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Review Article

Use of Fibrin Glue in Maxillofacial Surgery

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Abstract

Objective: To describe various applications of homologous fibrin glue in maxillofacial surgery. The clinical outcomes of the treated cases are discussed.

Methods: During the period January 1993 to July 1995, 71 patients underwent maxillofacial procedures in which homologous fibrin glue was utilized. The material used in each case was Tisseel™, which is composed of human fibrinogen and bovine thrombin. The material was used to provide close and secure re-approximation of soft tissue in 20 patients requiring coronal flaps. Bone or alloplast fixation was undertaken with fibrin sealant in 14 patients. In 13 cleft lip and palate patients, the material was used in the repair of residual fistulas or clefts. Twelve patients had sinus lift procedures where the material fixated the bone graft and repaired the torn mucoperiosteal lining. Finally, 12 patients with coagulopathies had fibrin glue placed following exodontia. All patients were followed for a minimum of 6 months postoperatively.

Results: Seventy patients treated with Tisseel™ had successful outcomes as determined by preoperative criteria. A single oral antral fistula recurred 3 weeks after surgery. No adverse reaction to the material was noted in any of the patients.

Conclusions: Homologous fibrin glue has various applications in the field of maxillofacial surgery and can be used with safe and predictable results.

Sommaire

Objectif: Décrire les applications variées de la colle de fibrine homologue dans la chirugir maxillo-faciale. L'évolution clinique des cas traités est discutée.

Méthodes: Au cours de la période de janvier 1993 à juillet 1995, 71 patients ont subi des interventions mexillo-faciales au cours desquelles de la colle de fibrine homologue fut employée. Le matériel employé dans chaque cas fut le "Tisseel"™, qui est composé de fibrinogène humain et de thrombine bovine. Le matériel fut employé pour assurer une ré-approximation serrée et sécuritaire des tissus mous dans 20 patients nécessitant des lambeaux de type coronal. La fixation d'os ou d'alloplast fut faite avec la colle de fibrine chez 14 patients. Chez 13 patients avec fissure labiale et palatine, le matériel fut employé pour la réparation de fissures ou de fistules résiduelles. Douze patients subirent des interventions pour remonter le sinus au cours desquelles le matériel a fixé la greffe osseuse et réparé le revêtement mucopériosté déchiré. Finalement, 12 patients avec coagulopathies eurent une application de colle de fibrine à la suite d'une exodontie. Tous les patients eurent un suivi postopératoire de 6 mois au minimum.

Résultats: Soixante-dix patients traités avec le "Tisseel" eurent une évolution favorable selon les critères déterminés en préopératoire. Seule une fistule oro-antrale a récidivé 3 semaines après la chirugie. Aucune réaction adverse au matériel ne fut notée chez aucun des patients.

Conclusions: La colle de fibrine homologue a des applications variées dans le champ de la chirugie maxillo-faciale et peut être employée avec des résultats sécuritaires et prévisibles.

Key words: fibrin glue, maxillofacial surgery

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Surgeons have long sought a product that could act as both a tissue adhesive and a hemostatic agent. Unfortunately, the ideal characteristics of an adhesive differ from those of a hemostatic agent. Presently, fibrin glue demonstrates the best equilibrium between both properties.

Fibrin was first used by Bergel[1] in 1909 to establish hemostasis. In 1915, Grey[2] used topical fibrin to provide for hemostasis while performing cerebral surgery. In 1940 Young and Medawar[3] noted that fib-

rinogen could act as a tissue adhesive. Cronkite et al.[4] in 1943, mixed bovine thrombin with plasma fibrinogen to produce the first biologic adhesive. One year later, Tidrick and Warren[5] were using fibrin to fixate skin grafts. In 1972, Matras et al.[6] enhanced the effectiveness of fibrin glue (FG) by increasing its fibrinogen concentration. Fearing possible viral transmission, the U.S. Food and Drug Administration banned the sale of homologous fibrin glue in 1978. Virally inactivated homologous fibrin glue has been available in Europe and Canada for numerous years. Presently, only autologous FG products are available in the United States, but phase-two clinical trials involving homologous fibrin glue are now underway.

Several homologous FG preparations exist. These include Tisseel™, Beriplast™, Biscol™, and Hemacure™. These products differ primarily in the concentration of their components. The various components of Tisseel™ are listed in Table 1.[7]

Preparation of the FG involves several steps and can be performed in approximately 10 minutes. The vials containing the Tisseel™ and aprotinin solution are placed in the Fibrinotherm™ heating and mixing unit. The unit heats both components to 37°C. The aprotinin is then transfered using a supplied syringe into the Tisseel™ vial. This forms component I. The Tisseel™ vial contains a tiny mixing rod. When the vial is placed in the mixing part of the Fibrinotherm™ unit, a uniform mixing and disolving of the product results. The clinician may choose the desired thrombin concentration, either 4 IU/mL or the faster setting 500 IU/mL. The calcium chloride is added to the heated thrombin via a second syringe. This forms component II. Components I and II are mixed together at delivery using the Duploject™ syringe system. This supplied dual-syringe system allows the simultaneous application of both components, ensuring that they are quickly and thoroughly mixed. This system has numerous optional attachments, including spray heads and application catheters.

Concern exists over the possibility of viral transmission when using a pooled homologous blood source. Tisseel™ is prepared from selected donors who undergo extensive screening. Virilogic testing and vapour heat treatment of all donor products is performed. To date, close to 2.5-million administrations of the product have occurred and not a single documented case of viral transmission has been noted. This article reports the results in 71 patients who received Tisseel™ during maxillofacial procedures.

Material and Methods

During the period January 1993 to July 1995, homologous fibrin glue was used in 71 patients who underwent procedures in the maxillofacial region. The material used in all cases was Tisseel™ (Immuno, Austria).

Table 1 Components of Tisseel™

1. Protein concentrate (human):	
Total protein	100–130 mg/mL
Factor XIII	10–50 U/mL
Fibrinogen	70–110 mg/mL
Fibronectin	2–9 mg/mL
Plasminogen	40–120 µg/mL
2. Aprotinin solution, bovine	3000 KIU/mL
3. Thrombin, freeze dried, bovine	500 or 4 IU/mL
4. Calcium chloride solution	40 mmol/L

The amount of material used and the postoperative course of each patient was noted. A breakdown of these data is noted in Table 2.

Sprayed FG was used to provide close and secure reapproximation of soft tissue in 20 patients requiring coronal flaps. In those patients undergoing esthetic procedures, FG was applied after addressing the frontalis, procerus, and corrugator supercilii muscles, and during the final reapproximation of the overlying flap to its new position.

Bone grafts or alloplasts were fixated with FG in 14 patients. Ten patients had cancellous grafts stabilized with FG. The grafts were placed for either augmentation of alveolar ridges (Figs. 1 and 2), the reconstruction of mandibular discontinuity defects, or the stabilization of osteotomy sites (Fig. 3). Three alloplastic implants were stabilized with FG. In all cases, the alloplast used was Biocoral™. Finally, in a single instance, an orbital-floor calvarial graft was fixated with FG (Fig. 4). The graft was used to reconstruct an orbital-floor defect in a patient with a zygomaticomaxillary fracture.

In 13 cleft lip and palate patients, persistent oronasal fistulae were repaired using local flaps and FG. All cases had failed earlier attempts at closure and presented with significant scarring of the palatal soft tissue. Fibrin glue was used in each instance to help with closure of the nasal lining. A combination of sutures and FG was used to provide oral closure.

Twelve patients underwent maxillary sinus lift bone grafting. Potential difficulties inherent with this technique include stabilizing the bone graft in the maxillary sinus. The second potential problem occurs when the thin mucoperiosteal-sinus lining is torn during the dissection. Fibrin glue was used to stabilize the cancel-

Table 2 Amount of Fibrin Glue Used for Various Indications

		Amount (mL)	
Indication	*n*	*Range*	*Mean*
Coronal flaps	20	3–6	4
Bone grafts	14	4–12	6.7
Oronasal fistula	13	6–7	6.5
Maxillary sinus lifts	12	6–7	6
Exodontia in coagulopathy patients	12	1–2	1.8

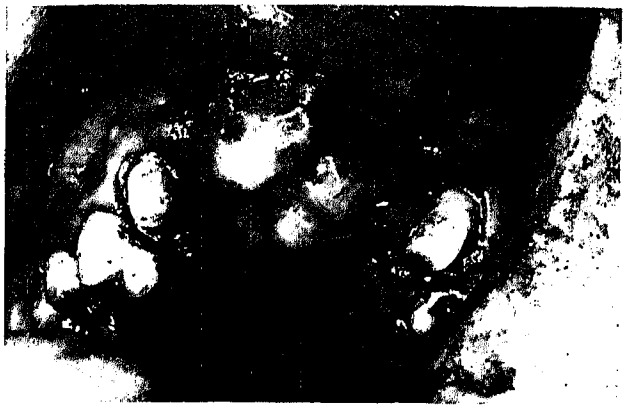

Figure 1 Alveolar crest cancellous bone graft secured with fibrin glue.

lous bone in the desired position and to repair the thin sinus lining, thus ensuring that the graft was isolated from the lumen of the maxillary sinus (Fig. 5).

Finally, FG was used to achieve hemostasis in 12 patients who underwent dental extractions. The patients in whom FG was used had either a congenital factor deficiency (factor VIII or IX) or factor deficiency secondary to advanced liver disease. Following extraction of the involved teeth, the sockets were curreted and irrigated, and FG was applied to the sockets using the Duploject™ syringe (Fig. 6). No further hemostatic measures were used.

Results

All patients were followed for a minimum of 6 months. The average amount of Tisseel™ used per case was 5 mL (range, 1–12 mL). Table 2 lists the means and ranges of the amount of Tisseel™ used for each procedure category.

Seventy patients treated with Tisseel™ had successful outcomes. No adverse reaction to the material was noted in any patient. There were no postoperative hematoma or seroma formations in the coronal flap patients. Bone grafts and alloplasts fixated with FG remained radiographically in place during the healing or incorporation phase. No further bleeding in the coagulopathy patients who underwent extractions was noted. Twelve of the 13 oronasal fistulae remained successfully closed at a minimum of 6 months follow-up. A single fistula recurred 3 weeks after surgery.

Discussion

Fibrin glue mimicks the final stage of the coagulation cascade in which thrombin cleaves fibrinopeptides A and B from fibrinogen forming a fibrin monomer. Crosslinking of the fibrin monomer by the action of factor XIII in the presence of calcium results in a stable fibrin clot. Hemostasis is thus possible, even in the face of a coagulation defect.

Presently, both homologous and autologous forms of fibrin glue have found numerous applications in various surgical specialties. In the field of orthopaedic surgery, FG has been used for the repair of osteochondral talar fractures and radial head fractures.

Cardiovascular surgeons have used the product for numerous years to seal both aortic and coronary artery leaks during bypass surgery, and to seal implanted vascular grafts. General surgeons have controlled gastrointestinal, hepatic, splenic, and pancreatic bleeding using FG. Thoracic surgeons have used FG to seal esophagogastric anastomoses and to close pleuropulmonary and bronchopleural fistula.[8] Postoperative chylothorax has also been successfully treated using FG.[9]

Neurosurgeons have controlled intracranial bleeding and repaired dural tears with fibrin glue.[10,11] Fibrin glue has also been successfully used to stop postoperative CSF leaks.[12] In the field of orbital surgery, FG has been used to reapproximate conjunctiva, repair corneal perforations, and treat retinal detachments.[13]

Otolaryngologists have used FG to decrease or eliminate the need for nasal packing following functional endoscopic sinus surgery.[14] A decreased hospital stay was also noted when FG was used during thyroidectomies.[15]

Figure 2 Tongue flap used for soft tissue coverage of graft.

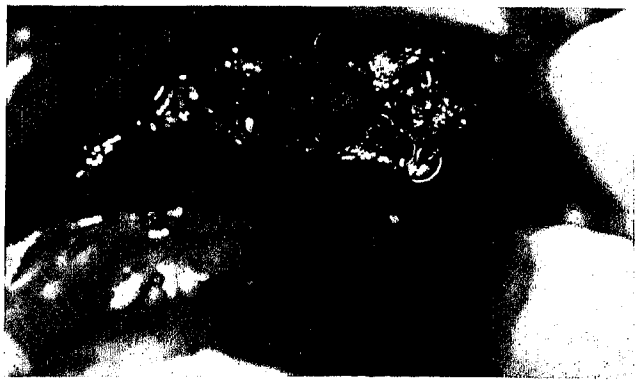

Figure 3 Bone graft secured with fibrin glue in LeFort I level osteotomy.

Figure 4 Split calvarial bone graft to orbital floor defect fixated with fibrin glue.

Compared to diathermy, an FG-treated group had decreased post-tonsillectomy pain, with no difference in primary or secondary bleeding noted between the two groups.[16] Fibrin glue has also been used to secure tympanic membrane grafts and in ossicular reconstruction.[17]

In the area of craniofacial surgery, Marchac and Renier[18] mixed FG with a bone paste. The paste was mixed with the fibrin/aprotinin component alone in a 1:1 ratio. The thick paste was then molded into the desired shape, after which the thrombin component was added causing it to solidify. The final product could be further shaped and was easier to secure to the recipient site than cancellous bone alone. Marchac and Sandor[19] demonstrated a statistically significant decrease in major hematoma development when FG was sprayed between the SMAS layer and the overlying skin flap in face-lift surgery. Blepharoplasty incisions have been closed with the aid of FG, necessitating fewer sutures. Grafts for the coverage of burns or difficult wounds have been successfully secured in place with FG alone or in combination with a minimal number of sutures.

Fibrin glue has numerous applications in oral and maxillofacial surgery. Tayapongsak et al.[20] used FG to secure cancellous bone grafts to homologous mandibles during reconstruction. In the rabbit model, FG allowed for easier soft-tissue reapproximation following osteoplasties of the mandibular condyle.[21] Several clinicians have noted that hydroxyapatite granules are much more easily handled and are less likely to become displaced when FG is used to secure them.[22]

Cavernous hemangiomas of the tongue and lip have been initially treated with intralesional injection of Tisseel™. Halling and Merten[23] claim that hemangiomas less than 15 mm in diameter will involute spontaneously after 1 or 2 intralesional injections of FG performed over a 4-week period. The often-difficult excision of ranulas has also been facilitated by the intraluminal injection of FG, resulting in easier dissection once the material has solidified.[24]

Fibrin glue has been used to provide hemostasis following dental extraction in patients with inhereted coagulation defects or advanced liver disease, or in those taking anticoagulants. Martinowitz et al.[25] described the use of FG in anticoagulated patients requiring exodontia with INR values above 2.5. Conventional hemostatic agents such as collagen matrices (Gelfoam™), oxidized cellulose matrices (Surgicel™), and topical thrombin are usually ineffective in patients with low platelet counts or deficient coagulation factors. Expensive replacement therapy is usually required in the factor-deficient patient. Rakocz et al.[26] showed very good success at providing postextraction hemostasis with Tisseel™ in all but the most severe of hemophiliacs. Martinowitz and Schulman[27] claim that the use of FG instead of factor concentrates in exodontia and minor surgery result in a ten-fold reduction in cost. Factor replacement may still be neccessary but in reduced amounts. An evaluation of this is currently underway.

Tisseel™ is one of the several commercially available homologous fibrin glues. The cost per mL is approximately Cdn$100, including the fibrin glue and applicator. This compares favourably with the quoted costs of autologous fibrin glue (US$103/mL *plus* US$50 for thrombin *plus* US$50 for the applicator).[28] Autologous and homologous fibrin glue products also differ in terms of the content and concentration of components.

The concentration of fibrinogen is usually considerably lower in the autologous FG products compared to homologous FG. Fibrinogen is important for the shear adhesive strength of the product. Saltz et al.[29] demonstrated experimentally that by increasing fib-

Figure 5 Maxillary sinus lift bone graft secured in place with fibrin glue.

rinogen levels from 20 to 70 mg/mL, the shear adhesive strength of fibrin glue is increased 19-fold.

The breaking strength of the clot is affected by fibrin crosslinking; therefore, factor XIII levels are also important. Native factor XIII, loosely bound to the fibrinogen, is present in concentrations of 10 U/mL and seems to be adequate for efficacy of the fibrin glue.[30]

The working time of the fibrin glue can be altered by varying the concentration of the thrombin. When 4 IU/mL of thrombin is used, the working time is 30 or more seconds before a fibrin clot will form. When 500 IU/mL of thrombin is used, the fibrin clot forms within 5 seconds. This is fairly constant for thrombin concentrations between 20 and 1000 IU/m.[30]

The addition of an antifibrinolytic to fibrin glue is controversial and is one reason the FDA has not yet approved its sale in the United States. The antifibrinolytic most commonly used in homologous fibrin glue is bovine aprotinin. Tranexamic acid and aminocaproic acid have also been used. The manufacturers of homologous glue claim that the absorption rate of the fibrin glue can be slowed by the addition of an antifibrinolytic. This is of particular benefit in areas of high-fibrinolytic activity, such as the oral cavity, but may not be important in other tissues, such as bone.[31]

Several reactions to the components of fibrin glue have been noted. Nonfatal anaphylactic reactions to aprotinin have been described. Wuthrich et al.[32] also demonstrated an IgE-mediated anaphylactic reaction to aprotinin. Aprotinin is a polypeptide derived from bovine lung and has potential antigenicity. Berguer et al.[33] described two cases, one fatal, in which profound hypotension developed after treating deep liver lacerations with nonaprotinin-containing fibrin glue.

Bovine thrombin also contains bovine factor V, which can be antigenic. The inhibitors of bovine factor V can crossreact with human factor V. This can result in a significant reduction in human factor V levels. Reexposure to FG will also increase the likelihood of developing inhibitors. Tissucol™ (Immuno, France) has overcome this problem by using human thrombin in their homologous FG preparations.

This article describes several new applications for homologous fibrin glue. The volume of FG used for some of the procedures is higher than expected as a result of a learning-curve phenomenon and operator and assistant errors, particularly during the early part of this series.

Broad conclusions on any of the procedures performed in our series are not possible due to the limited sample size and the lack of controls. We believe, however, that the use of FG improved our outcomes or facilitated the procedure in several ways.

Placement of osseointegrated implants in the posterior edentulous maxilla often requires bone grafting of this area. The graft, usually cancellous bone harvested from the ilium, is placed below an intact mucoperiosteal sinus lining. An intact lining stabilizes and isolates the graft from the remainder of the sinus. Several clinicians recommend aborting the procedure if large tears in the thin mucoperiosteal lining occur. Fibrin glue allowed us to stabilize the graft easily and repair tears in the lining, thus ensuring its isolation from the maxillary sinus.

Figure 6 Fibrin glue used to obtain hemostasis in extraction site of patient with coagulopathy.

Persistant oronasal fistulae are often challenging to repair. A double-layered closure is preferred, as it decreases the incidence of fistula recurrence. The nasal layer, however, can be difficult to close, particularly in redo cleft lip and palate cases. Fibrin glue allowed easier closure of the nasal layer.

Patients with coagulopathies of mild-to-moderate severity were able to undergo simple exodontia without the use of factor replacement. Fibrin glue, in this situation, appeared to be more cost effective, decreased the total treatment time, and in all but the most severe of coagulopathies, eliminated the risks involved with factor replacement.

Patient comfort was improved by spraying FG under coronal flaps during reapproximation, thus eliminating the need for postoperative drains. It would seem that this technique does not increase the risk of hematoma or seroma development.

In nonloaded areas, FG alone provided sufficient support for bone grafts. This not only eased the stabilization of cancellous grafts in particular, but also eliminated the potential need of having to remove the fixation hardware at a later date. There is, however, no contraindication to using FG in the presence of fixation hardware. This is often necessary in loaded areas requiring bone grafting of defects. Most recently, we have begun using FG together with bioresorbable plates (Lactosorb™, Walter Lorenz, Jacksonville, FL) for recontructing complex maxillofacial fractures. Fibrin glue has been used to stabilize nonloaded bone grafts, and the resorbable plates have been used to fix-

ate fractures. In our opinion, this is an ideal combination as it represents a completely biodegradable system.

Fibrin glue has numerous applications in the field of maxillofacial surgery. It is a safe, cost-effective, and clinically proven method of providing hemostasis, securing or glueing hard and soft tissue, and sealing friable or difficult-to-reach tissues. It does not, however, replace good surgical technique.

Future applications of this product include using FG as a vehicle for the delivery of antibiotics and growth factors. Improved methods of producing autologous fibrin glue and recombinant products are also under development. Presently, homologous fibrin glue offers several advantages over its autologous counterpart. These include lower cost, ease of procurement, and better mechanical properties. The only disadvantage is the possibility of disease transmission. To date, however, there has not been a single documented case of disease transmission in well over 2.5 million administrations of the product.

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