Versatility of use of fibrin glue in wound closure and vitreo-retinal surgery

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Abstract

Background: Fibrin glue is an absorbable blood-derived product, a biological tissue adhesive which imitates the final stages of the coagulation cascade, it produces a firm clot, forming a seal along the whole length of the wound, the resultant fibrin clot degrades physiologically into granulation tissue 2 weeks after the application. Biological glue has been used extensively in many forms of surgical procedures. Its use in eye surgery has grown lately as we have evidence that showed it was effective in securing conjunctival grafts in pterygium surgery, in securing wounds after glaucoma surgery and more importantly in 20G and 23G vitrectomy.

Purpose: The aim of this study is to present our experience in the use of fibrin glue in vitreoretinal surgery.

Material and methods: We included 281 eyes of 221 patients who underwent vitreoretinal surgery during the period of May 2009 to July 2012, the preoperative diagnoses were as following: proliferative diabetic retinopathy, rhegmatogenous retinal detachment, macular hole, epiretinal membrane, luxation of cataratous nucleous and cortex, intraocular lens luxation, penetrating trauma, silicone extraction, phaco + IOL + vitrectomy + Ahmed valve implant, vitreous biopsy and optic nerve pit associated to macular detachment. The procedures were performed with Alcon Accurus Surgical System 20-gauge, 23-gauge or a combination of both. We used fibrin glue in all of the 20-gauge sclerotomies and leaking 23-gauge sclerotomies, scleral wound for IOL extraction, conjunctival peritomy for buckle implantation, conjunctiva in Ahmed valve implant, corneal graft in corneal perforation in trauma and leaking corneal wounds for phacoemulsification, in an optic pit, and in subretinal space in a giant retinal tear.

Results: We did not use any suture in any of the patients throughout the different procedures, there was no leakage in any wounds in the postoperative period, we found no inflammatory reaction, infection, and whenever we had excess amount, it was trimmed. Two patients presented a small dehiscence of the wound that was corrected in-office with a small amount of fibrin glue in the post-operative period.

Conclusions: Fibrin glue reduces surgical time, it is a good sealant, safe, with minimal allergic or toxic reactions and inflammation, minimizes bleeding, easy to undo and that eventually degrades. This small series shows that fibrin glue is a viable alternative for tissue coaptation in vitreoretinal surgery. However, further studies are required before fibrin glue takes the place of sutures.

Keywords: Fibrin glue, Vitreoretinal surgery, Retinal detachment surgery, Rhegmatogenous retinal detachment

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established tissue adhesives as attractive alternatives to sutures. Currently, fibrin glue is being used for conjunctival closure following pterygium and strabismus surgery, lamellar corneal grafting, closure of corneal perforations and management of conjunctival wound leaks after trabeculectomy [1]. There is a limited number of reports of the use of tissue adhesives in vitreoretinal surgery as early as 1988, Zauberman et al. have reported its use for conjunctival wound closure following retinal detachment surgery [2]. Mentens compared the efficacy of fibrin glue in comparison with conjunctival closure by sutures following 20-gauge needle pars plana vitrectomy in 504 eyes [3, 4]. In these publications the authors reported that fibrin glue offers significantly better results than suturing for closure of conjunctival wounds. In another study, Bateman et al. supported the view of Mentens and suggested that in case of persistence of leaking wound following transconjunctival-sutureless vitreoretinal surgery, application of fibrin glue is a better alternative over suturing [5]. Fibrin glue has other intraoperative applications during vitreoretinal surgeries as well. It has been found to not have any toxic effects on retinal function or structure in a rabbit model [6]. Its use has also been reported in macular hole surgery, and has been described recently in the management of optic disc pit-associated macular detachments [7–9]. Fibrin glue has also been used to stabilize keratoprosthetic devices during vitreoretinal surgeries [10].

The latest literature supports procedures such as glue-assisted retinopexy for rhegmatogenous retinal detachment (GuARD). Anatomical success can be archived in retinopexy procedures without the use of gas or silicone oil tamponade. Advantages such as no need for maintaining a specific position during the post-operative period. However, a closer follow up is need due to suspected epiretinal proliferation [11].

Fibrin glue is a biological tissue adhesive which imitates the final stages of the coagulation cascade when a solution of human fibrinogen is activated by thrombin (the two components of fibrin glue). Fibrin glue includes a fibrinogen component and a thrombin component, both prepared by processing plasma. It can be prepared from the patients’ own blood or obtained as a commercially available preparation. Fibrin glue produces a firm clot, forming a seal among the whole length of the wound, the resultant fibrin clot degrades physiologically after granulation tissue two weeks after the application [12–14].

The aim of this study is to present our experience in the use of fibrin glue in wound closure and vitreoretinal surgery.

Methods
In our study, patient enrollment was performed in a consecutive manner, every patient with surgical indication for retinopexy and vitrectomy was considered for use of fibrin glue within their procedure.

The procedures were performed with Accurus Surgical System (Alcon Surgical, Forth Worth, TX, USA) at 20-gauge or 23-gauge. We used fibrin glue in all of the 20-gauge sclerotomies and leaking 23-gauge sclerotomies, (Fig. 1) scleral wound for IOL extraction, conjunctival peritomy for buckle implantation (Figs. 2, 3), conjunctiva in Ahmed valve implant, corneal graft in corneal perforation in trauma and corneal wounds for phacoemulsification, in an optic nerve pit, and in subretinal space in giant retinal tear to prevent slippage.

Technique for application
The two components of fibrin glue were applied sequentially to prevent clotting within the needle. We used both components loaded into two syringes. The thrombin is first applied on the area of interest, followed by a thin layer of fibrinogen. In a minute or two, coagulation starts and by two or three minutes, polymerization is complete. The physiological final pathway of coagulation is replicated. Factor XIII (present in the fibrinogen component of the glue) cross links and stabilizes the clot’s fibrin monomers while aprotinin inhibits fibrinolytic enzymes, consequently resulting in a stable clot. The tissue is pressed gently over the glue for 60 s for firm adhesion (Fig. 4). At the end of the procedure, pad and bandage is applied after instillation of steroid and antibiotic drops. The commercially available form of fibrin glue we used comes installed with double-barreled injection system, but due to lack of control over the mixing time of both injection components and the risk of a sudden burst of pressure when congealed glue frees outside the cannula, and risk of tissue damage, we opted out of the pre-installed system. Instead, we layered both components separately while at the same time holding both tissue borders together, until visible fixation was obtained.

Vitrectomy
Our use of fibrin glue during vitrectomy surgery for different diagnoses consisted of sealing sclerotomies whether they were leaking or not (Fig. 1). A thin layer of thrombin was applied around the sclerotomy borders and soon after, using curved forceps, pressure was applied to close the borders, then, a thin layer of fibrinogen was applied right after tissue repositioning was made to seal the port of entrance.
Results
We included 281 eyes of 221 patients who underwent vitreoretinal surgery during a 10-year period (Table 1). The preoperative diagnoses were as following: proliferative diabetic retinopathy, rhegmatogenous retinal detachment, macular hole, epiretinal membrane, luxation of cataratous nucleus and cortex, intraocular lens luxation, penetrating trauma, silicone extraction, phaco+IOL+vitrectomy+ahmed valve implant, vitreous biopsy and optic nerve pit associated to macular detachment.

Discussion
In this study, we aimed to describe the different applications of fibrin glue within vitreoretinal surgery. Throughout the development of our experience with fibrin glue, we noted several advantages that we will further discuss. This material is blood-derived, meaning it has a biological origin as first described by Tassman in 1950, who proposed its first application in ophthalmologic surgery mainly to unite tissues and eliminate the use of sutures [15]. We used commercially available fibrin glue in all our procedures due to its ease of use, however, as described by Bhatia et al., fibrin glue can be obtained by the recipient’s own blood, using cryoprecipitate, but low concentrations of fibrinogen (2–4 mg/ml) require large amounts of blood donated to obtain a very small amount of viable fibrin glue. These two limitants discourage the use of recipient-derived fibrin glue preparations [16].

One advantage in the use of fibrin glue is the absence of suture removal procedure in the post-operative period since it has been previously described the risk of endophthalmitis following suture removal [17]. Due to its plasticity and biodegradability it is very easy to use and it’s safe to manipulate in the postoperative period at the office, using the slit lamp.

Uy et al. described a decreased inflammatory tissue reaction, following pterygium surgery, which in our experience is compatible with less inflammatory reaction after...
using fibrin glue to seal a leaking sclerotomy or conjunctival fixation after peritomy for PPV (Fig. 5) [18]. Less inflammatory reaction provides the patient with more comfort after the procedure, something we have related to a better outcome.

There are several publications referring to the use of fibrin glue within wound closure in external procedures, however there is a limited number of evidence regarding its use in vitreoretinal surgery both internally and externally.

Since fibrin glue is a blood-derived product there are reports of its safety in the use within intraocular tissues without severe toxic reactions. Historically, the use of blood clots in management of macular hole surgery has been a coadyuvant technique for closure of macular hole, without toxic or adverse events reported with the eye. This past experience encourages the use of blood-derived

| Study procedures                                                                 | Number of patients | Number of eyes | Tamponade          | Gauge |
|---------------------------------------------------------------------------------|--------------------|----------------|-------------------|-------|
| Proliferative diabetic retinopathy (either vitrectomy or combined surgery—phacoemulsification, implant of intraocular lens and vitrectomy) | 86                 | 142            | SO 1000cs-46      | 20G-93|
|                                                                                 |                    |                | SO 5000cs-48      | 23G-49|
|                                                                                 |                    |                | SF6 gas-32        |       |
|                                                                                 |                    |                | C3F8 gas-1        |       |
|                                                                                 |                    |                | Air-4             |       |
|                                                                                 |                    |                | BSS-11            |       |
| Regmatogenus retinal detachment (either vitrectomy or combined surgery—phacoemulsification, intraocular lens implant and vitrectomy or lensectomy and vitrectomy) | 35                 | 36             | SO 1000cs-8       | 20G-15|
|                                                                                 |                    |                | SO 5000cs-6       | 23G-20|
|                                                                                 |                    |                | SF6 gas-14        |       |
|                                                                                 |                    |                | C3F8 gas-5        |       |
|                                                                                 |                    |                | Heavy silicon oil-3|      |
| Macular hole (either vitrectomy or combined surgery—phacoemulsification, intraocular lens implant and vitrectomy) | 28                 | 28             | SF6 gas-28        | 20G-11|
|                                                                                 |                    |                | 23G-17            |       |
| Epiretinal membrane (either vitrectomy or combined surgery—phacoemulsification, intraocular lens implant and vitrectomy) | 18                 | 19             | Air-8             | 20G-12|
|                                                                                 |                    |                | BSS-6             | 23G-7 |
|                                                                                 |                    |                | SF6-5             |       |
| Silicon extraction                                                               | 15                 | 15             | BSS-12            | 20G-15|
|                                                                                 |                    |                | Silicon oil 5000cs-1|  |
| Nucleus luxation                                                                 | 11                 | 11             | BSS-9             | 20G-8 |
|                                                                                 |                    |                | Air-2             | 23G-3 |
| Luxation of intraocular lens                                                     | 9                  | 9              | BSS-7             | 20G-8 |
|                                                                                 |                    |                | Air-1             | 23G-1 |
|                                                                                 |                    |                | SO 5000cs-1       |       |
| Penetrating trauma                                                               | 6                  | 6              | SF6-5             | 20G-20|
| Intraocular foreign body (4)                                                     |                    |                | C3F8 gas-1        |       |
|                                                                                 |                    |                | Air-1             |       |
| Combined surgery (cataract phacoemulsification + vitrectomy + Ahmed valve implantation) | 3                  | 5              | SO 1000cs-2       | 20G-4 |
|                                                                                 |                    |                | SOS5000cs-1       | 23G-1 |
|                                                                                 |                    |                | BSS-2             |       |
| Macular detachment associated to optic pit                                        | 1                  | 1              | C3F8 gas-1        | 23G   |
| Vitreous biopsy                                                                  | 1                  | 1              | BSS-1             | 23G   |
| Giant retinal tear                                                               | 1                  | 1              | SO1000cs          | 20G   |

SO silicon oil, BSS balanced-saline solution, SF6 sulfur hexafluoride, C3F8 octafluoropropane, CS centistokes, G gauge
products like fibrin glue as a safe tool for wound closure and application in vitreo retinal surgery [19].

Conclusions
In our experience, fibrin glue may be useful in reducing surgical time as it is a good sealant, safe, with minimal allergic or toxic reactions and inflammation, minimizes bleeding, easy to undo and that eventually disappears. This series shows us that fibrin glue is a viable alternative for tissue coaptation in vitreoretinal surgery. However, further and larger studies are required. A prospective point of view should be necessary to completely evaluate the fibrin glue role in the post-operative period. Comparative, randomized trials would be of great help to fully contrast fibrin glue vs conventional surgical techniques. Different surgical techniques in vitreoretinal diseases can be evaluated to fully exploit fibrin’s glue potential to aid in the outcome of patients’ procedures.

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Authors’ contributions
GLH: performed surgical interventions, preparation of data or images, revision of the manuscript. JLGN: preparation of data or images. MAMC: performed surgical interventions, preparation of data or images, revision of the manuscript. JFPV: redaction of the manuscript, submission of manuscript for publication. All authors read and approved the final manuscript.

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Availability of data and materials
The data that support the findings of this study are available on request from the corresponding author. [GLH]. The data are not publicly available due to restrictions in medical history access in the hospitals.

Declarations
Ethics approval and consent to participate
The patients signed a written informed consent to allow us to access their medical history (including publication of images). Information revealing the subject’s identity was avoided within the entire work. ClinicalTrials.gov Identifier: NCT01022164.

Consent for publication
Within the written informed consent noted previously, patients authorized the authors for publication of medical data and images.

Competing interests
The authors declare that they have no competing interests.

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References
1. Panda A, Kumar S, Kumar A, Bansal R, Bhartiya S. Fibrin glue in ophthalmology. Indian J Ophthalmol. 2009;57:371–9.
2. Zauberger H, Hemo I. Use of fibrin glue in ocular surgery. Ophthalmic Surg. 1988;19:132–3.
3. Mentens R, Devogelaere T, Stalmans P. Comparing fibrin glue to sutures for conjunctival closure in pars plana vitrectomy. Bull Soc Belge Ophthalmol. 2007;306:49–56.
4. Mentens R, Stalmans P. Comparison of fibrin glue and sutures for conjunctival closure in pars plana vitrectomy. Am J Ophthalmol. 2007;144:128–31.
5. Bateman C, Ozdamar Y, Aslan O, Sonmez K, Mutevelli S, Zilelioglu G. Tissue glue in sutureless vitreoretinal surgery for the treatment of wound leakage. Ophthalmic Surg Lasers Imaging. 2008;39:100–6.
6. Pardue MT, Hejny C, Gilbert JA, Phillips MJ, Geroski DH, Edelhauser HF. Retinal function after subconjunctival injection of carboplatin in fibrin sealant. Retina. 2004;24:776–82.
7. Blumenkranz MS, Ohana E, Shaikh S, Chang S, Coll G, Morse LS, et al. Adjuvant methods in macular hole surgery: intraoperative plasma-thrombin mixture and postoperative fluid–gas exchange. Ophthalmic Surg Lasers. 2001;32:198–207.
8. Al Sabti K, Kumar N, Chow DR, Kapusta MA. Management of optic disc pit associated macular detachment with Tisseel® fibrin sealant. Retin Cases Brief Rep. 2008;2:274–7.
9. Kumar N, Al SK. Optic disc pit maculopathy treated with vitrectomy, internal limiting membrane peeling, and gas tamponade: a report of two cases. Eur J Ophthalmol. 2009;19:897–907.
10. Uhlig CE, Gerding H. Fibrin sealant improves stability of corneal prostheses during vitreoretinal procedures. Retina. 2003;23:2.
11. Tyagi M, Basu S. Glue-assisted retinopexy for rhegmatogenous retinal detachments (GuARD): a novel surgical technique for closing retinal breaks. Indian J Ophthalmol. 2019;67(5):677.
12. Thompson DF, Letassy NA, Thompson GD. Fibrin glue: a review of its preparation, efficacy, and adverse effects as a topical hemostat. Drug Intell Clin Pharm. 1988;22:946–52.
13. Chhabat J, Tellier M, Porte P, Steinbuch M. Properties of a new fibrin glue stable in liquid state. Thromb Res. 1994;15:525–33.
14. Le Guinennec L, Layrollle P, Daculsi G. A review of bioceramics and fibrin sealant. Eur Cell Mater. 2004;8:1–10.
15. Tassman IS. Experimental studies with physiologic glue (autogenous plasma plus thrombin) for use in the eyes. Am J Ophthalmol. 1950;33:870–8.
16. Bhatia SS. Ocular surface sealants and adhesives. Ocul Surf. 2006;4(3):146–54. https://doi.org/10.1016/s1542-0124(12)70041-1.
17. Panchal B, Tyagi M, Pathengay A, Sharma S, Dave VP, Gandhi U, Balkrishnan D, Pappuru RR, Joseph J, Kekunnaya R, Das T. Endophthalmitis following suture removal-clinical outcomes and microbiological profile. In: Seminars in ophthalmology, vol. 34. Basingstoke: Taylor & Francis; 2019. p. 115–23.
18. Uy HS, Reyes JM, Flores JD, Lim-Bon-Siong R. Comparison of fibrin glue and sutures for attaching conjunctival autografts after pterygium excision. Ophthalmology. 2001;108:115–23.
19. Blumenkranz MS, Ohana E, Shaikh S, Chang S, Coll G, Morse LS, De Bostros S. Adjuvant methods in macular hole surgery: intraoperative plasma-thrombin mixture and postoperative fluid–gas exchange. Ophthalmic Surg Lasers. 2001;32(3):198–207.

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