Original Article

Preparation of two component Fibrin Glue and its clinical evaluation in skin grafts and flaps

Samir Saxena, Pradeep Jain, Jyoti Shukla

Department of Plastic Surgery and Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi.

Address for correspondence: Dr. Pradeep Jain, 2-B, Brij Enclave, Sunderpur, Varanasi-221005, India. E-mail: drpmjain@rediffmail.com

ABSTRACT

Tissue adhesive is one of the alternative to conventional suturing and has some added advantages. Fibrin glue has been used in obtaining haemostasis following trauma to spleen and liver. It has also been used in repair of dural tear and bronchial fistula. Fibrin glue is a biological tissue adhesive based on the final stage of coagulation wherein. Thrombin acting on fibrinogen converts it into fibrin. Thus, it has two components, one is fibrinogen and another is thrombin. We have prepared both components of fibrin glue. Fibrinogen was obtained from patient's own blood and thrombin from fresh frozen plasma of screened healthy donor. The glue was used in 20 cases requiring skin graft or flap. The results were compared with conventional suturing method. Use of the fibrin glue is simple, safe, cost effective, and rapid technique to fix the skin grafts and flaps with avoidance of peroperative bleeding and postoperative collection. It also has better overall results.

KEY WORDS

Fibrin Glue, Plastic Surgery, Fixation of Skin Grafts & Flaps.

INTRODUCTION

Through the centuries, surgeons have been using sutures made up of different materials to repair disrupted tissues. But these may have certain disadvantages like foreign body reaction, infection, scarring, need for removal and cost. Their application is slow and needs skill. In the search of solution of these problems, concept of tissue adhesive was floated. Although the use of fibrin as a biologic adhesive was first reported by Bergel as early as in 1909, it was not until 1944 that Tidrick and Warner used fibrin for skin graft fixation.[1] Fibrin glue is a biological tissue adhesive which initiates the final stages of coagulation when a solution of human fibrinogen is activated by thrombin (the two components of fibrin glue). Numerous uses of fibrin glue as a sealant, hemostatic agent and adhesive have been reported not only in the discipline of Plastic Surgery but also in other specialities.[1-9] Commercially available fibrin glue has been used extensively in Europe with has its own risks. This led to the development of numerous techniques to produce autologous glue preparation.[2-6] But these methods usually make only one component of glue (mainly fibrinogen) from blood of patients or donors. Many of these techniques are costly, cumbersome and time taking. Here, we present our experience of preparing both components of glue in a simple way with least monetary burden on the patients. Fibrinogen was obtained from patient's own blood and thrombin form fresh frozen plasma of healthy tested donors. The glue, thus prepared, was used for fixation of skin grafts

and insetting of flaps in 20 cases.

MATERIAL AND METHODS

20 patients for the clinical evaluation of fibrin glue were selected requiring raw areas to be covered by skin graft (split or full thickness) or reconstruction by a flap (10 in each group) and similar number of patients were taken as control in which conventional suturing was done. Two components (fibrinogen and thrombin) of fibrin glue were prepared in the following manner:

(a) **Fibrinogen** : It was prepared according to the technique of Hartman et al[10] with minor modification. A day before operation, 10 ml of patient's venous blood for every 100 cm^2 of anticipated skin graft/flap, was drawn in a heparinised syringe. It was centrifuged at 3,000 rpm for 10 minutes and the separated plasma was then aspirated with a spinal needle. The whole procedure was performed in strict sterile conditions. This plasma served as a source of fibrinogen and was stored in a syringe at less then -20 ^{0}C. The concentration of fibrinogen in this plasma was 350-450 mg/100 ml.

(b) **Thrombin** : It was prepared according to the method described by Armand J Quick.[11] This was obtained from fresh frozen plasma (FFP) of healthy donors screened negative for HIV and Hepatitis B. 10 ml of FFP was thawed to 2-4 ^{0}C and was 10 times diluted with distilled water, making 100 ml of solution. In this, 1 ml of 1% acetic acid was added to make the pH 5.3. and this resulted in the formation of precipitate. This was kept for half an hour and then centrifuged at 3000 rpm for 5 minutes. The precipitate was collected and in this, normal saline was added to make it 10 ml and then pH was brought up to approximately 7 by titrating with sodium carbonate. This was put in a water bath (37 ^{0}C) and 0.1 ml of 0.1 M $CaCl_2$ (Calcium Chloride) was added. The clot which formed in 45-120 seconds was removed by wrapping it around a stirring glass rod. The thrombin solution thus prepared was water clear and was constant in potency. The strength of thrombin was standardized to 10 second of thrombin time with the help of full strength thrombin solution. This thrombin solution was stored in deep freeze at less than -20^{0}C to maintain the potency and could be used up to a month.

Cold chain was maintained for both the components of fibrin glue till their application. Before use, the syringes containing two components of fibrin glue were taken out from the deep freeze and thawed to room temperature.

In the study group, one component (either) of fibrin glue in syringe was evenly sprinkled on the undersurface of graft or flap and the other over the recipient bed (Figures 1 & 2). 5 ml of each component

Figure 1: Fibrinogen applied on the bed after release of post-burn contracture of neck while thrombin on undersurface of graft

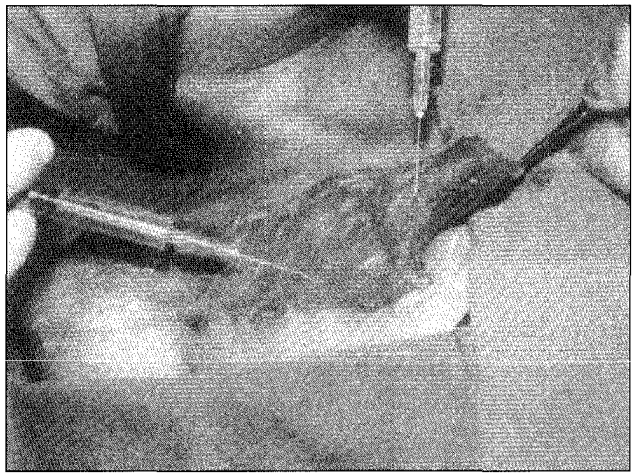

Figure 2: Fibrinogen applied on the bed and thrombin on undersurface of deltopectoral flap, which was being returned to donor site

solution was required for every 100 cm^2 wound area. The graft/flap was oriented and applied to the bed. No suturing was done in graft while few anchoring sutures were applied on the flap. Fibrin clot formation and adherence of graft/flap was noted within minutes. In the control group, Split-thickness sking graft was fixed with chromic calgut and Full thickness skin graft with Prolene. The flaps were sutured in conventional manner.

RESULTS

Observations in fibrin glue group (graft and flap) and control were noted and compared. Procedure of grafting/flap in setting was easy and comfortable when glue was used and difficult and cumbersome at time with conventional suturing particularly with large size defect situated deep in concavities. Duration of procedure was 50% less in glue group than in controls. It was noted that within 2-5 minutes of application of glue components, there was adherence between graft/flap and the bed in all the cases. This adherence was tested by pulling one edge of the graft/flap with a forceps and stickiness was felt. Besides, no hematoma/bleeding was seen at 5 minute in glue group while one case in graft and 4 cases in flap of control group had persistent oozing which was managed accordingly. In postoperative period, 20% cases in control group had collection in the wound while none in glue group. 30% of cases in conventional suturing group had developed suture tract infection at edges. Surface characteristics and graft-edge union in glue group was found to be better than in control cases. Final result as graft take was 96% in glue group and 88% in control group seen at two weeks while flap dehiscence at edge was 10% in control group. No adverse reaction or infection was noted in any of the patients (Table 1).

Table 1: Results at a glance

Parameters	*Fibrin Glue (n=20)*	*Control (n=20)*
Sub-graft/Flap Collection	None	4 (20%)
Suture Tract Infection	None	6 (30%)
Graft take	96%	88%
Flap dehiscence	None	2 (10%)
Adverse reaction	None	-

DISCUSSION

Since the conception of surgery, management of disrupted tissue with the sutures became the centerpoint of research and development. However, an ideal suture having multiple features in one e.g. easy to handle, non-reactivity, low cost, non-toxic, and not promoting infection, is still to be found. Concept of tissue adhesive evolved as the surgeons began to think of an alternative to suture which is devoid of its inherent disadvantages. All tissue adhesives, currently in use today, are organic compounds that form long-chained, covalently linked polymer. The two basic categories of tissue adhesives are – synthetic (commonest is n-butyl-2-cyanoacrylate) and biological (fibrin glue).

The principle behind the use of fibrin glue is taken from wound healing wherein the first phase is inflammation which involves formation of thrombus through series of events in coagulation cascade. The final outcome of this is conversion of fibrinogen to fibrin. Fibrin glue augments the induction of entire process of wound healing as whole of the coagulation cascade is bypassed and readymade fibrin is immediately produced with its adhesive function due to fibrin polymers.[2]

Beside the use of fibrin glue in plastic and reconstructive surgical procedures e.g. skin graft, flaps, microneurovascular repair, the glue is also used in other procedures like dural closure,[5] bronchial fistula,[6] ear surgeries,[7] blepharoplasty,[8] visceral trauma[12] etc.

Numerous techniques[1-4,10] have been used to prepare autologous fibrin glue. But in most of these, only one (fibrinogen) component is prepared from patient's or single donor's blood and other (thrombin) component is usually a commercial bovine one. This thrombin is very expensive, not readily available, has storage problem and may cause adverse reaction. We have obtained fibrinogen from patient's own blood by a simple and rapid method and thrombin from fresh frozen plasma of healthy donors. Thus, this fibrin glue is cost effective and safe alternative to commercially available glue and involves use of basic laboratory equipments only.

Fibrin glue provides numerous advantages for skin

grafting and flap insetting. Operation becomes easy and comfortable with more cosmetically acceptable wound. Glue causes good contouring of grafts particularly in depth, in difficult wounds (neck, axilla etc.) and large defects. This also obviates the need of stitching and bulk dressings for immobilization of skin graft. Thus, post-operative management also becomes handy.

Glue reduces the total operating time because time to control bleeding and meticulous suturing is saved. Haemostatic function of fibrin glue decreases the formation of haematoma/seroma in the post-operative period leading to good take of graft and good incorporation of flap. Buckley et al[1] have also shown such results in skin grafting. Glue also enhances the take of grafts when used on compromised bed (infections).[13]

The use of glue is also associated with least post-operative wound infection contrary to conventional suturing. No adverse reactions to fibrin glue were noted with its use. Use of autologous fibrinogen also minimizes the risk of transmission of blood borne infections though thrombin was obtained from screened healthy donors.

CONCLUSION

Autologous fibrin glue offers a simple, cost effective, easy and safe alternative to conventional methods for fixation of skin grafts and flaps with better final results and least postoperative care.

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