.

32. Bellocq D, Pierre-Kahn V, Matonti F, et al. Effectiveness and safety of dexamethasone implants for postsurgical macular oedema including Irvine-Gass syndrome: the EPISODIC-2 study. Br J Ophthalmol. 2017;101(3):333–41.

33. Pavesio C, Heinz C. Non-infectious uveitis affecting the posterior segment treated with fluocinolone acetonide intravitreal implant: 3-year fellow eye analysis. Eye (Lond). 2022;36(6):1231–7.

34. Chang-Lin JE, Burke JA, Peng Q, et al. Pharmacokinetics of a sustained-release dexamethasone intravitreal implant in vitrectomized and nonvitrectomized eyes. Invest Ophthalmol Vis Sci. 2011;52(7):4605–9.