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Assessing the Usage Anesthesia in the Surgical Treatment of Diabetic Macular Edema

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ABSTRACT

Diabetes-related macular edema is a fast-spreading condition that has damaged the lives of countless people throughout the globe. The current incorporation of subthreshold micropulse laser has indicated the precedence of laser therapy in the treatment of diabetic macular edema; nonetheless, vitreoretinal surgery in conjunction with anesthetics correlates with early mitigation of damage to the fovea. Surgery is a delicate procedure that necessitates careful consideration of the types and locations of anesthetics used. Depending on the individual being treated, various drugs and methods may be necessary. For example, some individuals may be allergic to conventional anesthetics, resulting in more severe consequences. In the surgical treatment of diabetic macular edema, the topical anesthetic was utilized more frequently than subconjunctival anesthesia, according to the review's statistical analysis. The examined literature indicated that topical lidocaine was the most employed anesthetic for vitreoretinal surgery; however, alternatives to lidocaine exist, and their effects should be investigated. Consequently, we would want to highlight the impacts of each of the several surgical medications and anesthetics used to treat diabetic macular edema.

Keywords

Diabetic macular edema
Topical anesthesia
Subconjunctival anesthesia
Lidocaine
Cooling anesthesia

INTRODUCTION

Diabetic macular edema (DME), defined as the leakage of fluids from blood vessels in the retina, is a frequent diabetic eye disease and the main cause of vision loss in developed nations [1]. In 2019, nearly 750,000 cases of diabetic retinopathy alone were documented in the United States [1]. When diabetic macular edema is left untreated, extra fluid in the retina causes swelling in the macula's surrounding tissue, resulting in permanent damage to the fovea [2]. DME symptoms can range from hazy vision and lack of contrast to total blindness. Due to the prevalence of DME, numerous novel and inventive therapeutic methods have been created. Integration of subthreshold micropulse lasers (SML) into laser therapy has been the most significant improvement in treating DME [2]. SML fulfills the same function as traditional continuous-wave lasers but without the associated negative side effects [2]. Although laser therapy is extensively used and significant advancements have been made in the field, the use of sophisticated anesthetics in vitreoretinal surgery has been found to correspond with more rapid DME intervention [2].

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In the case of DME, earlier surgery can minimize macula damage and avoid subsequent foveal degeneration. It is vital to consider the anesthetics used in these surgeries, as one of the key goals of healthcare providers is to minimize patient injury. We would like to review a variety of papers and examine the utilization and placement of anesthetics during DME surgical procedures. This investigation is a continuation of a previous study that was published in 2021 [3].

METHODS

Cases focusing on non-diabetic macular edema, diabetic retinopathy, cataracts, or failing to disclose the use of anesthetic medication were excluded from the study. Anesthesia was mentioned in relation to surgery to treat diabetic macular edema, therefore abstracts and titles were scrutinized. Only articles that were available in English or Spanish were included in our analysis. A total of 96 items were found after the database search using the specified criteria. 13 articles lacked the whole text, there were 64 duplicates, and two articles failed to meet the requirements for our study. Our search results included 17 papers that discussed surgical techniques including anesthetics and people with diabetic macular edema. The papers that were selected for this investigation can be seen in Table 1 [4-22]. The sample size, the application locations, the types of medications administered, and the types of anesthetics utilized were all information that was taken from each report (Figure 1).

LITERATURE REVIEW

Throughout the past two decades, numerous people with diabetic macular edema have had surgical treatment to eradicate the illness. The surgery is an invasive procedure that removes the vitreous around the posterior hyaloid detachment. Additionally, peeling removes any epiretinal and internal limiting membranes. Historically, detachment of the posterior vitreous has been associated with more rapid resolution of DME. Moreover, vitrectomy has been reported to ameliorate DME symptoms via multiple biological pathways [2]. These processes include enhanced retinal oxygenation, enhanced clearance of VEGF loads, and the release of aberrant vitreomacular adhesions [2]. According to the research, surgery is a highly effective treatment for diabetic macular edema. In order to reduce patient injury, it is necessary to evaluate the application and utilization of anesthetic during these procedures. There are two primary locations of the eye where anesthetics are administered during surgery to eliminate this condition. During DME surgery, the anesthetic is typically used topically or subconjunctivally [4]. Although some physicians use both topical and subconjunctival anesthetic,

Table 1: Summary of previous clinical studies of surgical procedures to treat diabetic macular edema

Author (year)	Area(s) of applied Anesthetic	Type(s) of anesthetic	Number of anesthetics used	Concentration of major anesthetic used	Drug(s) in injection	Sample Size (Eyes)
Besirli (2020) [4]	Subconjunctival	CA, LC	1	3.5%	AVEGF	44
Diaz-Llopis (2008) [5]	Topical	TC	1	1%	APE	18
Diaz-Llopis (2009) [6]	Topical	TC	1	1%	APE	16
Jonas (2004) [7]	Topical	LC	1	25 mg	TA	24
Jonas (2001) [8]	Topical	LC	1	20 mg	CC	2 (case report)
Kaderli (2006) [9]	Subconjunctival, Topical	LC	1	4%	TA	56
Karacorlu (2004) [10]	Topical	LC	1	4 mg	TA	2 (case report)
Koga (2005) [11]	Topical	LC	1	40 mg	TA	20
Kyto (2005) [12]	Subconjunctival	LC	1	4.8 mg	TA	2 (case report)
Lin (2007) [13]	Topical	LC	1	0.5%	TA	18
Massin (2004) [14]	Subconjunctival	LC	1	4 mg	TA	15
Ozkurt (2015) [15]	Topical	LC	1	40 mg	TA	42
Rifkin (2012) [16]	Topical	TV, TC, PR	3	N/A	AVEGF	120
Shirohima (2014) [17]	Topical	LC	1	2, 3.5, 5, 8, 12%	AVEGF	260
Song (2011) [18]	Topical	BC	1	4 mg	TA	58
Sutter (2004) [19]	Subconjunctival, Topical	LC	1	40 mg	TA	69
Xing (2014) [20]	Subconjunctival, Topical	PR, LC, TC	1	N/A	TA	75

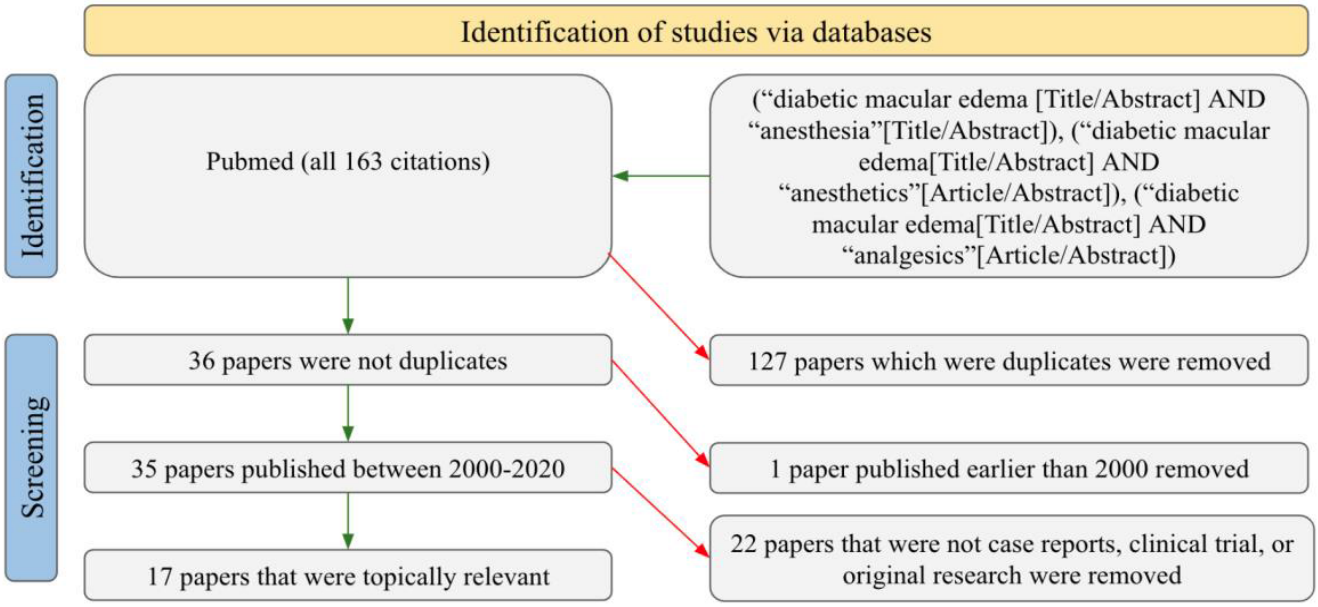

Figure 1: PRISMA Selection Diagram.

the vast majority of healthcare professionals only use topical anesthetics [4-20]. While subconjunctival anesthesia is known to reduce patient harm more than topical anesthetics, it has been demonstrated to increase the risk of subconjunctival bleeding [9] . This is likely why the majority of surgical treatments involving DME only employ topical anesthetic and not subconjunctival anesthesia.

Diabetic macular edema is treated surgically with injections of medications that counteract the disease's symptoms. In an effort to prevent damage to the patient's fovea, medication administration specifically targets the swelling of the macula [2]. In addition, surgical injections [21] aim to address the rupture of the blood-retinal barrier and the elevation of retinal vascular leukostasis. TA is the most commonly used medication by ocular surgeons for this surgery. This is perhaps because TA is a well-established anti-inflammatory in medical treatments [22]. Due to the anti-inflammatory actions of TA on the macula, it is one of the most effective treatments for alleviating the previously mentioned difficulties produced by DME. In the majority of research analyzed in Table 1, it was found that TA is the most frequently administered intravitreally during DME surgical treatments. Although TA is the most often used medication for this surgery, it is not the standard medication. This is most likely related to the fact that TA is a relatively new medicine on the pharmaceutical market [2 3] and AVEGF is the usual drug for this surgery. While both TA and AVEGF are anti-inflammatory drugs, TA has been shown to reduce central thickness and improve best-corrected visual acuity better [22]. In post-clinical trials, it has been demonstrated that TA has more lasting positive effects on patients' vision than AVEGF [22]. As additional clinical and translational research is conducted, it is possible that TA will replace AVEGF as the new standard of therapy. In order for surgeons to administer TA injections to patients with DME, the patients must first be anesthetized to prevent pain during surgery. Therefore, it is essential to evaluate the type of anesthetics while contemplating DME treatment.

The most prevalent anesthetic for DME surgical procedures is LC. LC is an amino acid-derived local anesthetic that inhibits nerve signal transmissions. Since LC is an antiarrhythmic chemical, it also decreases sodium channel transit and, consequently, the heart rate of the patient [2 4]. This approach is beneficial for minimizing blood leakage in the macula because it reduces total blood flow to the eyes. Numerous eye operations, such as cataract removal, LASIK, and DMEK, have made extensive use of LC [25-27] . Because LC is so versatile, it can be administered directly to the skin as well as to the mucous membranes. Despite the fact that LC often takes several minutes to three hours to take effect, its anesthetic impact is significant [2 4]. The majority of Table 1's studies are examined. LC is the most commonly utilized anesthetic in DME surgical procedures, but in some of the earliest research TC was used instead. This may be due to the fact that TC has been utilized in the medical sector for a longer period of time than LC, however clinical investigations have demonstrated that LC is more effective than TC at reducing patient pain [28-30] . So, despite

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Table 2: Statistical Analysis Using p-values and t-test scores for Anesthetic Usage.			
Group vs Group	**t-test**	**p-value**	**Proof of statistical significance**
Topical vs Subconjunctival	The mean of Topical minus Subconjunctival equals 0.47 95% CI (0.16, 0.78)	The two-tailed P value = 0.0042	Confirmed

the fact that TC has been used by physicians for a longer period of time, LC is the anesthetic of choice among surgeons for the treatment of DME, as it has been demonstrated to be more effective. As noted previously, LC is likely one of the greatest anesthetics utilized for DME surgery, but it is not a one-size-fits-all approach. Numerous people get allergic reactions when exposed to LC and other anesthetics [4] . In rare situations, LC might exacerbate the symptoms of DME by generating more inflammation in the macula. In order to provide therapy for those who are hypersensitive to conventional anesthesia, alternative anesthetic methods are actively being created and researched. CA is one such solution devised to meet these requirements. When ocular tissue is subjected to extremely cold temperatures, the body produces a stress-induced opioid-mediated analgesia [3,31] . CA is a treatment that entails freezing the patient's eyes to extremely low temperatures in order to enhance the patient's pain threshold, hence allowing the surgeon to conduct the procedure with minimal patient injury. CA is a type of anesthesia that does not rely on synthetically manufactured substances; hence, CA does not cause as many treatment issues as conventional anesthetics. Recent research has demonstrated that the CA reduces transient adverse effects by 12% relative to the normal standard of care [4] . Although CA is a viable alternative kind of anesthesia, it should be utilized with extreme caution. CA is known to produce the desired anesthetic effect when the temperature of human tissue falls below -10°C; however, lasting cell damage could occur if the temperature falls below -20°C [4].

Our study did have some limitations. Firstly, our analysis reveals only trends in anesthetic uses in vitreoretinal surgery, specifically within the context of diabetic macular edema. Hence, it is important to note that these trends may not be representative within other pathologies requiring vitreoretinal surgery. Furthermore, we were unable to ascertain the negative effects (ie. subconjunctival hemorrhage) associated with these anesthetics. More studies are needed to investigate the side effect profiles of these anesthetics within multiple contexts to better improve patient safety.

CONCLUSION

Diabetic macular edema may become a more prominent condition in the future, given how many patients presently suffer from diabetes. When combating this disease, it is vital to consider the numerous treatment choices and their long- and short-term impacts on individuals. Surgery is one of the therapeutic options for DME, and its effects can vary depending on the anesthetic used. Although lidocaine is the most predominantly utilized anesthetic in DME surgery, it may not be the most effective and safe anesthetic in the future, given the promising research and outcomes of cooling anesthesia. The literature appears to support the assumption that the anesthetic for this technique should be given topically and triamcinolone acetonide should be the primary pharmacological injection for conventional DME treatment. Possibly, future studies will demonstrate that non-medicated anesthetic treatments are more successful than the current standard of care.

An analysis of the usage of topical and subconjunctival anesthesia can be seen in Table 2. The statistical significance demonstrated through the unpaired t-test shows that a topical rather than subconjunctival anesthetic is more commonly utilized for local anesthesia in diabetic macular edema surgery. This suggests that in the past two decades (in which the dates of the studies range), physicians are still predominantly using lidocaine in DME surgery and its associated topical application. This shows that physicians have not fully recognized or feel comfortable using cooling anesthesia, because though given the benefits of a reduction in patient harm, the risk of the patient experiencing subconjunctival hemorrhage is still uncomfortable and not worth taking. Future studies on this topic could address current rates of subconjunctival hemorrhage and rates of application along with efficacy and physician comfort in application.

ABBREVIATIONS

TA triamcinolone acetonide, BC bevacizumab, LC lidocaine, N/A Not Applicable, PR proparacaine, TV tetravisc, TC tetracaine, CA cooling anesthetic, APE autologous plasmin enzymes, AVEGF anti-vascular endothelial growth factor, CC crystalline cortisone, DME diabetic macular edema

REFERENCES

1. Mansour SE, Browning DJ, Wong K, Flynn HW Jr, Bhavsar AR. The Evolving Treatment of Diabetic Retinopathy. Clin Ophthalmol. 2020 Mar 4;14: 653-678.

2. Stefánsson E. The therapeutic effects of retinal laser treatment and vitrectomy. A theory based on oxygen and vascular physiology. Acta Ophthalmol Scand. 2001 Oct;79(5):435-40.

3. Dang A, Akshay J Reddy. "The Application and Usage of Anesthetics in the Surgical Treatment of Diabetic Macular Edema.". Ophthalmology and Vision Care, 1(1); DOI: http;//doi.org/03.2021/1.1001.

4. Besirli CG, Smith SJ, Zacks DN, Gardner TW, Pipe KP, Musch DC, Shah AR. Randomized Safety and Feasibility Trial of Ultra-Rapid Cooling Anesthesia for Intravitreal Injections. Ophthalmol Retina. 2020 Oct;4(10):979-986.

5. Díaz-Llopis M, Udaondo P, García-Delpech S, Cervera E, Salom D, Quijada A. Vitrectomía enzimática por inyección intravítrea de plasmina autóloga como tratamiento inicial del edema macular diabético difuso [Enzymatic vitrectomy by intravitreal autologous plasmin injection, as initial treatment for diffuse diabetic macular edema]. Arch Soc Esp Oftalmol. 2008 Feb;83(2):77-84. Spanish.

6. Diaz-Llopis M, Udaondo P, Arevalo F, Salom D, Garcia-Delpech S, Quijada A, Romero FJ. Intravitreal plasmin without associated vitrectomy as a treatment for refractory diabetic macular edema. J Ocul Pharmacol Ther. 2009 Aug;25(4):379-84.

7. Jonas JB, Kreissig I, Degenring RF. Cataract surgery after intravitreal injection of triamcinolone acetonide. Eye (Lond). 2004 Apr;18(4):361-4.

8. Jonas JB, Söfker A. Intraocular injection of crystalline cortisone as adjunctive treatment of diabetic macular edema. Am J Ophthalmol. 2001 Sep;132(3):425-7.

9. Kaderli B, Avci R. Comparison of topical and subconjunctival anesthesia in intravitreal injection administrations. Eur J Ophthalmol. 2006 Sep-Oct;16(5):718-21.

10. Karacorlu M, Ozdemir H, Karacorlu S, Alacali N. Regression of optic nerve head neovascularization in proliferative diabetic retinopathy after intravitreal triamcinolone. Regression of diabetic optic disc neovascularization after intravitreal triamcinolone. Int Ophthalmol. 2004 Mar;25(2):113-6.

11. Koga T, Mawatari Y, Inumaru J, Fukushima M, Tanihara H. Trans-Tenon's retrobulbar triamcinolone acetonide infusion for refractory diabetic macular edema after vitrectomy. Graefes Arch Clin Exp Ophthalmol. 2005 Dec;243(12):1247-52.

12. Kytö, Janne P et al. "Intravitreal triamcinolone acetonide as an adjuvant therapy to panretinal photocoagulation for proliferative retinopathy with high risk characteristics in type 1 diabetes: case report with 22 weeks follow-up." Acta ophthalmologica Scandinavica vol. 83,5 (2005): 605-8. doi:10.1111/j.1600-0420.2005.00477.x

13. Lin JM, Chiu YT, Hung PT, Tsai YY. Early treatment of severe cystoid macular edema in central retinal vein occlusion with posterior sub-tenon triamcinolone acetonide. Retina. 2007 Feb;27(2):180-9.

14. Massin, Pascale et al. "Intravitreal triamcinolone acetonide for diabetic diffuse macular edema: preliminary results of a prospective controlled trial." Ophthalmology vol. 111,2 (2004): 218-24; discussion 224-5. doi:10.1016/j.ophtha.2003.05.037

15. Ozkurt YB, Akkaya S, Aksoy S, Evciman T, Haboğlu M. Posterior Subtenon's Capsule Triamcinolone Acetonide Injection for the Treatment of Diabetic Macular Edema. J Ocul Pharmacol Ther. 2015 Oct;31(8):455-60.

16. Rifkin L, Schaal S. Factors affecting patients' pain intensity during in office intravitreal injection procedure. Retina. 2012 Apr;32(4):696-700.

17. Shiroma HF, Nunes RP, Farah ME, Penha FM, Lorenzo JC, Grumann A, Rodrigues EB. Safety and efficacy of various concentrations of topical lidocaine gel for intravitreal injection. Expert Opin Drug Saf. 2014 Oct;13(10):1299-303.

18. Song JH, Lee JJ, Lee SJ. Comparison of the short-term effects of intravitreal triamcinolone acetonide and bevacizumab injection for diabetic macular edema. Korean J Ophthalmol. 2011 Jun;25(3):156-60.

19. Sutter FK, Simpson JM, Gillies MC. Intravitreal triamcinolone for diabetic macular edema that persists after laser treatment: three-month efficacy and safety results of a prospective, randomized, double-masked, placebo-controlled clinical trial. Ophthalmology. 2004 Nov;111(11):2044-9.

20. Xing L, Dorrepaal SJ, Gale J. Survey of intravitreal injection techniques and treatment protocols among retina specialists in Canada. Can J Ophthalmol. 2014 Jun;49(3):261-6.

21. Vinores SA. Breakdown of the Blood–Retinal Barrier. Encyclopedia of the Eye. 2010:216–22.

22. Aksoy S, Yilmaz G, Akkoyun I, Yazici AC. Comparison of intravitreal bevacizumab and triamcinolone acetonide theraphies for diffuse diabetic macular edema. Int J Ophthalmol. 2015 Jun 18;8(3):550-5.

23. Wenick AS, Bressler NM. Diabetic macular edema: current and emerging therapies. Middle East Afr J Ophthalmol. 2012 Jan;19(1):4-12.

24. Giordano D, Raso MG, Pernice C, Agnoletti V, Barbieri V. Topical local anesthesia: focus on lidocaine-tetracaine combination. Local Reg Anesth. 2015 Nov 27;8:95-100.

25. Pilger D, Maier AK, Bertelmann E, Joussen A, Torun N. Use of topical anaesthesia and peribulbar anaesthesia in Descemets membrane endothelial keratoplasty. Eur J Ophthalmol. 2020 Aug 27:1120672120950935.

26. Nebbioso M, Livani ML, Santamaria V, Librando A, Sepe M. Intracameral lidocaine as supplement to classic topical anesthesia for relieving ocular pain in cataract surgery. Int J Ophthalmol. 2018 Dec 18;11(12):1932-1935.

27. Lam DS, Law RW, Ng AS, Lam PT, Jhanji V, Lee VY, Fan AH, Rao SK. Randomized double-masked controlled trial comparing pain scores with and without the use of supplementary 2% lidocaine gel in LASIK. Am J Ophthalmol. 2012 Apr;153(4):627-31, 631.e1-3.

28. Ruetsch YA, Böni T, Borgeat A. From cocaine to ropivacaine: the history of local anesthetic drugs. Curr Top Med Chem. 2001 Aug;1(3):175-82.

29. Gordh T. Lidocaine: the origin of a modern local anesthetic. 1949. Anesthesiology. 2010 Dec;113(6):1433-7.

30. Chandra S, Sugiarto A, Hotasi R, Chrysantia Melati A, Harmani B. The Effectiveness of 2% Lidocaine Gel Compared to 0.5% Tetracaine Eye Drop As Topical Anesthetic Agent for Phacoemulsification Surgery. Anesth Pain Med. 2018 Apr 28;8(2):e68383.

31. Strigo IA, Carli F, Bushnell MC. Effect of ambient temperature on human pain and temperature perception. Anesthesiology. 2000 Mar;92(3):699-707.

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