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EDITORIAL

Enhancing the outcomes of diabetic vitrectomy with pharmacological adjuvants

Chun-Yao Cheng, Wen-Rui Hao, Tzu-Hurng Cheng

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Abstract

This editorial offers insights from a minireview by Venkatesh *et al*, who explored pharmacological adjuvants for diabetic vitrectomy. Specifically, they synthesized current knowledge and evaluated the efficacy of various adjunctive therapies in improving the outcomes of diabetic retinopathy and managing associated complications. Herein, we highlight the key roles of pharmacological adjuvants in optimizing surgical techniques, minimizing intraoperative challenges, and enhancing postoperative recovery. We further discuss the potential implications of this approach for clinical practice and future research directions in this evolving field. Overall, this editorial underscores the importance of incorporating pharmacological adjuvants into standard diabetic vitrectomy care to improve surgical outcomes and thus patients' quality of life.

Key Words: Diabetic vitrectomy; Pharmacological adjuvants; Surgical outcomes; Diabetic retinopathy; Clinical implications

Core Tip: Incorporating pharmacological adjuvants into diabetic vitrectomy can significantly enhance surgical outcomes and postoperative recovery. These therapies reduce intraoperative complications like bleeding and improve surgical precision while minimizing postoperative issues, including inflammation and fibrosis. Therefore, the incorporation of these adjunctive treatments into routine clinical practice is crucial for improving patient care, lowering complication rates, and enhancing long-term visual outcomes for those undergoing diabetic vitrectomy.

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INTRODUCTION

The field of diabetic vitrectomy surgery is evolving with the introduction of pharmacological adjuvants, as highlighted by Venkatesh *et al*[1]. Diabetic retinopathy, a leading cause of global blindness, often requires vitrectomy to address complications such as vitreous hemorrhage and tractional retinal detachment. Traditional surgical techniques face challenges like intraoperative bleeding and postoperative complications[1-3]. Pharmacological adjuvants offer promising solutions by reducing bleeding, enhancing visualization, and promoting retinal healing[4,5]. Venkatesh *et al*[1] provided a comprehensive review of these therapies, evaluating their efficacy and safety, underscoring their potential to transform diabetic vitrectomy practices[6]. Integrating these advancements into clinical protocols could simplify surgery and improve patient outcomes globally[7,8]. This editorial synthesizes key insights from recent research, highlighting the transformative role of pharmacological adjuvants in diabetic vitrectomy and advocating for their integration into standard surgical practice[9,10].

CURRENT CHALLENGES IN DIABETIC VITRECTOMY

Diabetic vitrectomy presents numerous challenges due to the complex pathology of diabetic retinopathy. A major issue is intraoperative bleeding, which obscures the surgical field and increases the risk of complications[2]. The presence of fibrovascular membranes adds further complexity, requiring delicate dissection to minimize retinal damage[4]. Incomplete vitreous clearance also remains a significant concern, contributing to postoperative complications like proliferative vitreoretinopathy (PVR) and macular edema[3]. Traditional surgical techniques, while effective, are limited in addressing these issues. Studies have demonstrated that preoperative anti-vascular endothelial growth factor (anti-VEGF) agents, such as ranibizumab, reduce intraoperative bleeding by decreasing neovascularization in fibrovascular membranes[6]. Enzymatic vitreolysis using reengineered collagenases offers an innovative method for improving vitreous clearance, reducing the need for mechanical manipulation[4]. Also, *in situ* cross-linked hyaluronan hydrogel shows promise in facilitating posterior vitreous detachment, aiding in vitreous removal[5]. Pharmacological adjuvants like mitomycin C have also been explored for their potential to prevent postoperative fibrosis and PVR, improving both functional and anatomical outcomes[3]. High-density silicone oil is another approach used to manage severe proliferative diabetic retinopathy (PDR), though it carries risks such as increased intraocular pressure[11]. Despite these advances, significant challenges remain in diabetic vitrectomy. The integration of pharmacological adjuvants and innovative surgical techniques is crucial for improving outcomes and reducing postoperative complications. As research progresses, combining traditional methods with emerging therapies will likely enhance the safety and efficacy of diabetic vitrectomy [1].

ROLE OF PHARMACOLOGICAL ADJUVANTS

Pharmacological adjuvants play a crucial role in enhancing the efficacy of diabetic vitrectomy by addressing both intraoperative and postoperative challenges. Anti-VEGF agents, such as ranibizumab and bevacizumab, have proven effective in reducing intraoperative bleeding and facilitating the removal of fibrovascular membranes, both essential for successful outcomes in patients with PDR. These agents inhibit neovascularization, improving intraoperative visualization and reducing the risk of postoperative vitreous hemorrhage[2,6]. Preoperative anti-VEGF administration also appears to mitigate the angiogenic and fibrotic responses associated with diabetic retinopathy, enabling more precise and safer surgeries[2]. Corticosteroids, particularly dexamethasone implants, play a pivotal role in controlling postoperative inflammation, which accelerates patient recovery. Their anti-inflammatory effects help minimize the risk of macular edema and fibrosis, thus improving both functional and anatomical outcomes[12]. Mitomycin C, an antifibrotic agent, has also been shown to reduce the risk of PVR, improving surgical outcomes in cases of severe tractional retinal detachment [3]. Enzymatic vitreolysis is another innovative approach in diabetic vitrectomy. Reengineered collagenases, such as those derived from *Vibrio mimicus*, facilitate vitreous liquefaction, simplifying its removal and reducing the need for mechanical

manipulation. This approach lowers the risk of retinal tears and postoperative complications[4]. Alike, cross-linked hyaluronan hydrogels have been explored to ease posterior vitreous detachment, further improving surgical efficiency [5]. As well, novel therapies like fibrin glue show promise in reducing the risk of postoperative vitreous hemorrhage, a common complication after diabetic vitrectomy. By promoting clot stabilization and reducing intraocular bleeding, fibrin glue contributes to better surgical outcomes[13]. Overall, the integration of pharmacological adjuvants in diabetic vitrectomy not only enhances surgical precision but also improves patient outcomes by addressing the complexities of diabetic retinopathy. As research continues to advance, the role of these adjuvants in clinical practice will likely expand, offering new avenues for improving the management of diabetic eye disease[1].

EVIDENCE FROM RECENT STUDIES

Recent studies have deepened our understanding of the role pharmacological adjuvants play in improving outcomes in diabetic vitrectomy. Venkatesh *et al*[1] provided comprehensive evidence on the efficacy and safety of these adjuncts in vitrectomy for diabetic retinopathy. Their research highlighted significant improvements in surgical success rates, visual acuity, and reductions in complications compared to traditional methods without adjuvants, underscoring the potential of these agents to mitigate the complexities of diabetic retinopathy surgery and enhance patient care. Similarly, Fadakar *et al*[2] investigated the effects of preoperative anti-VEGF treatment on fibrovascular membranes in patients with PDR. Their study found that anti-VEGF therapy not only reduces intraoperative bleeding but also modulates the angiogenic and fibrotic environment, contributing to more successful surgical outcomes. This aligns with the findings of Gao *et al*[6], who demonstrated the benefits of combining intravitreal ranibizumab with vitrectomy, particularly in cases involving neovascular glaucoma and diabetic vitreous hemorrhage. These therapies have been linked to improved anatomical and functional outcomes, further validating their role in enhancing surgical precision and reducing postoperative complications. Santra *et al*[4] explored enzymatic vitreolysis with collagenase to facilitate vitreous detachment in diabetic patients, showing promise in simplifying the surgical process. Building on this, Hisatomi *et al*[5] developed *in situ* cross-linked hyaluronan hydrogels, which aid in removing the posterior vitreous cortex, reducing the complexity of diabetic vitrectomy. Further supporting the use of pharmacological adjuvants, Gurelik *et al*[3] demonstrated that mitomycin C improves both functional and anatomical outcomes in patients with severe diabetic tractional retinal detachment, a challenging complication of PDR. Collectively, these studies underscore the importance of integrating pharmacological adjuvants into diabetic vitrectomy practice. These agents not only enhance surgical success rates and improve patient outcomes but also reduce the risk of complications such as recurrent hemorrhage and fibrosis. However, continued research is needed to fully elucidate their long-term benefits and refine optimal protocols for their use in clinical settings.

CLINICAL IMPLICATIONS AND ADOPTION CHALLENGES

Pharmacological adjuvants in diabetic vitrectomy have shown significant potential in improving surgical outcomes. Agents like anti-VEGF therapies (*e.g.*, ranibizumab and conbercept) and enzymatic vitreolysis agents help reduce intraoperative complications by facilitating the removal of fibrovascular membranes and controlling bleeding[1,2]. However, several challenges hinder their widespread adoption in clinical practice. One of the main barriers is the high cost associated with these treatments. Anti-VEGF medications are expensive, raising concerns about cost-effectiveness, particularly in regions with limited healthcare resources[1,6]. This financial burden restricts access for many patients, making it crucial for healthcare providers to balance the benefits of these therapies against their costs. As well, variability in efficacy across patient populations presents another challenge. While anti-VEGF agents improve outcomes for many, their effectiveness can depend on factors such as the timing of administration and disease severity[2,8]. For instance, preoperative anti-VEGF injections significantly reduce intraoperative bleeding in patients with PDR[2], but outcomes may vary based on individual patient characteristics. This variability necessitates a personalized approach, complicating efforts to standardize these treatments in clinical practice. A further concern is the lack of comprehensive long-term safety data. While short-term studies show promising results, particularly in reducing postoperative complications like macular edema, the long-term effects of repeated anti-VEGF injections or enzymatic vitreolysis remain under investigation[4,14]. There are concerns about potential adverse outcomes, including an increased risk of fibrosis or retinal detachment, which complicates the adoption of these therapies without more extensive evidence. Regulatory challenges also contribute to the slow adoption of newer pharmacological adjuvants, such as hyaluronan-based hydrogels. Issues with approval and regional availability make it difficult to integrate these therapies into routine care[5,7]. Healthcare providers must navigate these regulatory landscapes while staying updated on emerging pharmacological options to ensure the best care for their patients. To address these challenges, further research is essential. Ongoing clinical trials and studies are critical for refining treatment protocols, optimizing dosing strategies, and clarifying the long-term safety profiles of adjuvant therapies[1]. Large-scale, multicenter studies could help mitigate the variability in treatment outcomes and provide more definitive evidence to support broader adoption[3]. Additionally, developing cost-effective models and securing wider regulatory approval for innovative agents could enhance their clinical utility. Overall, while pharmacological adjuvants hold great promise in diabetic vitrectomy, their integration into routine practice faces barriers related to cost, variable efficacy and safety concerns. Ongoing research, along with collaborative efforts between clinicians, researchers and policymakers, is crucial to overcoming these challenges and ensuring that patients benefit from these advancements in diabetic retinopathy management.

FUTURE DIRECTIONS AND RESEARCH OPPORTUNITIES

The future of pharmacological adjuvants in diabetic vitrectomy is set to advance significantly through a comprehensive research strategy. A key focus will be refining existing therapies while exploring new agents and combination treatments to address the complexities of diabetic retinopathy. For example, ongoing work with hyaluronan-based hydrogels aims to simplify posterior vitreous cortex removal, potentially improving surgical outcomes[5]. Equally, research into reengineered collagenase demonstrates the promise of enzymatic vitreolysis for safer, more effective procedures[4]. Future studies should emphasize long-term efficacy and safety, particularly concerning outcomes like recurrence rates and visual stability. Randomized clinical trials will be critical in assessing the sustained benefits of preoperative anti-VEGF injections and other adjuvants, with early data suggesting reductions in intraoperative complications and postoperative inflammation[2]. Large-scale comparisons of agents like conbercept and ranibizumab are also needed to establish standardized protocols for different stages of diabetic retinopathy[6,8]. Moreover, research should explore the integration of pharmacological adjuvants with emerging surgical techniques. Combination therapies, such as intravitreal steroids with vitrectomy, could enhance both anatomical and functional outcomes by mitigating postoperative complications like macular edema[15]. Furthermore, the use of mitomycin C in conjunction with vitrectomy for severe tractional retinal detachment shows potential for improving functional results[3]. Another important area for research is the assessment of quality-of-life measures and patient-reported outcomes. Since diabetic retinopathy often requires long-term management and multiple interventions, understanding how pharmacological adjuvants affect patients' daily lives and overall satisfaction is essential. Incorporating these patient-centered outcomes into clinical trials will guide treatment decisions and ensure that new therapies align with patient needs and expectations[1]. To drive these innovations, interdisciplinary collaboration is crucial. Partnerships between ophthalmologists, pharmacologists and bioengineers will accelerate the development of advanced drug delivery systems and more effective adjuvants. Such collaboration will ensure a holistic approach to diabetic vitrectomy, moving the field toward more personalized and patient-centered care[7]. In brief, advancing the role of pharmacological adjuvants in diabetic vitrectomy requires robust clinical research and cross-disciplinary innovation. By focusing on long-term efficacy, personalized treatment approaches, and enhancing patient-reported outcomes, the field can improve the surgical management of diabetic retinopathy, ultimately delivering better visual outcomes and quality of life for patients.

CONCLUSION

The integration of pharmacological adjuvants into diabetic vitrectomy surgery marks a significant advancement in enhancing surgical outcomes and elevating patient care standards. As detailed, these adjunctive therapies effectively address critical challenges such as intraoperative bleeding, postoperative inflammation and complications associated with diabetic retinopathy (Table 1). The comprehensive review by Venkatesh *et al*[1] substantiates their efficacy and safety, providing a strong foundation for their strategic implementation in clinical practice[6]. Looking ahead, healthcare providers must navigate the challenges of adopting these therapies while leveraging evolving evidence to tailor treatment strategies that effectively meet individual patient needs. Continued research efforts are crucial for refining existing adjuvants, exploring novel therapeutic avenues, and establishing comprehensive guidelines for their optimal use[5,16]. Longitudinal studies focusing on long-term outcomes and patient-reported quality of life will further enhance clinical decision-making in this evolving field. In conclusion, incorporating pharmacological adjuvants into diabetic vitrectomy protocols holds great promise for significantly improving surgical outcomes and ultimately enhancing the quality of life for patients with diabetic retinopathy. By embracing these advancements, healthcare providers can achieve superior visual outcomes and effectively alleviate the global burden of diabetic eye disease[4,8].

Table 1 Comparison of novel and traditional treatment modalities for diabetic retinopathy: Advantages and disadvantages

Treatment modality	Advantages	Disadvantages	Ref.
Novel: Pharmacological adjuvants in vitrectomy	Enhances vitreous clarity, improving surgical visibility; mitomycin C and other agents can improve functional outcomes	Adverse effects such as retinal toxicity in some cases; not universally adopted	Venkatesh *et al*[1], 2024; Gurelik *et al*[3], 2024
Novel: Anti-VEGF therapy	Reduces neovascularization and macular edema; short-term reduction in angiogenic and fibrotic factors in fibrovascular membranes	Requires repeated injections; potential ocular pain with multiple intravitreal injections	Fadakar *et al*[2], 2024; Zhou *et al*[14], 2024; Damasceno *et al*[17], 2024
Novel: Hyaluronan hydrogel adjuvant in vitrectomy	Facilitates easier removal of posterior vitreous cortex; biocompatible and injectable, improving surgical outcomes	Still under clinical evaluation; potential complications in certain patients	Hisatomi *et al*[5], 2024; Suzuki *et al*[7], 2023
Novel: Conbercept and ranibizumab pre-vitrectomy	Enhances anatomical outcomes by reducing vitreous hemorrhage; improves outcomes in complex cases such as neovascular glaucoma	Costly and not universally accessible; timing of administration critical for efficacy	Gao *et al*[6], 2023; Yang *et al*[8], 2023; Wang *et al*[16], 2023
Traditional: Laser photocoagu-	Well-established, reduces risk of vision loss	Can cause permanent retinal scarring;	Venkatesh *et al*[1], 2024;

lation	from proliferative diabetic retinopathy	limited effect on macular edema	Chauhan *et al*[18], 2024
Traditional: Pars plana vitrectomy	Effective in treating advanced proliferative diabetic retinopathy; can remove vitreous hemorrhage and fibrovascular tissue	High risk of complications, including postoperative vitreous hemorrhage; prolonged recovery period	Mansour *et al*[13], 2023; Rohowetz *et al*[19], 2024; Thapa *et al*[20], 2024
Traditional: Intravitreal steroids	Reduces inflammation and macular edema; long-lasting effect compared to anti-VEGF	Increases risk of intraocular pressure elevation; risk of cataract formation	Salvetat *et al*[12], 2024; Wang *et al*[15], 2024

This table compares the advantages and disadvantages of novel and traditional treatments for diabetic retinopathy. Novel therapies, including pharmacological adjuvants and anti-vascular endothelial growth factor agents, offer advancements in managing complications but may involve higher costs and specific risks. Traditional approaches, such as laser photocoagulation and pars plana vitrectomy, remain effective but have limitations, including retinal scarring and extended recovery times. References are provided for further review of the supporting evidence. VEGF: Vascular endothelial growth factor.

FOOTNOTES

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