

CASE REPORT & REVIEW

Prevention of epiretinal membrane traction progression with topical indomethacin treatment: a case report and mini literature review

Amedeo Lucente¹, Andrea Taloni^{2,3,4}, Federico Fava⁵, Giuseppe Giannaccare⁶

¹Private Practice, Studio Lucente, 87012 Castrovillari, Italy; ²Department of Translational Medicine, University of Ferrara, Ferrara, Italy; ³Department of Ophthalmology, Ospedale Privato 'Villa Igea', Forlì, Italy; ⁴Istituto Internazionale per la Ricerca e Formazione in Oftalmologia (IRFO), Forlì, Italy; ⁵Department of Ophthalmology, University of Catania, Catania, Italy; ⁶Eye Clinic, Department of Surgical Sciences, University of Cagliari, Cagliari, Italy

Abstract

This case report explores the potential of 0.5% indomethacin eye drops (Indo0.5) in preventing the progression of epiretinal membrane traction. A 72-year-old patient with progressive vitreomacular traction was treated with Indo0.5, leading to a significant decrease in intraretinal cyst within 8 months, complete resorption after 16 months and full restoration of the retinal profile after 22 months. A mini literature review highlights the anti-inflammatory effects of indomethacin for various conditions affecting the anterior segment and suggests that the 0.5% concentration may also be effective in managing retinal inflammation. Indo0.5 could be a non-invasive option for

slowing epiretinal membrane traction progression, supporting further research to optimize treatment strategies.

Keywords: epiretinal membrane, inflammation, 0.5% indomethacin eye drops, internal limiting membrane, traction of the epiretinal membrane.

Citation

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Introduction

Pathological cell proliferation on the surface of the internal limiting membrane (ILM) underlies the formation of abnormal tissue at the vitreoretinal interface, leading to the development of epiretinal membranes (ERMs), also known as macular pucker.¹ These membranes can induce traction on the retina, resulting in a range of visual disturbances such as decreased visual acuity, distortion and blurring or shadowing of central vision.² ERMs can develop either spontaneously, without a known cause, in which case they are classified as idiopathic ERMs, or as a result of other conditions such as retinal diseases, eye surgery or trauma. Notably, the presence of vitreomacular traction and intraretinal oedema is often associated with thickening of the ILM.³

With advancing age, the ILM not only increases in thickness but also becomes stiffer, likely due to modifications in its protein composition, including a notable increase

in collagen IV and a decrease in laminin content.⁴ In the context of ERM formation, abnormal posterior vitreous detachment with vitreoschisis contributes to membrane proliferation.⁵⁻⁷ These pathological membranes, which adhere to the retina and incorporate hyalocytes, also attract monocytes from retinal vessels and glial cells, further consolidating the membranes. The traction and contraction associated with macular pucker are primarily attributed to the hyalocytes within these membranes.^{8,9}

Inflammation is a significant factor in ERM pathogenesis, and its modulation may offer therapeutic opportunities in this setting. Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase (COX) enzymes and suppress prostaglandin synthesis, including prostaglandin E₂ (PGE₂), which plays a central role in inflammation. In the eye, prostaglandins contribute to vasodilation, disruption of the blood-ocular barrier and leukocyte migration. By inhibiting COX, NSAIDs modulate inflammation and have demonstrated efficacy in treating retinal

diseases such as diabetic retinopathy^{10–14} and age-related macular degeneration.^{15–18} Furthermore, increasing evidence highlights the significant role of COX2 in retinal diseases, underscoring the therapeutic potential of targeting this pathway.¹⁹

Topical NSAIDs are commonly used after cataract surgery to prevent cystoid macular oedema and manage inflammation. Indomethacin, a non-selective COX2 inhibitor, was first shown to lower the incidence and severity of cystoid macular oedema by preventing blood–retinal barrier breakdown caused by prostaglandin release.²⁰ More recent studies have further supported the role of indomethacin in effectively decreasing vitreous PGE₂ levels in patients undergoing vitrectomy for macular pucker.^{21,22} These findings highlight the potential role of NSAIDs, including 0.5% indomethacin, 0.1% nepafenac, 0.09% bromfenac and 0.1% diclofenac, in managing posterior segment inflammation and provide valuable insights into their evolving clinical applications.

This article presents a case report illustrating changes in the vitreoretinal interface, particularly the formation of ERMs from the ILM, and explores the potential benefits of using 0.5% indomethacin eye drops. Additionally, a mini literature review highlights the clinical studies conducted so far on the use of topical indomethacin in treating various ocular conditions.

Methods

This is a retrospective case report describing the outcomes of a patient treated with single-dose vial eye drops containing an ophthalmic suspension with 0.5% indomethacin and hydroxypropylmethylcellulose (HPMC; INDOM 0.5%, Alfa-Intes, Italy), hereafter referred to as Indo0.5. The patient's data are presented anonymously, with no identifiable details provided, ensuring that the patient's identity cannot be determined in any way. Additionally, a mini review of the literature was conducted to examine clinical studies specifically evaluating the efficacy of indomethacin in treating various ocular conditions. A bibliographic search was performed on PubMed using the following keywords: 'Indomethacin' AND 'eye drops' AND 'clinical trials', limited to English-language articles published between 1 January 2000 and 6 January 2025. Studies were included if they were clinical studies assessing the efficacy of indomethacin eye drops in adults. Studies not focused on the topical use of indomethacin, as well as systematic reviews and meta-analyses, were excluded. Data were extracted focusing on key efficacy outcomes, and studies were synthesized narratively.

Case report

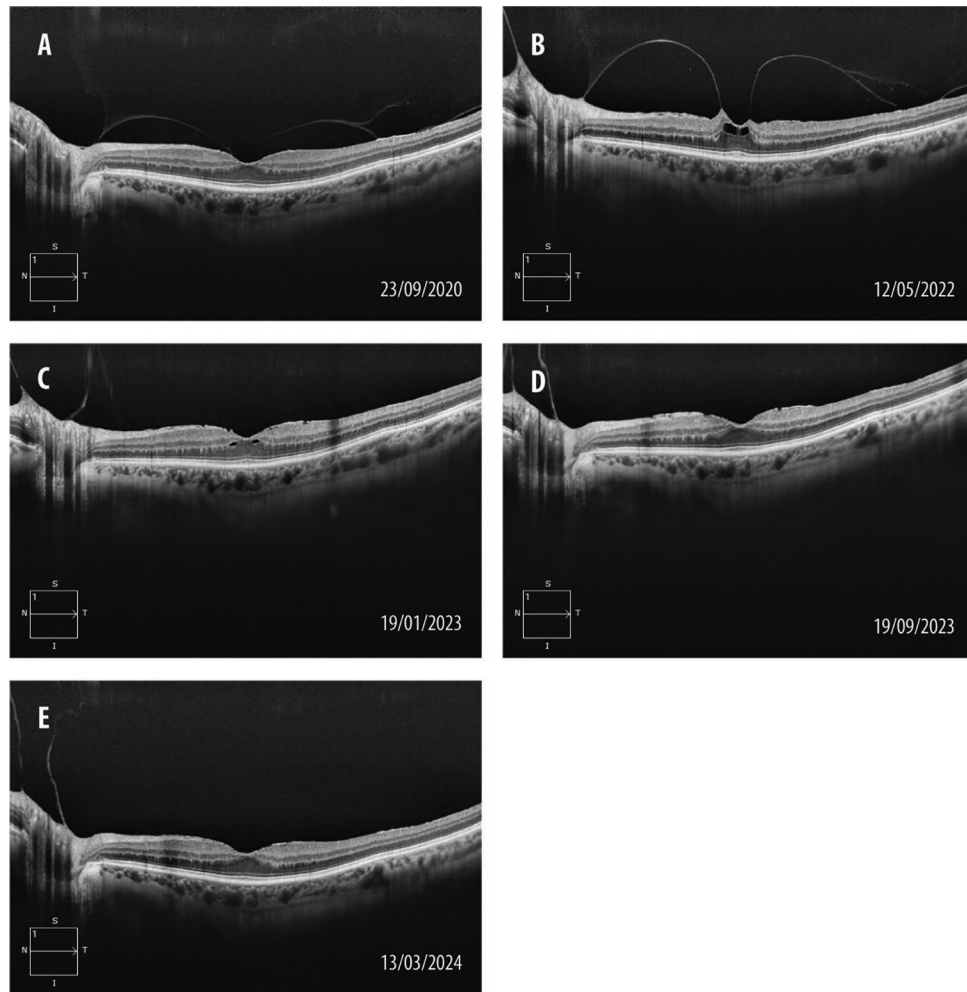
A 72-year-old woman with no significant systemic diseases and no history of diabetes was followed with serial ophthalmic evaluations for several years. A complete eye exam was conducted during follow-up visits, which included visual acuity assessment using the Snellen test, Amsler grid test, Ishihara test, Worth four-dot test, Goldmann tonometry, endothelial cell count using a Topcon SP-3000P™ specular microscope, Schirmer test, tear break-up time, widefield fundus photography with the Zeiss Clarus 500, and optical coherence tomography angiography with the Zeiss Angioplex 6000.

During a routine visit, an ERM was detected in the left eye. The membrane was highlighted by a 12-mm HD 1-Line B-Scan (100x). An incomplete vitreous detachment was observed, with retinal attachments at the foveal clivus, a few millimetres from the foveal area, symmetric and without retinal traction. Snellen visual acuity was 8/10 in both eyes due to the presence of early lens opacities. Macular thickness was 285 µm in the right eye and 295 µm in the left eye. No pharmacological treatment was given at this stage (Figure 1A).

At the next check-up visit, vitreomacular traction was observed at the same points where, 20 months earlier, mild, non-threatening adhesions of the hyaloid membrane to the ERM had been noted. In the macular cube 512x128 scan, central millimetre volumes were 285 µm in the right eye and 373 µm in the left eye. At this stage, intraretinal cavities developed at the foveal site, resulting in partial loss of the foveal pit. Visual acuity in the left eye decreased to 7/10, whilst the Amsler test remained unchanged from the initial assessment (Figure 1B).

The patient was prescribed topical Indo0.5 in single-dose vials to be administered twice daily for the first 60 days, then once daily without interruption (including in the healthy right eye) until the last observation on 13 March 2024. The chosen dosing strategy can be considered 'soft' as it follows a gradual, sustained approach with a lower administration frequency over time. This regimen allows for long-term management of the chronic inflammatory condition whilst minimizing the risk of adverse effects associated with higher dosing frequencies.

Eight months after Indo0.5 treatment, the intraretinal cysts had significantly decreased; however, occasional hyperreflectivity of the ILM persisted without any associated traction (Figure 1C). In the macular cube 512 × 128 scan, central millimetre volumes were 285 µm in the right

Figure 1. Optical coherence tomography scans.

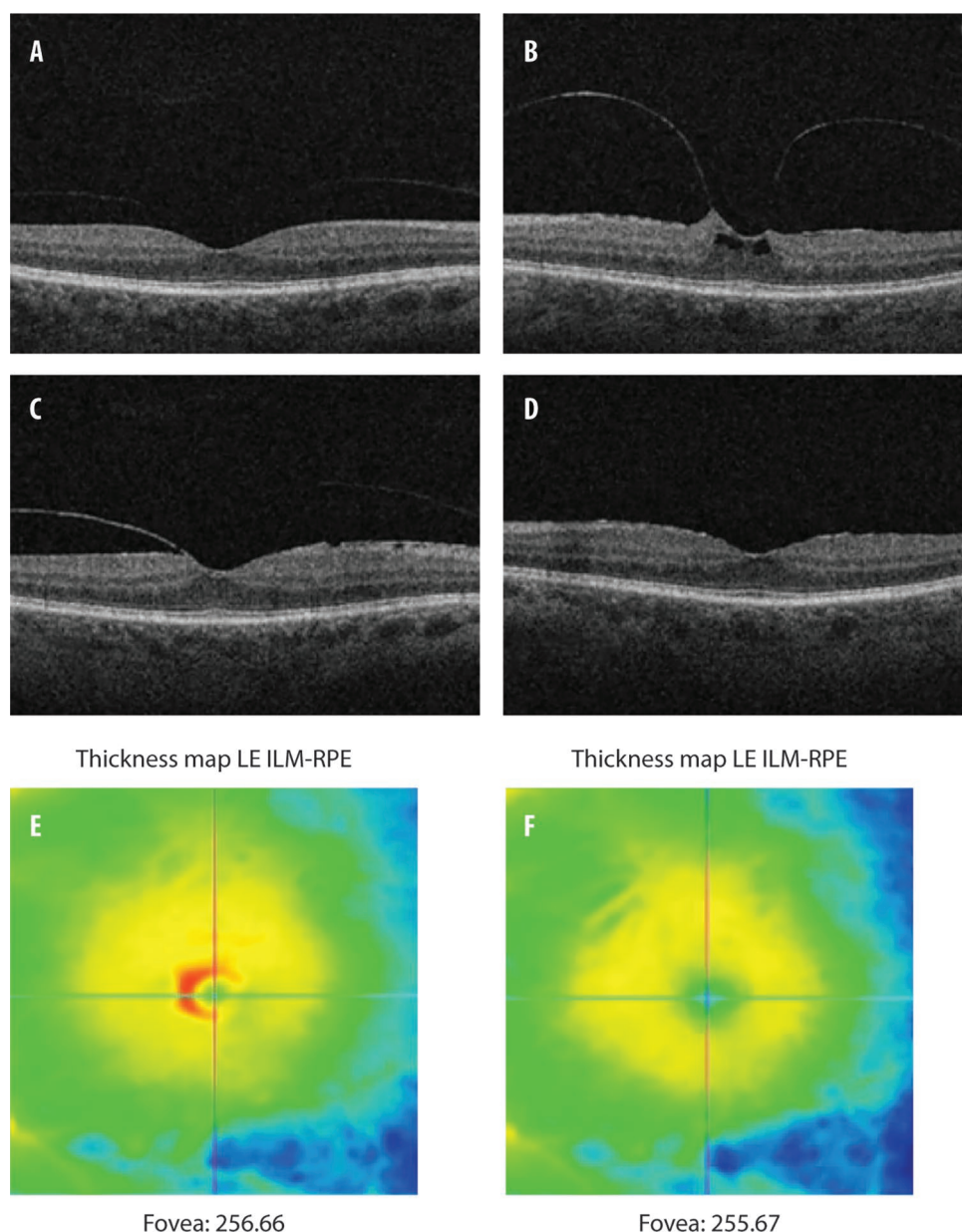
Optical coherence tomography scans obtained (A) during a routine visit, showing incomplete vitreous detachment with retinal attachments at the foveal clivus, located a few millimetres from the fovea in the left eye; (B) during a check-up visit, showing clear vitreous traction in the left eye, with intraretinal cavities observed in the foveal region and partial loss of the foveal pit; (C) after 8 months of 0.5% indomethacin eye drop treatment, showing a significant reduction in the intraretinal cysts in the left eye, with no evidence of traction; (D) after 16 months of 0.5% indomethacin eye drop treatment, confirming the complete disappearance of intraretinal cysts in the left eye; and (E) 22 months after the onset of traction, showing that the retinal profile in the left eye has nearly returned to normal. Reproduced with permission from Ref.³⁹

eye and 321 μm in the left eye. By month 16, the intraretinal cysts had completely resorbed (Figure 1D). Central millimetre volumes in the Macular Cube 512 \times 128 scan measured 355 μm in the right eye and 318 μm in the left eye.

Twenty-two months after the onset of the traction process, the retinal profile in the left eye had nearly returned to normal, though discontinuous ILM hyper-reflectivity persisted. Visual acuity had recovered to baseline levels (Figure 1E). In the right eye, initial traction

was noted in the foveal area, along with ILM thickening suggestive of early ERM formation; however, no subjective symptoms or visual acuity loss were reported. The lens opacities remained unchanged in both eyes, and visual acuity was 7–8/10. In the Macular Cube 512 \times 128 scan, the central millimetre volumes were 339 μm in the right eye and 313 μm in the left eye.

Figure 2 presents side-by-side optical coherence tomography images of both eyes at the onset of the traction process (in the left eye) and 22 months later.

Figure 2. Optical coherence tomography and macular cube scans of the eyes.

Optical coherence tomography scans of the right eye (A, C) and of the left eye (B, D) at the initiation of 0.5% indomethacin eye drop treatment (A, B) and 22 months later (C, D), showing initial traction in the foveal area and thickening of the internal limiting membrane (ILM), consistent with an epiretinal membrane in the right eye (C). (E, F) Macular cube scans of the left eye (LE) at the start of 0.5% indomethacin eye drop treatment (E) and 22 months later (F). RPE, retinal pigment epithelium. Reproduced with permission from Ref.³⁹

Additionally, the Macular Cube scans of the left eye at both time points are shown.

The Schirmer test, tear break-up time and endothelial cell count using specular microscopy showed no significant changes over time compared to baseline measurements or follow-up assessments. The patient reported no side-effects related to the prescribed eye drops and showed good tolerability.

Mini literature review

A summary of representative studies across various clinical conditions is presented in Table 1.

Most of the reviewed clinical trials focused on the use of 0.1% indomethacin eye drops, either alone^{23–27} or in combination with other treatments, such as gentamicin eye

drops,²⁸ or administered before intravitreal injections (IVIs) of bevacizumab, ranibizumab or aflibercept.²⁹ These studies have shown that 0.1% indomethacin is effective in several indications. When combined with gentamicin, it reduces pain and discomfort associated with traumatic corneal abrasion compared to gentamicin alone.²⁸ It was also found to reduce sub-clinical conjunctival inflammation before filtering surgery more effectively than fluorometholone.²³ In the context of cataract surgery, 0.1% indomethacin reduced postoperative ocular inflammation compared to 0.5% ketorolac²⁵ and was effective in preventing inflammation even when compared to 0.1% dexamethasone.²⁶ Additionally, it was shown to reduce pain after laser sub-epithelial keratomileusis treatment when compared to 0.1% fluorometholone.²⁷ A study by Toker et al.²⁴ reported that 0.1% indomethacin, similar to 0.5% ketorolac, was more effective than artificial tears in reducing conjunctival hyperaemia in patients with measles during the first 2 weeks of infection. However, neither treatment alleviated burning sensations, foreign body sensations or photophobia. Additionally, Sakallioğlu et al. found that, whilst 0.1% indomethacin administered before IVIs did not significantly reduce pain immediately afterwards, it significantly lowered visual analogue scale scores 6 hours post-administration.²⁹

Other clinical trials specifically examined the use of 0.5% indomethacin eye drops. Allegri et al. conducted a randomized, double-blind, placebo-controlled clinical trial to assess the efficacy and tolerability of Indo0.5 (administered four times daily over a 6-month treatment period) in patients with macular oedema due to various aetiologies of uveitis.³⁰ The study found that Indo0.5 significantly reduced macular oedema at the 6-month follow-up compared to placebo. However, vitreoretinal traction prevented the complete resolution of ME in some patients. Russo et al. conducted a prospective pilot study on patients with new-onset choroidal neovascularization (CNV), where participants were randomized to receive either intravitreal ranibizumab (IVR) injections alone or in combination with Indo0.5.³¹ All patients received monthly 0.5 mg IVR injections for 3 months, followed by additional monthly injections as needed. Patients in the indomethacin group also self-administered one drop of Indo0.5 three times daily for 12 months. At 12 months, both groups showed significant improvement in best-corrected visual acuity and central retinal thickness but the indomethacin group exhibited more pronounced benefits and required fewer IVR injections. The absence of treatment-related serious adverse events, along with the demonstrated safety and tolerability of the treatments throughout the 12-month period and high compliance with eye drop use, provides strong evidence supporting the overall safety and tolerability profile of Indo0.5.

Studies have evaluated the effects of topical NSAID administration, including 0.5% indomethacin, on vitreous PGE₂ levels in patients undergoing vitrectomy. One study found that treating patients with NSAIDs (three times daily for 7 days) before surgery reduced vitreous PGE₂ levels, particularly with 0.5% indomethacin, 0.09% bromfenac and 0.1% nepafenac.²¹ A more recent study indicated that 0.5% indomethacin and 0.09% bromfenac were more effective in reducing PGE₂ levels compared to 0.1% diclofenac and 0.3% nepafenac, with diclofenac associated with higher PGE₂ concentrations.²²

Discussion

We presented a clinical case detailing the evolution and management of ERM in an older patient using Indo0.5. No evident signs of progression in the traction process were observed. Significant reduction in intraretinal cysts was observed after 8 months of Indo0.5 treatment, with full resorption after 16 months and complete restoration of the retinal profile 22 months after the onset of traction. The therapy was also administered to the contralateral eye as a preventive measure. After several months of follow-up, a mild membrane appeared in the contralateral eye, initially showing traction but without functional consequences. These observations suggest that Indo0.5 may effectively prevent the progression of ERM-related traction, particularly in older patients, where early intervention can play a key role in slowing or halting the development of tractional complications that could result in significant visual acuity impairment, potentially requiring surgical intervention. In cases where traction from an ERM causes significant visual impairment or structural changes in the retina, surgical intervention, such as vitrectomy, is often necessary to directly remove the ERM and relieve the traction. However, in some cases, traction may spontaneously resolve over time. The resolution of traction can be monitored using imaging techniques, such as optical coherence tomography, which allows for the assessment of changes in traction and its eventual disappearance.³² Generally, spontaneous resolution occurs more frequently in individuals without other systemic conditions and when the vitreous detachment, through incomplete, does not lead to significant persistent adhesions within the vascular arcades.^{33,34}

NSAIDs are used to reduce retinal inflammation and control macular oedema. By addressing the inflammatory component, they can help decrease retinal oedema, which may, in turn, reduce the mechanical stress or traction on the retina caused by the ERM. Sub-Tenon's corticosteroid injections also manage inflammation and macular oedema but work through a different mechanism and are typically reserved for more severe cases

Table 1. Summary of clinical trials evaluating the efficacy of indomethacin eye drops in various clinical conditions.						
Reference	Study type	Medical condition	Groups	Treatment duration	Follow-up	Outcomes
Alberti 2001 ²⁸	Multicentre, randomized, double-masked	Traumatic corneal abrasion	Indomethacin 0.1% + gentamicin 300,000 IU/100 mL (group 1, n=62) versus gentamicin 300,000 IU/100 mL alone (group 2, n=61)	Four times daily for 5–6 days	5–6 days	Group 1 demonstrated greater pain reduction, better overall pain relief and a more significant decrease in ophthalmic symptoms than group 2
Baudouin 2002 ²³	Prospective, randomized, multicentre	Conjunctival inflammation following chronic application of antiglaucomatous drugs	Indomethacin 0.1% (n=46) versus fluorometholone 0.1% (n=43)	One drop, four times daily, for 1 month before filtering surgery	30 days	A significant reduction in sub-clinical conjunctival inflammation was observed after 1 month of treatment with 0.1% indomethacin prior to filtering surgery
Toker 2006 ²⁴	Prospective, double-masked, placebo-controlled, randomized	Measles-associated conjunctivitis	In the right eye: ketorolac 0.5% (n=31) versus indomethacin 0.1% (n=31). In the left eye: artificial tears	One drop in each eye, four times a day, for 2 weeks	14 days	Ketorolac and indomethacin were more effective than artificial tears in reducing conjunctival hyperaemia but had no effect on burning sensations, foreign-body sensations or photophobia
Weber 2013 ²⁵	Prospective, multicentre, investigator-masked, parallel-group, randomized, active-controlled	Ocular inflammation following cataract surgery	Indomethacin 0.1% (n=59) versus ketorolac 0.5% (n=62)	QID for 3 weeks, starting 24 hours before surgery	90 days	On day 1, 0.1% indomethacin was at least as effective as 0.5% ketorolac in treating ocular inflammation and was more effective by day 7. Additionally, indomethacin was better tolerated than ketorolac
Allegri 2014 ³⁰	Randomized, double-blind, placebo-controlled	Uveitic macular oedema	Indomethacin 0.5% (Indo0.5, n=16) versus placebo (vehicle of Indo0.5, n=15)	Four times per day for 6 months	6 months	The administration of 0.5% indomethacin resulted in a significant reduction in macular oedema at the 6-month follow-up, compared to placebo, in most patients
Russo 2016 ²¹	Prospective, investigator-masked, randomized	Vitrectomy for macular pucker	Indomethacin 0.5% (n=16), or bromfenac 0.09% (n=16), or nepafenac 0.1% (n=16), or placebo (n=16)	Three times per day for 7 days before surgery	7 days before surgery	All NSAIDs penetrated the vitreous and reduced basal PGE ₂ levels, with greater penetration in pseudophakic eyes than in phakic eyes. The indomethacin group showed the greatest PGE ₂ reduction, though differences were not significant compared to the bromfenac and nepafenac groups

(Continued)

Table 1. (Continued)

Reference	Study type	Medical condition	Groups	Treatment duration	Follow-up	Outcomes
Russo 2018 ³¹	Randomized, prospective pilot study	Neovascular age-related macular degeneration	Ranibizumab group versus ranibizumab + indomethacin group	All patients: monthly 0.5 mg intravitreal ranibizumab injections for 3 months, followed by as-needed monthly injections. Ranibizumab + indomethacin group: additionally, 0.5% indomethacin eye drops three times daily	12 months	At 12 months, both groups showed significant improvements in best-corrected visual acuity and central retinal thickness, with greater changes in the ranibizumab + indomethacin group. Indomethacin also significantly reduced the number of intravitreal ranibizumab injections
Pastore 2020 ²²	Prospective, randomized, investigator-masked	Pars plana vitrectomy for idiopathic epiretinal membrane or full-thickness macular hole	Diclofenac 0.1% (n=20), or indomethacin 0.5% (n=22), or nepafenac 0.3% (n=21), or bromfenac 0.09% (n=21), or placebo (n=20)	Diclofenac 0.1%; four times a day; indomethacin 0.5%; three times a day; nepafenac 0.3%; once a day; bromfenac 0.09%; twice a day. Placebo (hyaluronic acid 0.2% lubricating eyedrops): twice a day. All treatments: 3 days before surgery; 1 hour prior to surgery; a single drop of the assigned treatment	3 days before surgery	All NSAIDs reduced basal vitreous PGE ₂ levels compared to placebo, but the diclofenac group had significantly higher PGE ₂ levels than the other NSAIDs. Indomethacin and bromfenac led to greater PGE ₂ reductions than nepafenac. Pseudophakic eyes had significantly higher drug bioavailability and lower PGE ₂ levels than phakic eyes
Sakallioğlu 2024 ²⁹	Single-centre, cross-sectional, placebo and randomized-controlled, double-blinded, comparative case series	Patients receiving intravitreal injections for any indication	Nepafenac 0.1% (n=73), or nepafenac 0.3% (n=73), or ketorolac trometamol 0.5% (n=76), or diclofenac 0.1% (n=76), or flurbiprofen 0.03% (n=75), or indomethacin 0.1% (n=71), or bromfenac 0.09% (n=74), or pranoprofen 0.1% (n=70), or control (n=74) + IVIs of bevacizumab or ranibizumab or aflibercept	NSAIDs were applied 30–45 minutes before each IVI	VAS immediately after and 6 hours following the IVI	Nepafenac 0.3%, nepafenac 0.1% and bromfenac had the lowest VAS scores both immediately and after 6 hours, with no significant differences between them. Diclofenac and ketorolac had higher scores than the first group but lower than the control group. Flurbiprofen, pranoprofen and indomethacin did not significantly reduce pain immediately but had significantly lower scores at the 6-hour mark

IVI, intravitreal injection; NSAIDs, non-steroidal anti-inflammatory drugs; PGE₂, prostaglandin E₂; VAS, Visual Analogue Scale.

of inflammation.³⁵ NSAIDs, in the form of eye drops, are generally preferred due to their ease of use, non-invasive nature and lower risk of complications, making them more patient-friendly compared to sub-Tenon's corticosteroid injections, which are more invasive and associated with a higher risk of side-effects, particularly in individuals with systemic conditions such as diabetes or hypertension.^{36,37}

A study conducted by Allegri et al. reported that 7 out of 46 eyes treated with Indo0.5 four times daily did not achieve complete resolution of macular oedema due to vitreoretinal traction.³⁰ Whilst the 0.5% indomethacin formulation used in that study was the same as in the case report presented here, the findings highlight the importance of considering both the dosage regimen and the treatment duration in future studies to optimize therapeutic outcomes.

Furthermore, we provide an overview of clinical studies conducted with indomethacin eye drops. Whilst the dosage, follow-up duration and ocular conditions vary across studies, all have shown that indomethacin is well tolerated. Most studies have established the safety and efficacy of 0.1% indomethacin for treating anterior segment inflammation, whilst only a few have evaluated the more concentrated 0.5% formulation. This higher-dose suspension is indicated for treating inflammatory conditions of the anterior segment and inflammation following cataract surgery but it also appears to be effective for inflammatory conditions involving the vitreous and retina, as supported by the pharmacokinetic data. Bucolo et al.⁹ evaluated the ocular pharmacokinetics of two different indomethacin formulations (ophthalmic solution containing 0.1% indomethacin + hydroxypropyl- β -cyclodextrin (IND-CD) versus ophthalmic suspension containing 0.5% indomethacin + HPMC (IND-HPMC)) in rabbit eyes. The study found that 0.5% indomethacin exhibited better ocular distribution and higher drug concentrations in the posterior pole of the eye, making it more effective for managing retinal inflammatory conditions than the 0.1% formulation. The peak concentrations of indomethacin in the vitreous were achieved within 60 minutes after a single instillation of IND-CD and 30 minutes after IND-HPMC. The IND-HPMC formulation resulted in higher drug levels in the vitreous compared to IND-CD, with an AUC_{0-240} of 53.8 ng/mL per min for IND-HPMC versus 12.5 ng/mL per min for IND-CD. The maximum concentration in the vitreous was also significantly higher for IND-HPMC (31 ng/mL) compared to IND-CD (6.37 ng/mL). This difference is likely due to variations in drug concentration and the use of different vehicle formulations.⁹ HPMC is a viscosity enhancer that reduces surface tension, prolongs corneal contact time and improves ocular bioavailability.³⁸

Therefore, the presence of HPMC in the Indo0.5 formulation enhances ocular distribution, ensuring therapeutically relevant retinal concentrations of indomethacin, which may be particularly useful for treating posterior segment disorders.⁹

As an NSAID, indomethacin reduces inflammation by lowering the production of PGE_2 , a key inflammatory mediator. Studies in patients undergoing vitrectomy have shown that NSAIDs, such as 0.5% indomethacin, 0.09% bromfenac and 0.1% nepafenac, significantly lower vitreous PGE_2 levels.²¹ Another study found that 0.5% indomethacin and 0.09% bromfenac were more effective than 0.1% diclofenac and 0.3% nepafenac in reducing PGE_2 levels, with diclofenac associated with higher PGE_2 concentrations.²² Thus, monitoring prostaglandin levels in the aqueous and vitreous humour before and after indomethacin administration provides a valuable method for assessing its efficacy in reducing inflammation. By tracking these prostaglandin levels, it is possible to directly evaluate how effectively indomethacin decreases inflammatory markers in the eye.

Furthermore, studies on Indo0.5 have demonstrated its ability to significantly diminish inflammatory macular oedema³⁰ and provide an additive effect by reducing central retinal thickness in CNV,³¹ highlighting its capacity to reach the retina and effectively control inflammation. These findings suggest that 0.5% indomethacin may be particularly beneficial for managing posterior segment inflammation, a common concern in patients with ERM-related traction.

Although the frequency and duration of indomethacin treatment require further investigation, existing studies demonstrate that a higher concentration, such as 0.5%, may offer enhanced efficacy in managing retinal inflammation due to improved ocular distribution.

A more recent study compared the effects of eight different NSAIDs administered before IVIs to alleviate injection-related pain and found that 0.1% indomethacin, along with 0.03% flurbiprofen and 0.1% pranoprofen, did not significantly relieve pain immediately but provided notable benefits after 6 hours.²⁹ Based on the current understanding, it is possible that a higher concentration formulation of topical indomethacin eye drops could offer faster and more pronounced pain relief following IVIs. This effect may be attributed to higher drug concentrations reaching the site of inflammation, thereby potentially enhancing the therapeutic response.

Whilst 0.1% indomethacin is primarily indicated for inflammatory processes of the anterior segment,

pharmacokinetic data and limited clinical experience suggest that 0.5% indomethacin not only effectively controls anterior segment inflammation but may also offer additional benefits in managing retinal inflammation. This higher concentration could potentially improve outcomes in conditions such as ERM, macular oedema and CNV. Given these potential benefits, further studies are needed to optimize treatment protocols and explore the broader therapeutic applications of 0.5% indomethacin eye drops for posterior segment diseases, particularly in reducing PGE₂ levels, controlling inflammation and preventing ERM progression.

Conclusions

Whilst controlled clinical studies, particularly those employing a double-blind design, are essential for further elucidating the role of inflammation in ERM formation and the effects of indomethacin on tractional changes, the case presented herein suggests that Indo0.5 may represent a valuable conservative approach for controlling tractional forces at the vitreoretinal interface over time, thus preserving visual function. Further research is needed to deepen our understanding of this complex condition in the long term.

Contributions: AL collected and described the clinical case; GG conceptualized the study and drafted the manuscript; all authors contributed to the data analysis, manuscript preparation and edited the final version. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

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Correspondence: Giuseppe Giannaccare, Eye Clinic, Department of Surgical Sciences, University of Cagliari, Cagliari, Italy. Email: giuseppe.giannaccare@unica.it

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References

1. Fung AT, Galvin J, Tran T. Epiretinal membrane: a review. *Clin Exp Ophthalmol*. 2021;49:289–308. <https://doi.org/10.1111/ceo.13914>
2. Tsotridou E, Loukovitis E, Zapsalis K, et al. A Review of last decade developments on epiretinal membrane pathogenesis. *Med Hypothesis Discov Innov Ophthalmol*. 2020;9:91–110.
3. Matsunaga N, Ozeki H, Hirabayashi Y, et al. Histopathologic evaluation of the internal limiting membrane surgically excised from eyes with diabetic maculopathy. *Retina*. 2005;25:311–316. <https://doi.org/10.1097/00006982-200504000-00010>
4. Candiello J, Cole GJ, Halfter W. Age-dependent changes in the structure, composition and biophysical properties of a human basement membrane. *Matrix Biol*. 2010;29(5):402–410. <https://doi.org/10.1016/j.matbio.2010.03.004>
5. Sebag J, Gupta P, Rosen RR, Garcia P, Sadun AA. Macular holes and macular pucker: the role of vitreoschisis as imaged by optical coherence tomography/scanning laser ophthalmoscopy. *Trans Am Ophthalmol Soc*. 2007;105:121–129; discussion 129–131.
6. Sebag J. Vitreoschisis. *Graefes Arch Clin Exp Ophthalmol*. 2008;246:329–332. <https://doi.org/10.1007/s00417-007-0743-x>
7. Sebag J. Vitreous anatomy, aging, and anomalous posterior vitreous detachment. In: Dartt DA, ed. *Encyclopedia of the Eye*. Vol 4. Oxford: Academic Press; 2010:307–315.
8. Halfter W, Sebag J, Cunningham ET. II.E. Vitreoretinal interface and inner limiting membrane. In: Sebag J, ed. *Vitreous*. New York, NY: Springer; 2014:165–191. https://doi.org/10.1007/978-1-4939-1086-1_11
9. Bucolo C, Melilli B, Piazza C, Zurria M, Drago F. Ocular pharmacokinetics profile of different indomethacin topical formulations. *J Ocul Pharmacol Ther*. 2011;27(6):571–576. <https://doi.org/10.1089/jop.2011.0120>
10. Joussen AM, Poulaki V, Mitsiades N, et al. Nonsteroidal anti-inflammatory drugs prevent early diabetic retinopathy via TNF- α suppression. *FASEB J*. 2002;16:438–440. <https://doi.org/10.1096/fj.01-0707fje>
11. Ayalasomayajula SP, Kompella UB. Celecoxib, a selective cyclooxygenase-2 inhibitor, inhibits retinal vascular endothelial growth factor expression and vascular leakage in a streptozotocin-induced diabetic rat model. *Eur J Pharmacol*. 2003;458:283–289. [https://doi.org/10.1016/s0014-2999\(02\)02793-0](https://doi.org/10.1016/s0014-2999(02)02793-0)
12. Kern TS, Engerman RL. Pharmacological inhibition of diabetic retinopathy: aminoguanidine and aspirin. *Diabetes*. 2001;50(7):1636–1642. <https://doi.org/10.2337/diabetes.50.7.1636>
13. Kern TS, Miller CM, Du Y, et al. Topical administration of nepafenac inhibits diabetes-induced retinal microvascular disease and underlying abnormalities of retinal metabolism and physiology. *Diabetes*. 2007;56:373–379. <https://doi.org/10.2337/db05-1621>
14. Hattori Y, Hashizume K, Nakajima K, Nishimura Y, Naka M, Miyanaga K. The effect of long-term treatment with sulindac on the progression of diabetic retinopathy. *Curr Med Res Opin*. 2007;23:1913–1917. <https://doi.org/10.1185/030079907X218770>
15. Klein R, Klein BE, Jensen SC, et al. Medication use and the 5-year incidence of early age-related maculopathy: the Beaver Dam Eye Study. *Arch Ophthalmol*. 2001;119:1354–1359. <https://doi.org/10.1001/archophth.119.9.1354>
16. Wilson HL, Schwartz DM, Bhatt HR, McCulloch CE, Duncan JL. Statin and aspirin therapy are associated with decreased rates of choroidal neovascularization among patients with age-related macular degeneration. *Am J Ophthalmol*. 2004;137:615–624. <https://doi.org/10.1016/j.ajo.2003.10.025>
17. Takahashi H, Yanagi Y, Tamaki Y, Uchida S, Muranaka K. COX-2-selective inhibitor, etodolac, suppresses choroidal neovascularization in a mice model. *Biochem Biophys Res Commun*. 2004;325:461–466. <https://doi.org/10.1016/j.bbrc.2004.10.054>
18. Takahashi K, Saishin Y, Saishin Y, et al. Topical nepafenac inhibits ocular neovascularization. *Invest Ophthalmol Vis Sci*. 2003;44(1):409–415. <https://doi.org/10.1167/iovs.02-0346>
19. Chin MS, Nagineni CN, Hooper LC, Detrick B, Hooks JJ. Cyclooxygenase-2 gene expression and regulation in human retinal pigment epithelial cells. *Invest Ophthalmol Vis Sci*. 2001;42:2338–2346.
20. Miyake K. Prophylaxis of aphakic cystoid macular edema using topical indomethacin. *J Am Intraocul Implant Soc*. 1978;4:174–179.
21. Russo A, Morescalchi F, Vezzoli S, et al. Reduction of vitreous prostaglandin E2 levels after topical administration of indomethacin 0.5%, bromfenac 0.09%, and nepafenac 0.1. *Retina*. 2016;36:1227–1231. <https://doi.org/10.1097/IAE.0000000000000860>
22. Pastore MR, De Giacinto C, Cirigliano G, et al. Vitreous prostaglandin E2 changes after topical administration of diclofenac 0.1%, indomethacin 0.5%, nepafenac 0.3%, and bromfenac 0.09. *Retina*. 2020;40:1838–1845. <https://doi.org/10.1097/IAE.0000000000002674>

23. Baudouin C, Nordmann JP, Denis P, Creuzot-Garcher C, Allaire C, Trinquand C. Efficacy of indomethacin 0.1% and fluorometholone 0.1% on conjunctival inflammation following chronic application of antiglaucomatous drugs. *Graefes Arch Clin Exp Ophthalmol*. 2002;240:929–935. <https://doi.org/10.1007/s00417-002-0581-9>
24. Toker M, Erdem H, Erdogan H, et al. The effects of topical ketorolac and indomethacin on measles conjunctivitis: randomized controlled trial. *Am J Ophthalmol*. 2006;141(5):902–905. <https://doi.org/10.1016/j.ajo.2005.12.004>
25. Weber M, Kodjikian L, Kruse FE, Zagorski Z, Allaire CM. Efficacy and safety of indomethacin 0.1% eye drops compared with ketorolac 0.5% eye drops in the management of ocular inflammation after cataract surgery. *Acta Ophthalmol*. 2013;91:e15–21. <https://doi.org/10.1111/j.1755-3768.2012.02520.x>
26. Missotten L, Richard C, Trinquand C. Topical 0.1% indomethacin solution versus topical 0.1% dexamethasone solution in the prevention of inflammation after cataract surgery. The Study Group. *Ophthalmologica*. 2001;215(1):43–50. <https://doi.org/10.1159/000050825>
27. Badalà F, Fioretto M, Macrì A. Effect of topical 0.1% indomethacin solution versus 0.1% fluorometholon acetate on ocular surface and pain control following laser subepithelial keratomileusis (LASEK). *Cornea*. 2004;23(6):550–553. <https://doi.org/10.1097/01.icc.0000121704.40011.3d>
28. Alberti MM, Bouat CG, Allaire CM, Trinquand CJ. Combined indomethacin/gentamicin eyedrops to reduce pain after traumatic corneal abrasion. *Eur J Ophthalmol*. 2001;11:233–239. <https://doi.org/10.1177/112067210101100304>
29. Sakallioğlu AK, Kaya S, Garip R, Guclu, H. Comparison of the effects of eight different topical nonsteroidal anti-inflammatory drugs on reducing intravitreal injection-induced pain. *Retina*. 2024;44(7):1196–1202. <https://doi.org/10.1097/IAE.0000000000004085>
30. Allegri P, Murialdo U, Peri S, et al. Randomized, double-blind, placebo-controlled clinical trial on the efficacy of 0.5% indomethacin eye drops in uveitic macular edema. *Invest Ophthalmol Vis Sci*. 2014;55:1463–1470. <https://doi.org/10.1167/iovs.13-13202>
31. Russo A, Scaroni N, Gambicorti E, et al. Combination of ranibizumab and indomethacin for neovascular age-related macular degeneration: randomized controlled trial. *Clin Ophthalmol*. 2018;12:587–591. <https://doi.org/10.2147/OPTH.S159672>
32. Matoba R, Morizane Y. Epiretinal membrane: an overview and update. *Jpn J Ophthalmol*. 2024;68:603–613. <https://doi.org/10.1007/s10384-024-01127-6>
33. Schadlu R, Apte RS. Spontaneous resolution of an inflammation-associated epiretinal membrane with previously documented posterior vitreous detachment. *Br J Ophthalmol*. 2007;91:1252–1253. <https://doi.org/10.1136/bjo.2006.113597>
34. Gupta R, Leslie H, Zhang Y. Spontaneous regression and separation of idiopathic epiretinal membranes. *Cureus*. 2023;15:e44473. <https://doi.org/10.7759/cureus.44473>
35. Sato H, Naito T, Matsushita S, Takebayashi M, Shiota H. Efficacy of sub-Tenon's capsule injection of triamcinolone acetonide for refractory diabetic macular edema after vitrectomy. *J Med Invest*. 2008;55:279–282. <https://doi.org/10.2152/jmi.55.279>
36. Conti SM, Kertes PJ. The use of intravitreal corticosteroids, evidence-based and otherwise. *Curr Opin Ophthalmol*. 2006;17:235–244. <https://doi.org/10.1097/01.icu.0000193107.00089.ee>
37. Gaballa SA, Kompella UB, Elgarhy O, et al. Corticosteroids in ophthalmology: drug delivery innovations, pharmacology, clinical applications, and future perspectives. *Drug Deliv Transl Res*. 2021;11:866–893. <https://doi.org/10.1007/s13346-020-00843-z>
38. Pawar PK, Rathod RD, Jagadale SR. A review on topical ophthalmic drug delivery system: reference to viscosity enhancer. *Polim Med*. 2024;54:71–84. <https://doi.org/10.17219/pim/166413>
39. Lucente A. Patologie dell'interfaccia vitreo-retinica: case series. *Oftalmologia Domani*. 2024;4:2:74–89.