



ROLE OF AUTOLOGUS FIBRIN TISSUE ADHESIVE IN ABDOMINAL SURGERY

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rezime Fibrin tissue adhesive (FTA) is an agent developed for achieving better hemostasis and adhesion of living tissue. FTA appears to have no tissue toxicity, promotes a firm seal in seconds to minutes, is reabsorbed in days to weeks following application, and appears to promote local tissue growth and repair. It can be used in various surgical procedures. It has been used preoperatively, perioperatively and postoperatively in abdominal surgical procedures. There were no side effects. Improvement of surgical hemostasis was obvious in all patients. Anastomotic leakages were closed in a shorter time without surgical intervention. Sero-lymphatic drainage after surgical procedures that include extensive lymph node dissections was less. Use of FTA in treatment of fistula in ano was successful. The data would indicate that use of FTA may be a good alternative in solving various conditions in every day clinical practice, although a bigger randomized series, and longer follow up is needed.

Key words: fibrin tissue adhesive, wound healing

INTRODUCTION

Last step of coagulation process is characterised by proteolytic cleavage of fibrinogen to fibrin monomers by thrombin. Fibrin monomers polymerize into fibrin fibers, which in the presence of factor XIII, fibronectin, and ionized calcium forms a stabile, insoluble, nonfriable fibrin clot or seal.

Fibrin is main structural protein in blood responsible in conjunction with platelets in achieving hemostasis.

There is strong indirect evidence that of fibrin plays important role in wound healing. In wounds fibrin acts as a glue between wound edges, provides a scaffold for ingrowing fibroblasts, stimulates reparative cells (monocytes, macrophages, fibroblasts) either directly or by its degradation products.

Proteolitical cleavage of the fibrin cloth leads to absolute reabsorption of fibrin.

All these beneficial properties of fibrin argue in favour of its use in various surgical situations.

Fibrin tissue adhesive is a topical biodegradable plasma-derived product, which mimics the final stages of coagulation cascade.

FTA is based on two components mixture: (component 1) fibrinogen, factor XIII and fibrinogen concentrate and antifibrinolytic; (component 2) CaCl₂ solution and bovine or human trombin.

It could be obtained as commercially prepared fibrin glue systems or from blood banks, so called "homemade fibrin glue".

In commercially available products component 1 is obtained from multiple, pooled, human blood plasma. There is the potential risk of transmission of blood human plasma borne viruses (hepatitis, acquired immune deficiency syndrome, and other blood-transmitted diseases) in such products.

Using plasma from plasma donors who are regularly tested ("accredited donors") can reduce the risk of transmission of infection. (single donor fibrin tissue adhesive SD-FTA).

Autologous fibrin tissue adhesive (A-FTA) is prepared in advance of surgery from the patient's own blood (autologous blood). The use of an autologous source to prepare fibrin glue eliminates the risk of viral disease transmission.

A variety of simple and economical techniques (cryoprecipitation, polyethylene glycol or ammonium sulfate precipitation) for the production of component 1 from single-donor or autologous plasma have been described and evaluated. All this enables the FTA to be made in large quantities with no greater risk of disease transmission than the risk from transfusion of single-unit fresh-frozen plasma in almost every Blood Bank.

Table 3

Comparison between industrial and autologous fibrin tissue adhesives				
	Industrial products		Autologous	
	con	pro	con	pro
Rheological properties		High FB content FB purity 70-90% Elasticity Tensile strength Adhesiveness Higher expected performance	Low FB content FB purity <50% Lower performance?	Controlled processes ¹
Viral safety	Pooling	Donor selection Screening tests Viral reduction treatments GMP	Microbial or viral contamination is not excluded if processing is done in an open system No quality control test Less reproducible?	Single donor Controlled processes ¹
Reproducibility		Standardized Established specifications Quality control on samples		

FB=Fibrinogen

Modified from Fibrin Sealnat, Radosevich, Goubran, Barnouf. Vox Sang 1997,72;133-143

Comparison between industrial and A-FTA are shown on the table 1

MATERIALS AND METHODS

A/FTA and SD/FTA made in national Blood Transfusion Institute were used.

Component 1 was made by modified three cyclic cryoprecipitation procedure (by Bela Balint) in addition of commercial aprotinin (3000/10 000 KIU/mL). Characteristics of this so called "homemade" fibrin tissue adhesive were: total protein 121/165 mg/mL; plasmafibrinogen 73,11,2 mg/mL; factor XIII 7,530,47mg/mL.

Component 2: CaCl₂ solution (40 mM/L) with bowin thrombin (500NIH-U/mL)

Tensile strength of FTA was 1,1680,16 N/cm².

Component 1 and Component 2 were mixed in equal volume during the application. They were applied on, as much as possible, dry tissue by means of spraying or squirting it from separate syringes in a variety of surgical situations.

Urgent surgery

Perioperatively:

improvement of surgical hemostasis

Elective surgery

1. Preoperatively: hemostasis

2. Perioperatively: improvement of surgical hemostasis, reducing postoperative sero-lymphatic secretion, treatment of fistula in ano, pancreatic surgery.

3. Postoperatively: anastomotic leakage

RESULTS

From the 1st January 1997 to the 30th September 1999 in the Institute for Digestive Diseases, FTA was used in treatment of 142 patients. There were 164 male and 39 female patients, aged between 22 and 84 years (average 53,6 years).

Perioperatively:

a) FTA was applied to bleeding parenchymal wounds: perioperative spleen injury (7 pts.), salvage of injured spleen after blunt trauma (3 pts.) and in three patients sealing of the resected spleen; resections of the liver (16 pts.) and in one patient sealing of renal and liver tears after blunt trauma.

b) pancreatic surgery Whipple procedure (14 pts.) postoperative sero-lymphatic secretion 10050 mL distal pancreatectomy postoperative sero-lymphatic secretion 125100 mL;

c) reducing intraoperative hemorrhage and postoperative sero-lymphatic secretion: Miles procedure (32 pts.) perioperative blood loss average was 250 mL 125mL, and postoperative sero-lymphatic secretion average 125 mL 75

mL, extensive pelvic surgery for advanced rectal cancer perioperative blood loss average was 320 mL 140 mL and postoperative sero-lymphatic secretion was average 175 mL 75 mL;

d) treatment of fistula in ano (93 pts). There were 18 pts. operated previously (1 to 3 operations). 68 pts. Had transphinteric (23 pts. had high transphinteric fistula) and 17 pts. had intersphinteric fistula. Five patients had horse-shoe and three patients had multiple fistulas. Accessory fistula tracts had 58 pts. 24 patients healed completely, 4 healed after multiple attempts (max 3) and 2 showed no improvement. Postoperatively one patient had inersphinteric abscess (morbidity 0.3%). Median hospital stay was 3 days. Patient discomfort was minimal. 30 patients were followed for 3 to 11 months. There was no postoperative impairment of anal sphincter. Sealing of anastomotic leakage in 12 patients.

Attempts of closure ranged from 1 to 20 in average of 5 days (min 2 days max 28 days). In one patient sealing of the gastrostomy.

CONCLUSION

It may be concluded that fibrin sealing is a complication-free, highly effective and very useful operative sealant; it can be applied to bleeding parenchymal wounds; FTA reduces the need for parenchymal sutures that may be traumatic; it promotes splenic wound healing; FTA reduce operative blood loss; sero-lymphatic drainage after surgical procedures that include extensive lymph node dissections was reduced. The minimal postoperative care associated with early return to normal activities seems to increase the satisfaction of patients and nursing staff.

Bleeding, biliary fistula and subphrenic abscess are the major postoperative complications after liver surgery. Many different adjuvant methods have been developed for control of hemorrhage from the raw surface of liver, but the superiority of any single method remains to be proved. The use of two-component fibrin adhesive for the control of solid organ bleeding seems to be promising.

SAŽETAK

ULOGA AUTOLOGNOG FIBRINSKOG TKIVNO ADHEZIVA U ABDOMINALNOJ HIRURGIJI

Fibrinski tkivni adheziv (FTA) je materija sintetisana radi ostvarivanja bolje hemostaze i adhezije živog tkiva. Može se široko upotrebljavati u različitim hirurškim disciplinama. FTA nema toksični efekat na tkiva, omogućuje ostvarivanje čvrste veze, reabsorbuje se u loku od nekoliko dana i nedelja i ubrzava lokalni rast tkiva i zarastanje. Korišćen je preoperativno, perioperativno i postoperativno u različitim hirurškim disciplinama. Dobijeni podaci ukazuju da je fibrinski tkivni adheziv dobra alternativa za rešavanje različitih hirurških potreba.

Ključne reči: fibrinski tkivni adheziv, zarastanje rana

REFERENCES

1. Rutgeerts P, Rauws E, Wara P, Swain P, Hoos A, Solleder E, Haltunen J, Dobrilla G, Richter G, Prassler R. Randomised trial of single and repeated fibrin glue compared with injection of polidocanol in treatment of bleeding peptic ulcer. *Lancet* 1997 Sep 6; 360(9079):962-6
2. Martinowitz U, Spotnitz WD. Fibrin tissue adhesives. *Thromb Haemost* 1997 Jul; 78(1):661-6
3. Radosevich M, Goubran HI, Burnof T. fibrin sealant; scientific rationale. Production methods, properties, and current clinical use. *Vox Sang* 1997; 72(3):133-43
4. Jackson MR, Friedman SA, Carter AJ, Bayer V, Burge JR, MacPhee MH, Drohan WN, Alving BM. Hemostatic efficacy of a fibrin sealant-based topical agent in a femoral artery injury model: a randomized, blinded, placebo-controlled study. *J Vasc Surg* 1997 Aug; 26(2):274-80
5. Holcomb JB, Pusateri AE, Hess JR, Hetz SP, Harris RA, Tock Bb, Drohan WN, MacPhee MH. Implications of new dry fibrin sealant technology for trauma surgery. *Surg Clin North Am* 1997 Aug; 77(4):943-52
6. Imhof M, Verreet PR, Ohmann C, Roher HD. Endoscopic versus surgical therapy of gastroduodenal ulcer hemorrhage—results of a randomized study. *Langenbecks Arch Chir Suppl Kongressbd* 1997; 114:647-51
7. Spotnitz WD, Fasstrom JK, Rodeheaver GT. The role of sutures and fibrin sealant in wound healing. *Surg Clin North Am* 1997 Jun; 77(3):651-69
8. Kulber DA, Bacilious N, Peters ED, Gayle LB, Hoffman L. The use of fibrin sealant in the prevention of seromas. *Plast Reconstr Surg* 1997 Mar; 99(3):842-9; discussion 850-1
9. Suzuki Y, Kuroda Y, Morita A, Fujino Y, Tanioka Y, Kawamura T, Saitoh Y. Fibrin glue sealing for the prevention of pancreatic fistulas following distal pancreatectomy. *J Cataract Refract Surg* 1995 May; 21(3):320-5
10. Hjortrup A, Moesgaard F, Kjaergard J. Fibrin adhesive in the treatment of perineal fistulas. *Dis Colon Rectum* 1991 Sep; 34(9):752-4
11. Kirkegaard P, Madsen PV. Perineal sinus after removal of the rectum. Occlusion with fibrin adhesive. *Am J Surg* 1983 Jun; 145(6):791-4
12. Jakob H, Campbell CD, Stemberger A, Wriedt-Lubbe i, Blumel G, Replogle RL. Combined application of heterologous collagen and fibrin sealant for liver injuries. *J Surg Res* 1984 Jun; 36(6):571-7
13. Sakon M, Monden M, Gotoh M, Kobayashi K, Kambayashi J, Mori T, Okamura J. Use of microcrystalline collagen powder and fibrinogen tissue adhesive for hemostasis and prevention of rebleeding in patients with hepatocellular carcinoma associated with cirrhosis of the liver. *Surg Gynecol Obstetr* 1989 May; 168(5):453-4
14. Kram HB, del Junco T, Clark SR, Ocampo HP, Shoemaker WC. Techniques of splenic preservation using fibrin glue. *J Trauma* 1990 Jan; 30(1):97-101
15. Ochsner MG, Maniscalco-Theberge ME, Champion HR. Fibrin glue as a hemostatic agent in hepatic and splenic trauma. *J Trauma* 1990 Jul; 30(7):884-7