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Research Article

Exploring the Efficacy and Safety of Intravitreal Fluocinolone Acetonide Implant (ILUVIEN®) in the Management of Irvine-Gass Syndrome: Insights from a Retrospective Case Series Analysis

João Alves Ambrósio*, Vítor Miranda, Catarina Aguiar, Raquel Soares, João Chibante Pedro and Miguel Ruão

Ophthalmology Department, Centro Hospitalar de Entre o Douro e Vouga, Santa Maria da Feira, Portugal

***Corresponding Author:** João Alves Ambrósio, Ophthalmology Department, Centro Hospitalar de Entre o Douro e Vouga, Santa Maria da Feira, Portugal.

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Abstract

Introduction: Irvine-Gass Syndrome (IGS), also known as pseudophakic cystoid macular edema (CME), is a postoperative complication that can lead to reduced visual acuity following cataract surgery. While many cases resolve spontaneously, those that persist pose therapeutic challenges. Currently, there is no standardized treatment for recurrent cases. However, clinical evidence and theoretical reasoning support the use of intravitreal corticosteroids. The 0.19-mg sustained-release fluocinolone acetonide (FAc) implant (ILUVIEN®, Alimera Science) is approved for the treatment of chronic diabetic macular edema and the prevention of relapse in non-infectious posterior uveitis. This study aims to evaluate the efficacy and safety of the off-label use of ILUVIEN® in patients with IGS.

Methods: Five eyes from five patients with IGS who underwent FAc implants at Centro Hospitalar de Entre o Douro e Vouga were retrospectively reviewed. Patients were examined at baseline, at months 1, 3, and quarterly thereafter.

Results: Two patients were female, and the mean age was 78.8 ± 11.1 years. Before receiving ILUVIEN®, all eyes received short-term corticosteroid therapies with triamcinolone and/or dexamethasone (3.5 ± 0.5 intravitreal injections). The mean duration of CME before the FAc implant was 1.9 ± 0.9 years. The mean follow-up time after the FAc was 14.4 ± 5.2 months. The study demonstrated significant improvements in anatomical and functional outcomes, with either maintained or reduced central foveal thickness (CFT) and either maintained or improved best-corrected visual acuity (BCVA). The median BCVA at baseline and at the last observation was 0.30 [0.10; 0.65] logMAR, and 0.10 [0.10; 0.10] logMAR, respectively. The median CFT before FAc was 423 [371; 487] µm. At the last observation, it significantly decreased to 262 [282; 305] µm. No significant intraocular pressure (IOP) increase was observed. Two eyes required IOP-lowering medication before the FAc implant and continued it throughout.

Conclusions: In this study, both BCVA and CFT improved from baseline after treatment with FAc in patients with IGS in a routine clinical setting. ILUVIEN® may play a role in eyes with recurrent CME, providing longer recurrence-free periods and reducing the burden of short-acting corticosteroids. In this series, there were no safety concerns regarding the increase in IOP.

Keywords: Cataract Surgery; Irvine–Gass Syndrome; Cystoid Macular Edema; Fluocinolone Acetonide; Intravitreal Implant; Iluvien

Abbreviations

BCVA: Best-Corrected Visual Acuity; CFT: Central Foveal Thickness; CME: Cystoid Macular Edema; DEX: Dexamethasone; ERM: Epiretinal Membrane; F: Female; FAc: Fluocinolone Acetonide; HTN: Systemic Hypertension; IGS: Irvine-Gass Syndrome; IOL: Intraocular Lens; IOP: Intraocular Pressure; IV: Intravitreal; IVTA: Intravitreal Triamcinolone Acetonide; M: Male; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; OD: Right Eye; OS: Left Eye; PEX: Pseudoexfoliation; SD-OCT: Spectral-Domain Optical Coherence Tomography; T2DM: Type 2 Diabetes Mellitus

Introduction

Irvine-Gass Syndrome (IGS), also known as pseudophakic cystoid macular edema (CME), is a well-recognized postoperative complication that can significantly reduce visual acuity following cataract surgery, occurring even after uneventful surgeries [1-3].

The reported incidence of IGS varies widely due to differences in definitions and diagnostic criteria, ranging from 1% to 30%. However, a clinically significant CME incidence of 1% to 2% has been observed in patients without any risk factors [3]. Despite the significant reduction in IGS incidence due to the widespread adoption of phacoemulsification and small incision cataract surgery, it remains a prevalent postoperative morbidity, primarily because cataract surgery is one of the most performed surgical procedures worldwide. Nonetheless, surgical complications elevate the risk of IGS, namely posterior capsule rupture, secondary capsulotomy, vitreous loss, vitreous prolapse into the wound, iris incarceration, aphakia, and the insertion of an anterior chamber intraocular lens [4,5].

Inflammation plays a pivotal role in the development of IGS, triggered by increased levels of intraocular prostaglandins, cytokines, and other vasopermeability factors released as a response to surgical trauma. These mediators disrupt the integrity of the blood-retinal barrier, leading to increased capillary permeability and the accumulation of intraretinal and/or subfoveal fluid in the peri-foveal region [6,7]. Multiple risk factors contribute to the development of IGS, with preexisting ocular conditions and systemic factors adding to the susceptibility of developing pseudophakic CME. This risk is particularly notable in patients with a history of uveitis, diabetic retinopathy, retinal vein occlusion, epiretinal membrane (ERM), retinal detachment, or topical application of prostaglandin analogues [5]. Systemic conditions such as diabetes mellitus and systemic hypertension are also known to facilitate the development of pseudophakic CME, even in the absence of preexisting retinopathy [8].

While most cases resolve on their own, persistent cases pose a therapeutic challenge to ophthalmologists and entail considerable costs for the healthcare system [9]. Various strategies have been employed with varying levels of success [5,10,11]. The primary app.roach to managing IGS usually involves the use of topical corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs). However, topical treatments have limitations, including issues with patient compliance and inadequate diffusion to the posterior segment, and are therefore frequently insufficient in the treatment of chronic postoperative CME [12]. Although there is no standardized treatment for recurrent cases, there is clinical evidence and theoretical rationale to support the use of periocular/intravitreal (IV) corticosteroids in refractory cases [11]. IV triamcinolone acetonide (IVTA) and dexamethasone (DEX) IV implant (Ozurdex®, Allergan Inc., Irvine, CA) are generally associated with a duration of action lasting up to 3 to 6 months [5]. The high peak drug concentrations necessary for the effectiveness of short-acting corticosteroids elevate the risk of local corticosteroid-related adverse effects, such as ocular hypertension, and in phakic individuals, the development of cataracts [13].

The 0.19-mg sustained-release fluocinolone acetonide (FAc) IV implant (ILUVIEN®; Alimera Science, Apharetta, GA) has shown potential benefits for the treatment of various inflammatory eye conditions, being approved for the treatment of chronic diabetic macular edema and the prevention of relapse in non-infectious uveitis affecting the posterior segment of the eye. It has a potential duration of action of up to 3 years [11,14,15]. The development of sustained-delivery IV corticosteroid implants for treating inflammatory disorders in the posterior segment has tackled numerous limitations. This implant provides a stable, low-dose corticosteroid delivery to the posterior segment, reducing inflammatory episodes, treatment frequency and burden, and improving the quality of life for patients [16].

Limited reports, often based on small samples of patients, have documented the off-label use of FAc implants in managing IGS [17,18]. This study aims to assess the efficacy and safety of FAc IV implants in patients with pseudophakic CME at our institution, while providing a comprehensive report on a larger patient sample, enhancing the body of literature on the subject.

Materials and Methods

This retrospective observational case series investigates the utilization of FAc implants in patients with recurrent CME following cataract surgery at Centro Hospitalar de Entre o Douro e Vouga, Santa Maria da Feira, Portugal. We included consecutive eyes of patients with recurrent CME following cataract surgery who underwent FAc implantation. Excluded from the study were patients with secondary causes of CME, such as diabetic retinopathy, retinal vein occlusion, exudative age-related macular degeneration, and clinical uveitis.

All patients underwent comprehensive ophthalmic assessments, which included spectral-domain optical coherence tomography (SD-OCT) scans at baseline, (corresponding to the last visit before FAc implantation) and subsequently at months 1, 3, and then on a quarterly basis.

We documented patient demographic information, ocular comorbidities, prior treatment history, and CME recurrence. The

measured variables consisted of best-corrected visual acuity (BCVA), quantified using standardized Snellen charts and converted to logMAR, central foveal thickness (CFT) within the 1 mm circle centered on the fovea as determined by SD-OCT scans, and safety data, including intraocular pressure (IOP) variations, measured in mmHg with a Goldmann applanation tonometer, and the need for IOP-lowering medication.

Statistical analysis was conducted using IBM® SPSS® Statistics software (version 27.0 for MacOS; SPSS Inc., Chicago, IL, USA). We assessed the normal distribution of variables using skewness, kurtosis, and the Kolmogorov–Smirnov test. Parametric or non-parametric tests were selected for comparing variables based on the data distribution. The level of significance was defined at a *P* value less than 0.05.

This case series adheres to the guidelines for human studies and was conducted ethically in accordance with the principles of the Declaration of Helsinki. Comprehensive information regarding the potential risks and benefits associated with this off-label treatment was provided to all patients included in the study. The decision to undergo treatment was made collectively with active patient involvement. Informed consent was waived due to the retrospective nature of the study and the absence of reported data that could identify individual patients. All cases have been anonymized in this manuscript.

Results and Discussion

Results

A total of five eyes from five patients who had developed CME following cataract surgery and subsequently received IV FAc implants were retrospectively reviewed.

Among these patients, two (40%) were female, and the mean age was 78.8 ± 11.1 (61 – 88) years. Three (60%) of the patients had pseudoexfoliation syndrome (PEX), and two (40%) had diabetes, with none of them having diabetic retinopathy. Additionally, four (80%) patients had systemic hypertension, and three (60%) had dyslipidemia. Further details on systemic conditions can be found in Table 1.

Patient	Age (years)	Sex	Eye	Systemic history	Ocular history	Prior IOP-lowering medication	Prior IVTA	Prior IV DEX implant	Recurrence of CME after	Follow-up after FAc IV implant (months)
1	77	F	OS	T2DM; HTN; dyslipidemia; hyperuricemia; chronic gastritis	-	-	3	0	IVTA 3 - 4 months	6
2	88	M	OS	HTN; dyslipidemia	PEX; inferior subluxation IOL; secondary replacement with anterior chamber lens via scleral tunnel	Timolol and dorzolamide	1	2	IVTA 1 month DEX 3 - 4 months	18
3	88	M	OD	HTN	PEX	-	3	1	IVTA 1 - 3 months DEX 9 months	18
4	61	F	OD	-	-	-	3	1	IVTA 1 -2 months DEX 7 months	18
5	80	M	OD	T2DM; HTN; dyslipidemia	PEX; disinsertion complex IOL-capsular bag; secondary anterior chamber lens implantation; angle-closure glaucoma due to pupillary block following a triamcinolone IV injection; ERM	Timolol and dorzolamide	2	0	IVTA 1 – 2 months	12

CME: cystoid macular edema; DEX: dexamethasone; ERM: epiretinal membrane; F: female; FAc: fluocinolone acetonide; HTN: systemic hypertension; IOL: intraocular lens; IOP: intraocular pressure; IV: intravitreal; IVTA: intravitreal triamcinolone acetonide implant, M: male, OD: right eye, OS: left eye, PEX: pseudoexfolation syndrome, T2DM: type 2 diabetes mellitus

Table 1: Baseline characteristics of patients treated with fluocinolone acetonide intravitreal implant.

In our study, four (80%) patients experienced uneventful cataract surgery procedures, while one (20%) patient faced complications resulting in the disinsertion of the complex intraocular lens (IOL) and capsular bag. This required a secondary anterior chamber lens implantation two months later. In addition, one (20%) eye experienced inferior subluxation of the IOL, leading to lens replacement with an anterior chamber lens through scleral tunnel surgery 11 years later. Notably, this eye developed CME three months after the secondary procedure.

All five eyes were prescribed standard post-operative medications, which included a topical NSAID for four weeks, corticosteroids for four weeks, and antibiotics for two weeks.

Before receiving the FAc IV implant, all eyes had undergone short-term IV corticosteroid therapies with triamcinolone and/or dexamethasone (mean number of injections 3.2 ± 0.7; 2 – 4). All patients presented with recurring CME. The mean duration of CME prior to IV FAc implantation was 1.9 ± 0.9 (1 – 3) years. The mean follow-up period after FAc implantation was 14.4 ± 5.2 (6.0 – 18.0) months. Detailed data for each patient is provided in Table 1.

At baseline, the median BCVA was 0.30 [0.10; 0.65] logMAR. At the last observation, the median BCVA had improved to 0.10 [0.10 ; 0.10] logMAR. Throughout the follow-up period, all eyes either maintained or experienced an improvement in vision, as shown in Figure 1.

The median CFT before FAc treatment was 423 [371; 487] µm.

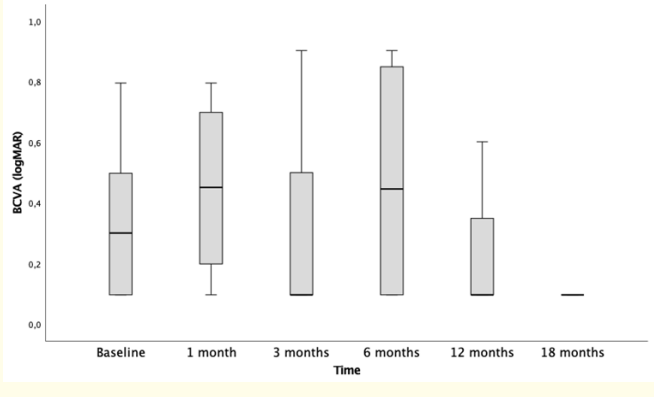

Figure 1: Best-corrected visual acuity (BCVA) evolution.

At the last observation, it had significantly decreased by 161 µm to 262 [282; 305] µm. Over the course of the follow-up, all eyes either maintained or reduced their CFT, as depicted in Figure 2. It is noteworthy that one eye exhibited an increase in CFT at 1 and 3 months compared to the baseline due to the development of an ERM. This patient underwent an IV injection of triamcinolone, resulting in a reduction in CFT from 613 µm at month 6 to 244 µm at month 12.

In terms of IOP, it remained stable during the follow-up period, with a slight reduction observed at the final visit (12 mmHg [10; 16 mmHg] vs. 10 mmHg [10; 15 mmHg), as shown in Figure 3. Initially, two (40%) eyes required IOP-lowering medications (timolol and dorzolamide) before the FAc, and they continued this treatment throughout. In contrast, three eyes did not require IOP-lowering drugs. Within our study cohort, one patient presented a notable case of angle-closure glaucoma due to pupillary block following a triamcinolone IV injection. This condition was effectively managed with a combination of IOP-lowering medications, a miotic agent, and a laser peripheral iridotomy.

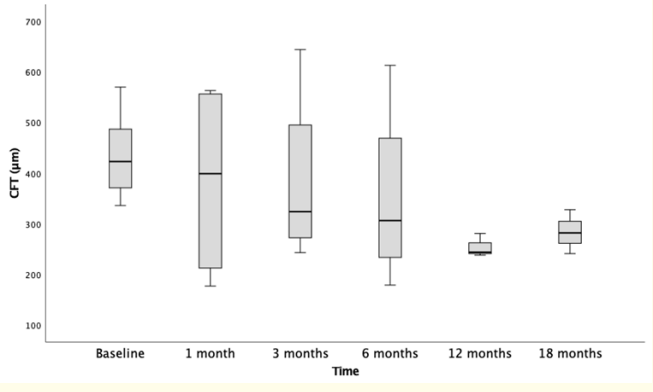

Figure 2: Central foveal thickness (CFT) evolution.

Given that all patients were already pseudophakic before FAc implantation, the assessment of cataract formation risk was not applicable.

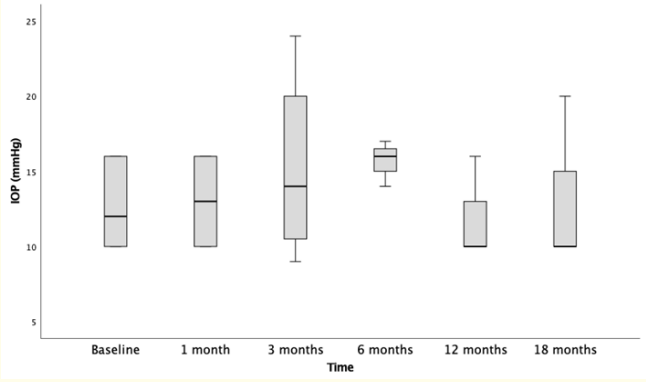

Figure 3: Intraocular pressure (IOP) evolution.

Discussion

Although many cases of IGS resolve spontaneously, a significant proportion poses challenges in management and can have a notable impact on the visual outcomes of cataract surgery. The conventional approach to managing IGS typically involves the use of topical NSAIDs and corticosteroids administered multiple times a day. Sub-Tenon triamcinolone and IV corticosteroids (including IV anti-vascular endothelial growth factor agents) have also been employed, but their success rates vary [5,10,11].

Inflammation plays a pivotal role in the pathophysiology of PCME, making steroids a crucial component of its treatment. Small case series have reported the high efficacy of IVTA in managing refractory CME [19-22]. Additionally, dexamethasone, a potent corticosteroid, is available in the form of a biocompatible IV implant (Ozurdex®, Allergan Inc., Irvine, CA), gradually releasing 0.7 mg over a period of up to 6 months. Limited case series and individual reports have demonstrated its effectiveness in managing refractory CME [23-27].

The use of sustained-release IV implants offers the advantage of extended drug delivery. When comparing the efficacy of IVTA and DEX in IGS, they appear to have similar effects on improving VA and reducing CFT. However, IVTA typically requires repeat injections within 6 months for 40% of treated eyes, and often leads to a more frequent, pronounced, and sustained increase in IOP [28]. Despite the extended duration of action provided by the DEX implant compared to IVTA, approximately 60% of patients require multiple implants to manage CME [27].

A significant limitation of traditional forms of anti-inflammatory treatments for chronic IGS is the need for frequent and repetitive dosing. This not only adds to the financial cost but also places a burden on the patients. While officially approved for addressing chronic diabetic macular edema and preventing relapse in non-infectious posterior uveitis, the off-label use of the 0.19-mg sustained-release FAc IV implant may be a viable option, particularly in cases of recurrent CME after IVTA and DEX implants, as its effects can last for up to 3 years [11,14].

This study presents five cases of IGS following cataract surgery. All the eyes had previously undergone treatment with IVTA and/or DEX implants, resulting in favorable anatomical responses. Nonetheless, CME recurred within 1 to 9 months. The introduction of a single FAc IV implant led to a significant improvement in both anatomical and functional outcomes, with an average reduction of 161 µm in CFT and a mean improvement of 0.20 logMAR in BCVA.

During the follow-up period of 14.4 ± 5.2 (6.0 – 18.0) months, there were no instances of CME recurrence in any of the eyes, except for one case of ERM with the development of vitreomacular traction syndrome (VMT), which was successfully resolved after a single IVTA injection. It's worth noting that both VMT and ERM can independently contribute to CME formation due to the anteroposterior and tangential tractions on the fovea, being well-established risk factors for the development of IGS [29].

To the best of our knowledge, the existing literature consists of reports based on small samples of IGS patients treated with FAc implants [17,18]. In addition to these isolated case reports, our case series provides further evidence of the effectiveness of a single FAc implant in controlling CME, establishing it as a viable option for managing IGS.

Diabetes and systemic hypertension are recognized risk factors for pseudophakic CME, even in the absence of preexisting retinopathy. In our study, 40% of the patients had diabetes, but none of them had diabetic retinopathy, and 80% had systemic hypertension. This underscores the importance of recognizing these systemic factors in the development of pseudophakic CME [3,8].

Regarding IOP, at baseline, two eyes were already receiving topical treatment due to a hypertensive response from prior steroid treatment. Following the FAc implant, IOP remained within the

normal range, and no additional interventions were required. The maximum IOP measured after the FAc implant showed no significant difference from the baseline levels.

While our study provides valuable insights, it does have several limitations. Firstly, its retrospective nature resulted in varying degrees of patient follow-up and the potential loss of some information. Secondly, this is a single-center study, which inherently limit the sample size. Thirdly, IOP measurements were not performed by a single examiner, introducing some variability to the measurements, and the decision to administer hypotensive eye drops was at the discretion of the attending physician.

The volume of published data on the use of FAc IV implant for IGS remains limited, and therefore its use is considered off-label. Further, larger studies are needed to reliably assess the efficacy and safety of the FAc implant in these cases.

Conclusion

In the context of recurrent CME after cataract surgery, IV corticosteroid injections have proven to be effective as a treatment option. This case series highlights that a single FAc implant not only maintained a dry macula anatomically but also provided extended visual improvement when compared to previous steroid treatments in a routine clinical setting. Both the mean BCVA and mean CFT improvements from baseline underscore the potential of the FAc implant as a therapeutic alternative for cases of IGS that are resistant to other treatments. It offers longer recurrence-free periods and reduces the burden of frequent IV short-acting corticosteroid injections. Notably, in this series, there were no safety concerns regarding increased IOP. Further studies with larger sample sizes and longer follow-ups are needed to enhance confidence in the efficacy and safety of the FAc implant in managing IGS.

Conflict of Interest

No financial interest or any conflict of interest exists.

Bibliography

1. L Kodjikian., *et al*. "Management of Irvine-Gass syndrome". *Journal Français d'Ophtalmologie* 40.9 (2017): 788-792.
2. S R Irvine. "A Newly Defined Vitreous Syndrome Following Cataract Surgery*". *American Journal of Ophthalmology* 36.5 (1953): 599-619.
3. A Grzybowski., *et al*. "Pseudophakic cystoid macular edema: update 2016". *Clinical Interventions in Aging* 11 (2016): 1221-1229.
4. SM Cohen., *et al*. "Cystoid macular edema after pars plana vitrectomy for retained lens fragments". *Journal of Cataract and Refractive Surgery* 32.9 (2006): 1521-1526.
5. D Zur and A Loewenstein. "Postsurgical Cystoid Macular Edema". (2017): 178-190.
6. K Miyake and N Ibaraki. "Prostaglandins and Cystoid Macular Edema". *Survey on Ophthalmology* 47 (2002): S203-S218.
7. L Ersoy., *et al*. "Aqueous flare is increased in patients with clinically significant cystoid macular oedema after cataract surgery". *British Journal of Ophthalmology* 97.7 (2013): 862-865.
8. A J Flach. "The incidence, pathogenesis and treatment of cystoid macular edema following cataract surgery". *Transactions of the American Ophthalmological Society* 96 (1998): 557-634.
9. J K SCHMIER., *et al*. "EVALUATION OF COSTS FOR CYSTOID MACULAR EDEMA AMONG PATIENTS AFTER CATARACT SURGERY". *Retina* 27.5 (2007): 621-628.
10. A Daruich,. *et al.* "Mechanisms of macular edema: Beyond the surface". *Progress in Retinal and Eye Research* 63 (2018): 20-68.
11. S S Ong., *et al*. "BILATERAL INTRAVITREAL 0.19-MG FLUOCINOLONE ACETONIDE IMPLANT FOR PERSISTENT NONDIABETIC CYSTOID MACULAR EDEMA AFTER VITRECTOMY". *Retinal Cases and Brief Reports* 15.3 (2021): 261-265.
12. D H Geroski and H F Edelhauser. "Drug delivery for posterior segment eye disease". *Investigative Ophthalmology and Visual Science* 41.5 (2000): 961-964.
13. V Sarao., *et al*. "Intravitreal Steroids for the Treatment of Retinal Diseases". *The Scientific World Journal* 1-14 (2014).
14. P A Campochiaro., *et al*. "Sustained Delivery Fluocinolone Acetonide Vitreous Inserts Provide Benefit for at Least 3 Years in Patients with Diabetic Macular Edema". *Ophthalmology* 119.10 (2012): 2125-2132.

15. D F Kiernan. "Sustained-release Low-dose Fluocinolone Acetonide Intravitreal Implant for Chronic Postoperative Cystoid Macular Edema: Two Case Reports". *Retinal Cases and Brief Reports* (2023).

16. J R de Oliveira Dias., *et al*. "New Drugs and New Posterior Delivery Methods in CME". *Current Ophthalmology Report* 5.2 (2017): 160-168.

17. A Chronopoulos., *et al*. "Intravitreal fluocinolone acetonide implant for chronic postoperative cystoid macular edema - two years results". *European Journal of Ophthalmology* 33.2 (2023): 1054-1060.

18. JH Marques., *et al*. "Fluocinolone Acetonide 0.19 mg Implant in Patients with Cystoid Macular Edema Due To Irvine-Gass Syndrome". *International Medical Case Reports Journal* 14 (2021): 127-132.

19. C KOUTSANDREA., *et al*. "INTRAOCULAR TRIAMCINOLONE ACETONIDE FOR PSEUDOPHAKIC CYSTOID MACULAR EDEMA". *Retina* 27.2 (2007): 159-164.

20. F Boscia., *et al*. "Intravitreal Triamcinolone Acetonide in Refractory Pseudophakic Cystoid Macular Edema: Functional and Anatomic Results". *European Journal of Ophthalmology* 15.1 (2005): 89-95.

21. N Benhamou., *et al*. "Intravitreal triamcinolone for refractory pseudophakic macular edema". *American Journal of Ophthalmology* 135.2 (2003): 246-249.

22. MD Conway., *et al*. "Intravitreal triamcinolone acetonide for refractory chronic pseudophakic cystoid macular edema". *Journal of Cataract and Refractive Surgery* 29.1 (2003): 27-33.

23. LM Meyer and CL Schönfeld. "Cystoid Macular Edema after Complicated Cataract Surgery Resolved by an Intravitreal Dexamethasone 0.7-mg Implant". *Case Reports in Ophthalmology* 2.3 (2011): 319-322.

24. T Brynskov., *et al*. "Longstanding refractory pseudophakic cystoid macular edema resolved using intravitreal 0.7 mg dexamethasone implants". *Clinical Ophthalmology* (2013): 1171.

25. RN Khurana., *et al.* "Dexamethasone Intravitreal Implant for Pseudophakic Cystoid Macular Edema in Patients With Diabetes". *Ophthalmic Surgery, Lasers and Imaging Retina* 46.1 (2015): 56-61.

26. D Bellocq., *et al*. "Effectiveness and safety of dexamethasone implants for post-surgical macular oedema including Irvine-Gass syndrome: the EPISODIC study". *British Journal of Ophthalmology* 99.7 (2015): 979-983.

27. D Bellocq., *et al*. "Effectiveness and safety of dexamethasone implants for postsurgical macular oedema including Irvine-Gass syndrome: the EPISODIC-2 study". *British Journal of Ophthalmology* (2016).

28. Y Dang., *et al.* "Comparison of dexamethasone intravitreal implant and intravitreal triamcinolone acetonide for the treatment of pseudophakic cystoid macular edema in diabetic patients". *Drug Design, Development and Therapy* (2014): 1441.

29. R Frisina., *et al*. "Cystoid macular edema after pars plana vitrectomy for idiopathic epiretinal membrane". *Graefe's Archive for Clinical and Experimental Ophthalmology* 253.1 (2015): 47-56.