Aprotinin

Comparative effectiveness of fibrin sealants in cardiac surgery.

Authors: Arnold M.R., Ito D., Magee G., Xiong Y., Testa D., Rubinstein M., Tackett S.

Publication Date: 2015

Abstract:

Objectives: While effectiveness of fibrin sealants for controlling bleeding in cardiac surgery has been demonstrated, there is a paucity of research on other clinical outcomes of fibrin sealants. In this retrospective observational study we analyzed the clinical outcomes of two different fibrin sealants in a population of patients undergoing cardiac surgical procedures. Methods: Data from patients undergoing coronary artery bypass grafting (CABG), valve and valvular procedures with CABG during the years 2008 - 2012 were extracted from Premier's Hospital Database. The Premier Hospital Database is a comprehensive database containing data from over 6 million US hospital discharges annually. Only surgeries in which a fibrin sealant was utilized were included; all other hemostatic agents were excluded from the study. The following clinical outcomes were assessed: major and minor complications, transfusions, surgical revisions for bleeding, operative mortality (hospitalization), OR time and hospital and ICU length of stay (LOS). Logistic regression analyses were performed on categorical outcome variables and GLM regression analyses were performed on continuous outcome variables. Study covariates included: age, primary procedure, Charlson Co-morbidity Index (CCI) score, heparin use, protamine use, admission type, gender, race, teaching hospital, bed size and region. Results: A total of 2,560 inpatient cardiac procedures using fibrin sealant with synthetic aprotinin (FS-apr) were compared to 1,019 procedures using fibrin sealant without aprotinin (FS). Results suggested that FS-apr was associated with significantly lower rates of minor complications (21.1% vs. 27.1%, $p = 0.002$), Day 1 Transfusions (28.6% vs. 36.8%, $p = 0.015$) and ICU LOS (4.7 days vs 7.1 days, $p < 0.0001$) as compared to FS. No significant differences were found between FS-apr and FS on the other clinical outcomes. Conclusions: FS-apr

was associated with signficantly lower rates of Day 1 Transfusions, avoidable minor complications and lower average ICU LOS as compared to FS.

Pharmacological strategies to decrease transfusion requirements in patients undergoing surgery.

Authors: Porte R.J., Leebeek F.W.G.

Publication Date: 2002

Abstract:

Surgical procedures are inevitably associated with bleeding. The amount of blood loss may vary widely between different surgical procedures and depends on surgical as well as non-surgical factors. Whereas adequate surgical haemostasis may suffice in most patients, pro-haemostatic pharmacological agents may be of additional benefit in patients with (diffuse) surgical bleeding or in patients with a specific underlying haemostatic defect. In general, surgical haemostasis and pharmacological therapies can be complementary in controlling blood loss. The use of pharmacological therapies to reduce blood loss and blood transfusions in surgery has historically been restricted to a few drugs. Antifibrinolytic agents (aprotinin, tranexamic acid and aminocaproic acid) have the best evidence supporting their use, especially in cardiac surgery, liver transplantation and some orthopaedic surgical procedures. Meta-analyses of randomised, controlled trials in cardiac patients have suggested a slight benefit of aprotinin, compared with the other antifibrinolytics. Desmopressin is the treatment of choice in patients with mild haemophilia A and von Willebrand disease. It has also been shown to be effective in patients undergoing cardiac surgery who received aspirin up to the time of operation. However, overall evidence does not support a beneficial effect of desmopressin in patients without pre-existing coagulopathy undergoing elective surgical procedures. Topical agents, such as fibrin sealants have been successfully used in a variety of surgical procedures. However, only very few controlled clinical trials have been performed and scientific evidence supporting their use is still limited. Novel drugs, like recombinant factor VIIa (eptacog alfa), are currently under clinical investigation. Recombinant factor VIIa has been introduced for the

treatment of haemophilia patients with inhibitors, either in surgical or non-surgical situations. Preliminary data indicate that it may also be effective in surgical patients without pre-existing coagulation abnormalities. More clinical trials are warranted before definitive conclusions can be drawn about the safety and the exact role of this new drug in surgical patients. Only adequately powered and properly designed randomised, clinical trials will allow us to define the most effective and the safest pharmacological therapies for reducing blood loss and transfusion requirements in surgical patients. Future trials should also consider cost-effectiveness because of considerable differences in the costs of the available pro-haemostatic pharmacological agents.

The role of fibrin sealants in hemostasis.

Authors: Mankad P.S., Codispoti M.

Publication Date: 2001

Abstract:

Hemostasis is a prerequisite for wound healing, and under normal physiologic conditions, it is achieved by means of the coagulation cascade. However, there are a number of surgical procedures where there may be considerable benefits to the patient, surgeon, or health-care costs if hemostasis can be achieved more efficiently. The rapid and effective control of bleeding during and after surgery reduces blood loss and can help reduce postoperative complications. These improved outcomes can reduce the need for transfusion, with the associated risk of viral transmission, and have a positive impact on operative and hospital stay times. Fibrin sealants are surgical hemostatic agents derived from human plasma that reproduce the final steps in the coagulation pathway and form a stable fibrin clot. Fibrin sealants are used in a broad range of surgical procedures to assist hemostasis, including cardiovascular, hepatic, and splenic surgery, gastrointestinal hemorrhage, skin grafting, and dental extractions in anticoagulated patients. Patients with coagulopathies are at high risk of prolonged or excessive bleeding during or after invasive surgery, and these patients may also benefit from the use of fibrin sealants. This article reviews the role of fibrin sealants in hemostasis, citing a number of key clinical studies that report a significant reduction in blood loss or chest drain output after surgery with fibrin sealant compared with controls.

Fate of fibrin sealant in pericardial space.

Authors: Hattori R., Otani H., Omiya H., Tabata S., Nakao Y., Yamamura T., Osako M., Saito Y., Imamura H.

Publication Date: 2000

Abstract:

Background. Although fibrin sealant (Beriplast, Aventis Behring, Marburg, Germany) has been widely used as a supplementary measure for hemostasis during cardiac surgery in Europe and is becoming popular in the United States, the pharmocokinetics of fibrin sealant applied in pericardial space has not been elucidated. Methods. A small incision was made on the epicardial surface of the left ventricle of a rat, and the incision was sutured. Total 0.2 ml of fibrin sealant containing iodine 125 (¹²⁵I)-labeled fibrinogen, aprotinin, blood coagulation factor XIII and thrombin was applied to the area around the suture line. Results. Distributions of ¹²⁵I-labeled fibrinogen in the heart on postoperative days 1, 3, 7, and 14 were 48.2% +/- 1.8%, 20.7% +/- 2.2%, 0.15% +/- 0.02%, and 0.01% +/- 0.02%, respectively. The radioactivity was negligible in the blood, liver, spleen, and kidney except for the thyroid in which the radioactivity increased to 7.9% +/- 0.7% and 4.3% +/- 0.4%, respectively, on postoperative days 7 and 14. Iodine 125-labeled fibrinogen concentrations of the heart and other organs showed a similar change in the time course of distribution. Dense and thick fibrin network, observed on postoperative day 1, had dissipated and was thinner with collagen formation by postoperative day 7. Conclusions. Fibrin sealant applied to the pericardial cavity regresses rapidly and plays an important role in wound healing.

Four years' experience with fibrin sealant in thoracic and cardiovascular surgery.

Authors: Matthew T.L., Spotnitz W.D., Kron I.L., Daniel T.M., Tribble C.G., Nolan S.P.

Publication Date: 1998

Abstract:

A single-donor fibrin sealant system was used in 689 thoracic and cardiovascular surgical procedures over the 4-year period between April 1, 1985, and March 31, 1989. An excellent overall success rate (646/689, 94% effective) was achieved with specific applications, including reduction of leakage of air (29/33, 88% effective), blood (595/ 634, 94% effective), and fluid (14/14, 100% effective), as well as positioning of anatomical structures such as coronary bypass grafts (8/8, 100% effective). Application methods included use of spray bottles (477/497, 96% effective), syringes (165/186, 89% effective), and a Silastic cannula through the flexible fiber-optic bronchoscope (4/6, 67% effective). The system was used in a wide variety of cardiac, pulmonary, esophageal, and vascular procedures to seal staple lines, suture lines, anastomoses, conduits, fistulas, and raw surfaces. No complications with this single-donor system secondary to blood-borne disease have been documented. Overall infection occurred at a nominal rate (16/689, 2%). Thus, fibrin sealant has been a useful tool to control the leakage of air, blood, acid fluid during a wide variety of thoracic and cardiovascular procedures and may be of benefit to other surgeons.

Fibrin sealant, aprotinin, and immune response in children undergoing operations for congenital heart disease [2] (multiple letters).

Authors: Schlag G., Seifert J., Ziemer G., Scheule A.M.

Publication Date: 1998

Abstract:

Not Available

Efficacy of hemostatic agents in improving surgical hemostasis.

Authors: Green D., Wong C.A., Twardowski P.

Publication Date: 1996

Abstract:

Not Available

Immunization against bovine antigens after cardiac surgery.

Authors: Bastien O., Berruyer M., Fffrench P., Paulus S., Belleville J., Amiral J., Estanove S.

Publication Date: 1994

Abstract:

Not Available

Bleeding hearts.

Authors: Estafanous F.G.

Publication Date: 1991

Abstract:

Not Available

Clinical experience with fibrin glue in cardiac surgery.

Authors: Koeveker G., De Vivie E.R., Hellberg K.D.

Publication Date: 1981

Abstract:

Cardiac surgery is often associated with hemostatic abnormalities leading to severe bleeding. Special problems are to be expected, if prosthetic material has to be implanted. Preclotting of Dacron prostheses with blood is well established but failures are sometimes encountered. Several years ago a new hemostatic sealing system (fibrin glue) was introduced into therapy. Since 1978 fibrin glue has been applied in 176 patients. The indications were: 1. sealing of woven-Dacron prosthesis, 2. bleeding from suture-holes (Gore-Tex), 3. diffuse myocardial bleeding and 4. prevention of kinking of coronary artery grafts. In 32 patients with an aortoventriculoplasty operation using Dacron the 'blood preclotting' and 'fibrin sealing' methods were compared. In the fibrin glue group there was a significant reduction in postoperative blood loss as well as shortening of the operation time (period of protamin administration to skin closure). No fibrinolytic dissolution of the fibrin layer on the prostheses was observed.

Aprotinin in fibrin tissue adhesives induces specific antibody response and increases antibody response of high-dose intravenous application.

Authors: Scheule AM, Beierlein W, Wendel HP, Jurmann MJ, Eckstein FS, Ziemer G

Publication Date: 1999

Abstract:

BACKGROUND: In cardiac operations, aprotinin therapy is used either locally as a component of commercially available fibrin tissue adhesives, intravenously, or combined. Our aim was to examine the formation of aprotinin-specific antibodies with regard to the application mode.

METHODS: Sera of 150 patients who had undergone cardiac operations and were receiving aprotinin therapy for the first time were sampled before the operation and at medians of 3.5 and 13.3 months after the operation. Aprotinin-specific IgG including all subgroups and aprotinin-specific IgE were analyzed. Aprotinin was given locally (as contained in fibrin sealant; n = 45; median dose, 6000 KIU), intravenously (n = 46; 2.000 x 10(6) KIU), and combined (n = 59; 2.012 x 10(6) KIU).

RESULTS: At 3.5 months, the prevalence of aprotinin-specific IgG antibodies was 33% (15/45 patients) after local, 28% (13/46 patients) after intravenous, and 69% (41/59 patients) after combined exposure (P =.0001). At 13.3 months, the prevalence of aprotinin-specific IgG antibodies was 10% (4/41 patients) after local, 31% (13/42 patients) after intravenous, and 49% (28/57 patients) after combined exposure. Total aprotinin dose was similar in patients who were antibody positive and negative. Before the operation, no aprotinin-specific antibodies were detected. Aprotinin-specific IgE were not found after the operation.

CONCLUSION: Local aprotinin contact induces a specific immune response and reinforces that of intravenous exposure. The antibody spectrum is identical to the immune response induced by intravenous exposure. Any exposure should be documented. For use in cardiac operations as a hemostyptic, the necessity itself and alternatives for aprotinin as a stabilizing agent merit consideration.

Fibrin sealant, aprotinin, and immune response in children undergoing operations for congenital heart disease.

Authors: Scheule AM, Beierlein W, Wendel HP, Eckstein FS, Heinemann MK, Ziemer G

Publication Date: 1998

Abstract:

OBJECTIVE: Most commercially available fibrin sealants contain aprotinin in doses of 1500 kallikrein inactivator units per milliliter. They are used in many operative disciplines. An elevated risk of hypersensitivity reactions exists at reexposure to aprotinin. Our aim was to examine the immunogenic potency of aprotinin as a fibrin sealant content.

METHODS: We investigated 49 children with operatively treated congenital heart disease. All patients received aprotinin only topically as contained in fibrin sealant. Serum samples were drawn preoperatively, 1 week, 2 weeks, 6 weeks, and approximately 1 year after operation. They were analyzed for aprotinin-specific immunoglobulin G antibodies with a standard enzyme-linked immunosorbent assay and a fluorescence enzyme immunoassay for aprotinin-specific immunoglobulin E antibodies.

RESULTS: At 1 week, 2 weeks, 6 weeks, and 1 year, we found prevalences of 8% (2 of 26), 8% (2 of 24), 6% (3 of 49), and 0% for aprotinin-specific Immunoglobulin E, and for aprotinin-specific immunoglobulin G 8% (2 of 26), 17% (4 of 24), 39% (19 of 49), and 12% (5 of 41). The doses of aprotinin given did not differ significantly in antibody-negative and antibody-positive patients; no significant factors could predict the immune response.

CONCLUSIONS: Our findings show the existence of a subgroup of patients who had

aprotinin-specific antibodies develop after topical aprotinin application. Any use of aprotinin must be carefully documented. If aprotinin use is planned in patients who previously underwent a surgical procedure, preexposure to aprotinin in any form must be sought to avoid unexpected anaphylactic reactions. The necessity itself and alternatives for aprotinin as a stabilizing agent in fibrin sealants merit consideration.

Convulsive seizures following subdural application of fibrin sealant containing tranexamic acid in a rat model.

Authors: Schlag M.G., Hopf R., Redl H., Chandler W.F., Friedman W.A., Bruce J.N., Sekhar L.N.

Publication Date: 2000

Abstract:

OBJECTIVES: Tranexamic acid (t-AMCA) has been shown to cause severe convulsions in humans and cats when applied topically to the central nervous system. We wanted to determine whether pure t-AMCA or fibrin sealant (FS) containing t-AMCA would induce similar effects when applied to the spinal cord in a rat model. METHODS: Following low-thoracic laminectomy, the dura was incised to expose the dorsal surface of the lumbar enlargement. Rats were allocated to one of the following treatments: 1) t-AMCA (10 mg/ml), 2) vehicle (phosphate buffered saline), 3) FS containing t-AMCA, 4) FS containing aprotinin. The response of the rats was evaluated based on neurological and behavioral observations. Additionally, motor function was scored in the rats that had received FS. RESULTS: Application of either 10 mg/ml t-AMCA or FS containing t-AMCA caused severe hind limb spasms that developed into spontaneous generalized convulsions. Two of the three rats that had received FS containing t-AMCA died of respiratory failure. In contrast, application of vehicle or FS containing aprotinin did not cause any abnormal conditions of the animals. CONCLUSION: Tranexamic acid may cause severe complications when used in the central nervous system. Thus, fibrin sealants containing t-AMCA should not be used in neurosurgery.

Evaluation of a fibrin sealant free of bovine-derived components in an experimental vas anastomosis study.

Authors: Vankemmel O., De La Taille A., Burnouf T., Rigot J.M., Duchene F., Mazeman E.

Publication Date: 2000

Abstract:

Objectives: The risk of transmission of bovine spongiform encephalopathy cannot be excluded from the use of bovine-derived products. The present study was undertaken to evaluate the performance of a new fibrin glue free of bovine-derived components in vas anastomosis and to compare this product to conventional vas anastomosis with fibrin glue. Methods: Bilateral delayed vas anastomosis was performed in 40 Sprague-Dawley rats. All animals underwent a fibrin glue-assisted vas anastomosis with three transmural sutures tied prior to fibrin glue application. The composition and preparation of fibrin glue was similar for all vas anastomoses except the fibrinolysis inhibitor component which was aprotinin (3,000 KUI/ml) in group 1 and tranexamic acid (10 mg/ml) in group 2. The animals (20 rats in both groups) were sacrificed 7 weeks postoperatively and evaluated for gross patency, presence of sperm granuloma and tensile strength measurements at the anastomosis site. Results: No difference was found between the 2 groups for all parameters evaluated whether a bovine-derived or a synthetic fibrinolysis inhibitor component was used. Conclusion: This study showed that tranexamic acid, a fibrinolysis inhibitor, can be substituted for conventional fibrin glue thereby avoiding the risks of bovine products.

The influence of aprotinin on fibrosis in peripheral nerve sutures. [German]

Authors: Herter T., Windmann D.

Publication Date: 1992

Abstract:

Although fibrin-glue has been used in many areas of surgery, it has not become fully established in nerve coaptation. Initially, significant advantages were expected: however, as the fibrin clot dissolved prematurely and gapping occurred, antifibrinolytic substances were added to the glue. Following this procedure, fibroses occurred frequently, which remains a problem. In this study, the influence of aprotinin's fibrosis-inducing effect was investigated. Aprotinin demonstrated no additional fibrosis-promoting effect.

The preparation of divided nerve ends.

Authors: Moss A.L.H.

Publication Date: 1990

Abstract:

Divided peripheral nerves often require trimming due to the 'mushrooming' of the fascicles. However, in practice, it can be very difficult to perform atraumatically as the nerve tends to behave like 'soggy spaghetti'. A technique is described which helps to stabilise the cut end of the fascicles, thus allowing satisfactory trimming. This involves the use of fibrin glue.

Pilot-study for the production and the application of self-made human-fibrin-glue. [German]

Authors: Beleites E., Tietz U., Forberger Ch., Gudziol H.

Publication Date: 1983

Abstract:

Not Available

The Use of a Fibrin Glue with a Low Concentration of Thrombin Decreases Seroma Formation in Postbariatric Patients Undergoing Circular Abdominoplasty.

Authors: Pilone V., Vitiello A., Borriello C., Gargiulo S., Forestieri P.

Publication Date: 2014

Abstract:

Background: The serum collection under the abdominal flap is the most common complication after a lipo-abdominoplasty. The frequency of seroma increases further among obese patients, who have achieved massive weight loss after bariatric surgery. The purpose of this study is to demonstrate the effectiveness of fibrin glues with a low concentration of thrombin in reducing seroma formation after a lipo-abdominoplasty.Methods: Thirty patients, that had achieved a significant weight loss after an intervention of laparoscopic adjustable gastric banding (LAGB), underwent a circular lipo-abdominoplasty at our bariatric surgery department. Patients were divided into two groups of 15 subjects each: group A underwent traditional surgery; in group B, we applied a slow-clotting variant of fibrin glue (ARTISS, Baxter) under the abdominal flap. All subjects were evaluated clinically using an ultrasound device on postoperative day 15. We considered positive for seroma, those cases with a liquid collection greater than 20 cc.Results: The groups were homogeneous for age, BMI, male/female ratio, and diabetic or smoker patients. The mean hospital stay was significantly longer in group A than in group B. We found eight cases of serum collection >20 cc in group A and only one case in group B. Hematoma, umbilicus necrosis, and surgical site infection occurred in both groups, but overall complication rate was lower in group B.Conclusions: The use of a fibrin glue with a low concentration of thrombin could be useful during wound closure and may decrease seroma formation in postbariatric patients undergoing lipo-abdominoplasty.

Safety and effectiveness of a new fibrin pleural air leak sealant: A multicenter, controlled, prospective, parallel-group, randomized clinical trial.

Authors: Gonfiotti A., Santini P.F., Jaus M., Janni A., Lococo A., De Massimi A.R., D'Agostino A., Carleo F., Di Martino M., Larocca V., Cardillo G.

Publication Date: 2011

Abstract:

Background: This study evaluated the sealing capacity and safety of a new fibrin sealant (FS) to reduce alveolar air leaks (AALs) after pulmonary resections in a randomized controlled clinical trial conducted in 3 Italian centers. Methods: The study randomized (1:1) 185 patients with an intraoperative AAL graded 1 to 3 according to the Macchiarini scale: 91 received FS and 94 had standard lung closure. The primary outcomes were the length of postoperative AAL duration and the mean time to chest drain removal. Other end points included the percentage of patients without AAL, the development of serum antibodies against bovine aprotinin, and any adverse event related to FS. Chest drains were removed when fluid output was 100 mL/day or less, with no air leak. Results: The study groups were comparable with respect to demographic variables and surgical procedures. The FS group showed a statistically significant reduction in duration of postoperative AALs (9.52 vs 35.8 hours; $p < 0.005$) and in the percentage of patients with AALs at wound closure (81.11% vs 100%; $p < 0.001$); the difference in time to chest drain removal was not significant. Pleural empyema developed in 1 patient with FS treatment vs in 4 with standard treatment, and antibodies against bovine aprotinin were found in 34 of 91 FS-treated patients. Conclusions: The present study showed that the new FS is safe and effective in preventing AALs after lung resections and in shortening the duration of postoperative AALs.

The effects of sheet-type absorbable topical collagen hemostat used to prevent pulmonary fistula after lung surgery.

Authors: Miyamoto H., Sakao Y., Sakuraba M., Oh S., Takahashi N., Miyasaka Y., Akaboshi T., Inagaki T.

Publication Date: 2010

Abstract:

Background: Numerous reports have been published on the application of fibrin glues, biological adhesives used as sealants for air leaks after pulmonary resection; however, the use of blood products has been questioned from both safety and economic perspectives. Therefore we were prompted to attempt the use of Integran (method C), a sheet-type absorbable topical collagen hemostat that is neither expensive nor derived from blood. Objective: To compare the efficacy of method C with that of method G, a combined approach in which TachoComb or a polyglycolic acid (PGA) sheet was fixed with a fibrin glue in a randomized controlled trial to prevent pulmonary fistula formation after lung surgery. Materials and Methods: Of the patients who were scheduled to undergo pulmonary resection in 2006 at the Department of General Thoracic Surgery, Juntendo University, and who provided informed consent for the study before surgery, those who developed visible air leaks during lobectomy, segmentectomy, partial resection for lung tumor or pulmonary cyst, or intractable pneumothorax were included as the subjects of this study. The subjects were randomized for treatment with either of 2 procedures, namely, method C or method G. Pulmonary fistula was defined as an obvious air leak persisting until day 3 after surgery. Results: A total of 38 patients were assigned to method C and 34 to method G. Three patients (7.9%) assigned to method C (including 1 who underwent lobectomy and 2 who underwent partial resection), and 6 (17.6%) patients assigned to method G, including 3 who each underwent a lobectomy and partial resection, developed postoperative pulmonary fistula. The incidence of pulmonary fistula was significantly

lower in the group assigned to method C, with a statistically significant difference of p = 0.044. Conclusions: In a Randomized Controlled Trial of Sealing with a Sheet-type Collagen vs. a Combined Approach of Fixing a Collagen Sponge, Using Fibrin Glue for Closure of Air Leaks, the use of Integran, a sheet-type absorbable topical collagen hemostat, is feasible to prevent pulmonary fistula after lung surgery. It is also affordable and safe because it is not a blood product.

Modern glue compositions in thoracic surgery. [Russian]

Authors: Perel'man M.I., Zykov A.S., Kononenko S.N., Pavlenko I.A., Limonchikov S.V.

Publication Date: 2002

Abstract:

Not Available

Four years' experience with fibrin sealant in thoracic and cardiovascular surgery.

Authors: Matthew T.L., Spotnitz W.D., Kron I.L., Daniel T.M., Tribble C.G., Nolan S.P.

Publication Date: 1998

Abstract:

A single-donor fibrin sealant system was used in 689 thoracic and cardiovascular surgical procedures over the 4-year period between April 1, 1985, and March 31, 1989. An excellent overall success rate (646/689, 94% effective) was achieved with specific applications, including reduction of leakage of air (29/33, 88% effective), blood (595/ 634, 94% effective), and fluid (14/14, 100% effective), as well as positioning of anatomical structures such as coronary bypass grafts (8/8, 100% effective). Application methods included use of spray bottles (477/497, 96% effective), syringes (165/186, 89% effective), and a Silastic cannula through the flexible fiber-optic bronchoscope (4/6, 67% effective). The system was used in a wide variety of cardiac, pulmonary, esophageal, and vascular procedures to seal staple lines, suture lines, anastomoses, conduits, fistulas, and raw surfaces. No complications with this single-donor system secondary to blood-borne disease have been documented. Overall infection occurred at a nominal rate (16/689, 2%). Thus, fibrin sealant has been a useful tool to control the leakage of air, blood, acid fluid during a wide variety of thoracic and cardiovascular procedures and may be of benefit to other surgeons.

Use of a fibrin glue in partial pulmonary excision surgery. Results of a controlled trial in 50 patients. [French]

Authors: Wurtz A., Chambon J.P., Sobecki L., Batrouni R., Huart J.J., Burnouf T.

Publication Date: 1991

Abstract:

A controlled study concerning the surgical use of a fibrin glue was conducted in 50 patients undergoing partial pulmonary excision. In 25 of these patients, chosen at random, hemostasis and aerostasis of the fissural, and/or intersegmentary dissection planes were achieved by electrocoagulation, in the other 25 by the application of fibrin glue. The statistical study did not show any significant difference between the two groups in terms of the surgical indication, the type of excision and the associated surgical procedures (pleurectomy and parietectomy). No significant statistical difference was observed concerning the quality of aerostasis, the post-operative drainage, the persistance of residual collection or faulty reexpansion after removal of the latter, and the necessity for repeated drainage. The same applied to the length of post-operative hospital stay. This study seems to demonstrate that the surgical application of fibrin glue on the fissural and/or intersegmentary dissection planes is feasible but, as compared to electrocoagulation, does not significantly improve the quality of the surgical results for partial pulmonary excision; however its use could reduce the duration of post-operative drainage.

Treatment of postoperative chylothorax with intrapleural fibrin glue.

Authors: Akaogi E., Mitsui K., Sohara Y., Endo S., Ishikawa S., Hori M.

Publication Date: 1989

Abstract:

Two patients with chylothorax after pulmonary resection for lung cancer were successfully treated without thoracotomy by injection of fibrin glue components into the pleural cavity. This new technique for closing the chylous leak is described.

Therapy of malignant pleural effusion by fibrin gluing. [German]

Authors: Kreuser E.D., Seifried E., Hartmann R.

Publication Date: 1984

Abstract:

Not Available

Closure of lung lacerations by fibrin adhesive. Experimental investigations. [German]

Authors: Turk R., Weidringer J.W., Wried-Lubbe I., Blumel G.

Publication Date: 1982

Abstract:

The effect of the fibrin adhesive on the gas density of pleura-lung-sutures was investigated in 28 male Wistar rats. Standardized pleura-lung-lacerations were closed by additional fibrin adhesive application in combination with fibrinolytic inhibitors. 30 minutes and 5 days after operation the animals were sacrificed and manometric and micromorphological examinations performed. In good histo-compatibility the additional application of the fibrin adhesive proved to be a proper technique in elevating the pressure tolerance of pleura-lung-sutures significantly.

Hemostatic efficacy of latest-generation fibrin sealant after hepatic resection: a randomized controlled clinical study.

Authors: Bektas H., Nadalin S., Szabo I., Ploder B., Sharkhawy M., Schmidt J.

Publication Date: 2014

Abstract:

Purpose This randomized, controlled, single-blinded multicenter study evaluated the efficacy of latest-generation fibrin sealant containing synthetic aprotinin as fibrinolysis inhibitor as supportive treatment for hemostasis after elective partial hepatectomy. Methods Adult subjects undergoing resection of at least one liver segment were assigned to treatment with fibrin sealant or manual compression with a surgical gauze swab if persistent oozing necessitated additional hemostatic measures after primary control of arterial and venous bleeding. The primary outcome measure was the proportion of subjects with intraoperative hemostasis at 4 min after start of randomized treatment application. Secondary efficacy outcome measures included intraoperative hemostasis at 6, 8, and 10 min, intra- and postoperative rebleedings, transfusion requirements, and drainage volume. Results Seventy subjects were randomized. Hemostasis at 4 min was achieved in 29/35 (82.9 %) fibrin sealant subjects compared with 13/35 (37.1 %) control subjects ($p < 0.001$). Significantly more fibrin sealant subjects achieved hemostasis at 6 ($p < 0.001$), 8 ($p = 0.028$), and 10 min ($p = 0.017$). The number of rebleedings was low in both study arms. Transfusion requirements and 48-h drainage volumes were similar between the study arms. No adverse events related to study treatment were reported. Conclusions Fibrin sealant was shown to be safe and superior to manual compression in the control of parenchymal bleeding after hepatic resection. The use of synthetic aprotinin as fibrinolysis inhibitor further improves the safety margin of fibrin sealant by eliminating the risk of transmission of bovine spongiform encephalopathy and other bovine pathogens.

Reversible portal vein embolization in a rabbit model using fibrin glue and aprotinin.

Authors: Olthof P.B., Huisman F., Van Lienden K.P., Meijer J.C., Verheij J., Van Gulik T.M.

Publication Date: 2015

Abstract:

Background: Portal vein embolization (PVE) is used to increase future remnant liver volume in patients requiring major hepatic resections. The aim of this study was to modulate lysis time of a fibrin-glue (FG) based embolization material by addition of the fibrinolysis inhibiting agent aprotinin to establish reversible PVE. Material and Methods: PVE of the cranial liver lobes was performed in 30 rabbits, divided into 6 groups using FG with 150 to 1000 KIU aprotinin. Caudal liver lobe hypertrophy was determined by CT-volumetry and recanalization of the embolized segments was asessed by portal reperfusion on CT images. The rabbits were sacrificed after 7 or 49 days and results were compared to a previous series using permanent embolization materials. Results: A dose dependant effect of aprotinin on caudal lobe hypertrophy was found, with 500 KIU providing the highest regeneration rate over the first 3 days (P<0. 05 compared to 300, 150 and permanent embolization groups). Lower concentrations of aprotinin (150, 300 KIU) resulted in fast recanalization of the embolized segments. Despite adequate embolization, higher concentrations of aprotinin (700, 1000 KIU) also displayed a lower hypertrophy response. When using 500 KIU aprotinin, 4 of 5 animals had adequate recanalization after 49 days. Conclusion: PVE using FG with a concentration of 500KIU aprotinin resulted in adequate hypertrophy with 80% recanalization after 49 days. At higher concentrations, an inhibitory effect of aprotinin on the hypertrophy response was found.

Effect of fibrin glue in liver regeneration after laparoscopic surgery.

Authors: Stanojkovic Z., Antic A., Dencic S., Stojanovic M., Stanojkovic M.

Publication Date: 2015

Abstract:

Background: Fibrin glue (FG) is a natural chemical - adhesive system with an important role in blood coagulation and wound healing. It consists of two basic components - fibrinogen and thrombin, where activation of fibrinogen and its transformation into fibrin under the action of thrombin is the third phase of blood coagulation. It is known that the use of FG in laparoscopic cholecystectomy reduces the complication rate in terms of stopping diffuse bleeding in the liver parenchyma, preventing extravasation of bile and the reduction of abdominal adhesions. The main objective of this study was to determine whether the use of FG in laparoscopic surgery has an effect on the speed of healing and regeneration of liver tissue. Material and methods: The study included a total of 40 experimental pigs in which was performed laparoscopic cholecystectomy and intraoperative standardized artificially damage of gallbladder boxes, which was repaired using FG in animals of experimental group (EG) or using standard means in animals of the control group (CG). FG was homemade (Blood Transfusion Institute Nis), prepared from two components, of which the first one was prepared from the cryoprecipitate with the addition of antifibrinolytic agents (aprotinin). The second component was a commercial bovine thrombin with calcium chloride. Animals were monitored for 30 days, 4 animals were sacrificed on the fifth, seventh, tenth, fourteenth and thirtieth day of follow- up. During autopsy we have taken liver tissue and prepared for pathological research on which basis is calculated the histopathologic regeneration score (HRS: 0-3), which shows the level of liver regeneration. Results: HRS was statistically significantly higher in EG on the fifth and seventh day ($P > 0.05$) and extremely higher on the tenth and fourteenth day ($P > 0.0001$). On the thirtieth postoperative day HSR in EG was 3.75 which is verified as a high level of regeneration and

indicates the completion of liver regeneration after thirty days from the application of FG. In the course of liver regeneration, necrosis and hemorrhage fields were lower in EG compared to CG (P = 0.03, respectively). Verified cytoplasmic vacuolization was significantly higher in CG compared CG. Conclusions: Application of fibrin glue in laparoscopic surgery affects the optimal and rapid flow of the process of healing and regeneration of the liver. Its application is recommended especially in the occurrence of diffuse intraoperative liver bleeding or in the bile duct injury, in patients who are on anticoagulant therapy, with liver cirrhosis and severe coagulation disorders.

Fibrin glue for closure of conjunctival incision in strabismus surgery: A report by the American academy of ophthalmology.

Authors: Yang M.B., Melia M., Lambert S.R., Chiang M.F., Simpson J.L., Buffenn A.N.

Publication Date: 2013

Abstract:

Objective: To evaluate the severity of postoperative inflammation, degree of patient discomfort, adequacy of wound closure, and length of operating time when using fibrin glue compared with sutures to close limbal conjunctival incisions after strabismus surgery. Methods: Literature searches of the PubMed and Cochrane Library databases were last conducted on January 24, 2013, and resulted in 24 citations, including 2 not in the English language. All citations were reviewed in full text. Five studies compared fibrin glue (68 eyes) with sutures (74 eyes) for closure of limbal conjunctival incisions in patients undergoing strabismus surgery and were included in this assessment; no studies were found that evaluated fornix incisions. A quality rating was assigned to each study using criteria specifically developed for this assessment. Results: No level I studies were found, and 5 level II studies were identified. There was significantly less postoperative inflammation and patient discomfort for 1 to 3 weeks after strabismus surgery for eyes treated with fibrin glue compared with sutures. In 3 studies that evaluated wound apposition, 2 of 50 eyes (4%) with conjunctival incisions that were initially closed using fibrin glue subsequently developed a wound gap that required suture repair. In the 2 studies that compared surgical time, fibrin glue required 1 to 5 minutes less time than suturing in 1 study and 55% less time (3.8 vs. 8.4 minutes) in a second study. These 5 studies did not evaluate the cost-effectiveness or risk of viral transmission from fibrin glue. Conclusions: Studies in the literature suggest that the off-label use of fibrin glue to close limbal conjunctival incisions in strabismus surgery resulted in less postoperative inflammation and required shorter operating time compared with sutures, but it increased the percentage of wounds requiring

subsequent repair with sutures. Financial Disclosure(s): The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Hemostatic efficacy of latest generation fibrin sealant after hepatic resection; a randomized controlled clinical study.

Authors: Bektas H., Nadalin S., Schmidt J., Szabo I., Ploder B., Sharkhawy M.

Publication Date: 2013

Abstract:

The objective of this randomized, controlled, multicenter study was to evaluate the hemostatic efficacy of latest generation fibrin sealant (FS) containing synthetic aprotinin as fibrinolysis inhibitor as supportive treatment to improve hemostasis in adult patients (>=18 years) undergoing partial hepatectomy involving resection of at least one anatomical liver segment. Subjects were randomized (1:1) to receive either FS or manual compression with a surgical gauze swab (MC) to control oozing from the cut liver surface persisting after primary hemostasis of major vessels had been achieved using sutures, ligations, clips, vascular staplers, point electrocautery or focal radiofrequency ablation. The primary endpoint, hemostasis at 4 minutes from the start of treatment application, was achieved in 82.9% (29/35) of FS-treated subjects compared to 37.1% (13/35) of subjects receiving MC ($p < 0.001$ in the likelihood ratio chi-squared test with a 5% two-sided significance level). In addition, significantly more FS-treated subjects achieved hemostasis at 6 (91.4% vs. 57.1%; $p < 0.001$), 8 (91.4% vs. 71.4%; $p = 0.028$), and 10 minutes (94.3% vs. 74.3%; $p = 0.017$). The number of intra and postoperative re-bleedings was small in both groups. Transfusion requirements and 48-hour drainage volumes were similar between FS and MC. (For categorical outcomes see Table 1.) This randomized, controlled, multicenter study demonstrated that FS is safe and its efficacy superior to MC for hemostasis in subjects undergoing hepatic resection. The use of synthetic aprotinin further improves the safety margin of FS by eliminating the risk of transmission of bovine spongiform encephalopathy and other bovine pathogens. (Table Presented).

L-PRP/L-PRF in esthetic plastic surgery, regenerative medicine of the skin and chronic wounds.

Authors: Cieslik-Bieleck A., Choukroun J., Odin G., Dohan Ehrenfest D.M.

Publication Date: 2012

Abstract:

The use of platelet concentrates for topical use is of particular interest for the promotion of skin wound healing. Fibrin-based surgical adjuvants are indeed widely used in plastic surgery since many years in order to improve scar healing and wound closure. However, the addition of platelets and their associated growth factors opened a new range of possibilities, particularly for the treatment of chronic skin ulcers and other applications of regenerative medicine on the covering tissues. In the 4 families of platelet concentrates available, 2 families were particularly used and tested in this clinical field: L-PRP (Leukocyte- and Platelet-rich Plasma) and L-PRF (Leukocyte- and Platelet-Rich Fibrin). These 2 families have in common the presence of significant concentrations of leukocytes, and these cells are important in the local cleaning and immune regulation of the wound healing process. The main difference between them is the fibrin architecture, and this parameter considerably influences the healing potential and the therapeutical protocol associated to each platelet concentrate technology. In this article, we describe the historical evolutions of these techniques from the fibrin glues to the current L-PRP and L-PRF, and discuss the important functions of the platelet growth factors, the leukocyte content and the fibrin architecture in order to optimize the numerous potential applications of these products in regenerative medicine of the skin. Many outstanding perspectives are appearing in this field and require further research.

Delayed reaction to fibrin sealant after facelift surgery: A case report and literature review.

Authors: Pugao R., Perenack J.

Publication Date: 2012

Abstract:

Fibrin sealants are commonly used in facelift surgery to diminish postoperative ecchymosis and edema, and to support soft tissues during healing.1 Fibrin sealants are two-component systems consisting of fibrinogen and thrombin with aprotinin as a fibrin-clot stabilizer, which potentially could lead to adverse reactions due to its bovine origin.2 This case report is about a patient undergoing facelift surgery in which fibrin sealant was used followed by a type-IV allergic reaction to the sealant. A literature review was also performed using the electronic database, Pubmed, and entering keywords such as fibrin tissue sealant, fibrin glue, allergy, adverse reaction, face-lift, and rhytidectomy. A 55-year-old Caucasian female presented to an affiliatecosmetic surgical center for evaluation and improvement of moderate facial and neck skin laxity. Patient described a history of asthma, rosacea, angioedema, vertigo, migraine headaches, and arthritis. Medications taken by the patient were amitriptyline, Aleve, Epipen, meclizine, promethazine, minocycline, hydroquinone, and cyclobenzaprine. She noted an allergy reaction to penicillin and Neosporin, as well as to certain fabrics. Patient revealed a surgical history of anterior cervical fusion in 1988 and tonsillectomy in 1960. Patient denied any general anesthetic complications during and after both surgeries. The patient underwent a facelift procedure with upper and lower blepharoplasty. The facelift procedure involved extensive pre- and posterior-auricular undermining with submental platysmalplasty. Fibrin sealant was applied at the end of the facelift procedure prior to closure. No complications were encountered before, during, and after surgery. The patient had uneventful follow-ups at post-op day one and five. At 4 weeks, patient presented with mild swelling below the chin not extending past the

hyoid bone. She denied fevers or chills and was maintaining her own airway without any distress. Upon physical examination, there was firm but fluctuant edema with urticaria and erythema along the submental region without tenderness to palpation. Lymphadenopathy was also present. No other signs of urticaria, edema, and erythema noted elsewhere on the face or torso. Submental aspirate collections revealed 1.5mL of pink, clear fluid, which flattened the submental region. Aspirate was sent for cultures, and the patient was prescribed antibiotics and a steroid dose-pack. At 6 weeks, surgical exploration was performed via submental incision and midline platysma-plication sutures were removed. Initial thought was that the patient experienced an allergic reaction to the silk suture. Surgical exploration was uneventful which noted no obvious granulation formations, except for thin, serous fluid. A biopsy was performed and submitted for pathology. Cultures and gram stain were negative, and the patient appeared to respond well to the steroid dose-pack. Pathology reported chronic inflammatory infiltrates. Over the next 6 months, erythema and swelling were evident but gradually subsided while surgical incisions healed well. Patient's symptoms eventually resolved completely without any further events. Type-I reactions to aprotinin are well documented in the literature. It is important to note that reactions related to aprotinin use involved mostly intravascular administration and a previous history of exposure.3 Other case reports describe anaphylactic reactions to fibrin sealants after topical application.4 On this patient, fibrin sealant was applied topically, but the symptoms clinically resembled a delayed hypersensitivity reaction. This is the first recorded incident of a type-IV hypersensitivity to fibrin sealant use in facelift surgery.

ADverse effects of fibrin sealants in thoracic surgery. The safety of a new fibrin sealant: Multicentre, controlled, prospective, parallel group randomised clinical trial.

Authors: Cardillo G., Lococo A., De Massimi A.R., D'Agostino A., Carleo F., Larocca V., Santini P.F., Gonfiotti A.

Publication Date: 2011

Abstract:

Objectives: The safety of fibrin sealants has been questioned in the light of recent reports of adverse effects, mainly thromboembolic events and fatal anaphylaxis. We evaluated the safety of a new fibrin sealant (FS) in a randomised controlled trial (RCT). Methods: Multicentre, prospective, open-label phase II/III RCT to evaluate the safety of FS. The trial was approved by the Ethic Committee. FS includes two components (component 1: fibrinogen; component 2: thrombin), each of them subjected to two viral inactivation procedures. Out of 200 screened patients, 185 eligible patients (49 females, 136 males), aged between 18 and 75 years, undergoing major thoracic surgery were randomised to receive FS (# 91 patients) as an adjuvant for air leak control or no treatment (#94 patients). Safety variables were: percentage of subjects with adverse events associated with the therapy; formation of antibodies against bovine aprotinin; vital signs (blood pressure, body temperature, heart and respiratory rate); laboratory parameters (haematology and blood chemistry). Results: None of the adverse events was considered as treatment-related. Atrial fibrillation (five patients in the FS group and four in the control group) and hyperpyrexia (five and seven patients, respectively in the two groups) were the most common adverse events. No patient reported thromboembolic events (pulmonary embolism or deep vein thrombosis) during the inhospital stay or within one month from discharge. The formation of bovine aprotinin antibodies was reported in a total of 34 patients (37.4%) in the FS group and was not related to any adverse effect.

Conclusions: The present RCT did not show any increased risk of serious and non-serious adverse events, and of surgical complications, related to the use of FS. The proportion of treated patients that developed bovine aprotinin antibodies was in compliance with literature data.

Sutureless patch graft for sterile corneal melts.

Authors: Gupta N., Sachdev R., Tandon R.

Publication Date: 2010

Abstract:

An innovative technique to seal large paracentral corneal melts is being presented. Two patients with sterile corneal melts sized 3-5 mm in diameter were treated with a full-thickness patch graft punched using a dermatological trephine and secured with the fibrin-aprotinin biological tissue adhesive, supplanting the need for sutures. The defect was adequately sealed, and successful tectonic support with postoperative best-corrected visual acuity of 6/24 was achieved in both cases, circumventing the need for an emergency full-thickness penetrating keratoplasty.

The use of fibrin glue in plastic surgery.

Authors: Mooney E., Loh C., Pu L.L.Q.

Publication Date: 2009

Abstract:

Fibrin glue has been used as an adjunct to hemostasis for many years. This article provides an overview of fibrin glue, including its composition, mechanism of action, availability, safety, efficacy, and potential applications in plastic surgery.

Clinical application of topical sealants in liver surgery: Does it work?.

Authors: Berrevoet F., De Hemptinne B.

Publication Date: 2007

Abstract:

Hepatic resections are considered as a standard intervention in abdominal surgery. However there is still a remarkable complication rate. Despite all recent developments in surgical techniques during liver surgery, blood loss is still one of the main causes for postoperative morbidity and mortality. In addition to patient-dependent factors, aspects of the surgical technique play a major role, in particular with regard to the occurrence of peri-operative bleeding, fluid accumulation and bile leakage. Nowadays, the use of topical sealants is often recommended as an additional tool to decrease postoperative bleeding and bile fistula. Fibrin sealants are able not only to enhance clot formation and wound healing, but possibly work as a sealing device for the small biliary branches. In this overview we will try to evaluate the efficacy in terms of time to complete haemostasis, the need for blood transfusions and the incidence of bile leakage according to recent trials. Furthermore the clinical benefit for the liver surgery patient will be discussed.

In vitro experiment of aprotinin/tranexamic acid improved injectable fibrin glue. [Chinese]

Authors: Wang J.-X., Zhu L.-X., Jin A.-M., Zhang S.-H., Huang R., Lan X.-Y.

Publication Date: 2008

Abstract:

Background: Injectable fibrin glue brings a new direction for the clinical application of cartilage-defect tissue-engineered complete repair and regeneration, the key issue of which is-regulation of the degradation speed. Objective: To observe the influence of concentration on the degradation rate of the fibrin glue scaffold by adding different concentration of the aprotinin and tranexamic acid into the injectable fibrin glue. Design, time and setting: The in vitro cytology experiment was performed at the Laboratory of Tissue Construction and Detection of Guangdong Province from February to August 2008. Materials: Fibrin glue was prepared with fibrinogen, thrombin and calcium chloride. Methods: The chondrocytes from articular cartilage of 3-weeks-old New Zealand rabbit were isolated and monolayer cultured in vitro, then the cultured chondrocytes were seeded onto the standard fibrin glue scaffold and improved fibrin glue scaffold (adding with aprotinin 7 500, 12 500, 17 500 MIU/L and tranexamic acid 15, 20, 25 g/L compound liquid) and were cultured and amplified in vitro for 6 weeks. Main outcome measures: The degradation of scaffold. Results: At 3 weeks of in vitro culture, the standard group had completely disintegrated, and the volume of each improved group was 1/2 of its original volume. After 6 weeks of culture, the scaffold remained a certain shape with thickness and elasticity. The degrading speed of the fibrin glue was greatly alleviated by adding aprotinin and the tranexamic acid with various concentrations. No significant effect could be found on multiplication of chondrocyte, maintaining of surface type and cytoplasm secretion when the concentration was lower than 12 500 MIU/ L aprotinin and (or) 20 g/L tranexamic acid, however, the higher concentration of aprotinin and (or) tranexamic acid would

greatly inhibit multiplication of cbondrocyte, maintaining of surface type and cytoplasm secretion. Conclusion: The degradation rate of the fibrin glue scaffold can be controlled by regulate the content of aprotinin and tranexamic acid in the fibrin glue.

Use of aerosolized fibrin glue fixation after liposuction of the arms [22].

Authors: Prado A., Castillo P.

Publication Date: 2005

Abstract:

Not Available

Use of mesh fibrous dressing covered with fibrin glue (TachoComb) in hemostasis after vascular anastomoses in the groin.

Authors: Pupka A., Rucinski A., Pawlowski S., Barc P., Janczak D., Kaluza G., Szyber P.

Publication Date: 2004

Abstract:

We present in this paper application of haemostatic device TachoComb onto bleeding after vascular anastomosis of dacron vascular prosthesis (branch of aortobifemoral or bypass aortofemoral) with common femoral artery in the groin. Hemorrhagic complications have influence onto clinical status of operated patients. Haemostatic TachoComb dressing was applied at 30 cases and results were compared to control group consist of 25 cases, in which gas compresses were applied. Mean loss blood in group I with the usage of TachoComb was statistical characteristic ($p < 0.003$) smallest than in group II. Also mean time of hemostasis was shortest than in group II ($p < 0.01$). We proved that use of TachoComb limits bleeding from suture line connecting artery with vascular prosthesis.

Intraoperative hemostasis during kidney transplantation and the use collagen mesh dressing covered by fibrin glue (TachoComb).

Authors: Pupka A., Chudoba P., Barc P., Kaluza G., Rucinski A., Janczak D., Pawlowski S., Szyber P.

Publication Date: 2003

Abstract:

In this paper we present influence of use of haemostatic dressing TachoComb, onto bleeding from surface of transplanted kidney. Kidney transplantation (KTX) seems to be main method of treatment of terminal renal failure. Enlarging number of KTX results in growing frequency of intra and postoperative complications. Hemorrhagic complications can impact clinical status of recipient and graft function. Haemostatic dressing was applied at 29 cases. Control group in which only gas compresses were used consisted of 25 patients. It was proved, that use of dressing from collagen mesh covered by fibrin glue TachoComb, after kidney transplantation diminished parenchymal bleeding and time necessary to get complete hemostasis.

Fibrin sealants in supporting surgical techniques: The importance of individual components.

Authors: Wozniak G.

Publication Date: 2003

Abstract:

Fibrin sealants have many different uses across a broad range of surgeries, where they have proved successful in controlling bleeding, providing suture support and tissue sealing. The action of all fibrin sealants depends on the thrombin-catalyzed formation of a fibrin clot. However, neither the purity nor the concentration of the main components of fibrin sealants (thrombin and fibrinogen) is uniform across all commercial products and this will affect performance. In addition, the optional inclusion of other components such as factor XIII and antiproteolytic inhibitors may also influence the quality of clot formation. Properties that vary among different fibrin sealants, such as the clotting rate, viscosity, adhesiveness, clot strength and resistance to proteolysis, are all-important considerations for the surgeon. The application of fibrin sealants in a very wide spectrum of surgical procedures means that some fibrin sealants may be more suitable for a particular procedure than others. One of the advantages of commercial fibrin sealants is that the high level of quality control ensures that their composition is extremely consistent between batches. On the other hand, blood bank-derived fibrin sealants may vary in their composition from one preparation to the next and hence be less predictable in their performance. This paper discusses how individual components contribute to the overall performance of fibrin sealants, thereby providing to the surgeon the necessary information to select the optimal fibrin sealant for a specific procedure.

Characterizing fibrin glue performance as modulated by heparin, aprotinin, and factor XIII.

Authors: Marx G., Mou X.

Publication Date: 2002

Abstract:

We describe the performance of fibrin glue (FG) as modulated by heparin, aprotinin, or factor XIII levels. In vitro tests and a rat kidney excision model demonstrated that the hemostatic efficacy of fibrin was not modulated by aprotinin. Overlapping rat skin sections demonstrated that adhesion strength (AS) was proportional to the area of overlap as well as to fibrinogen levels. AS was not modulated by exogenous heparin or aprotinin and was independent of the endogenous factor XIII in fibrinogen. SDS-PAGE developed by Coomassie or Western blots with anti-gamma chain antibody confirmed that normal skin sections contain adequate trans-glutaminase to maximally cross-link normal, as well as XIII-depleted, fibrin. Fibrin glue (FG) sprayed onto rat skin incision wounds with a dual channel spray applicator acted in 2 phases: initially (day 1), compared to wounds stapled without or treated with only thrombin, FG significantly increased breaking strength. In the second phase of wound healing (after day 3), all groups achieved increased but equivalent breaking strength. FG containing aprotinin (to 3000 U/m; Immuno, Behringwerke, Germany) exhibited initial tissue bonding strength equivalent to fibrin without aprotinin, but histological examination showed delayed fibrinolysis and a concomitant slower regeneration of granulation tissue. Thus, our data indicated that aprotinin was not particularly beneficial to wound healing and that the endogenous factor XIII level in the fibrinogen did not contribute significantly to skin bonding. Rather, the tissue supplied adequate trans-glutaminase activity required to crosslink fibrin to itself and to the tissue.

Treatment of chylous fistula with fibrin glue and clavicular periosteal flap.

Authors: Yoshimura Y., Kondoh T.

Publication Date: 2002

Abstract:

We describe a new treatment for chylous fistula using fibrin glue and clavicular periosteal flap.

Wound healing: Role of commercial fibrin sealants.

Authors: Amrani D.L., Diorio J.P., Delmotte Y.

Publication Date: 2001

Abstract:

This paper focuses on the use of commercial fibrin sealant (FS) in specific wound healing applications. This review is not intended to be all inclusive, but to examine in vitro and in vivo models, as well as select clinical conditions that are representative of specific wound healing applications of FS.

Collagen patch coated with fibrin glue components. Treatment of suture hole bleedings in vascular reconstruction.

Authors: Czerny M., Verrel F., Weber H., Muller N., Kircheis L., Lang W., Steckmeier B., Trubel W.

Publication Date: 2000

Abstract:

Background. Bleeding from suture holes during vascular reconstruction, particularly when polytetrafluoroethylene (PTFE) prostheses are used, is still a problem which can lead to intraoperative delay and increased blood loss. The aim of this prospective, randomised, open, controlled multicentre study was to evaluate whether the use of a new local haemostyptic would reduce intraoperative blood loss and the time to haemostasis. Methods. Thirty patients received a new haemostyptic (TachoComb H, Nycomed Pharma AG), whereas another 30 patients were treated with compresses. The vascular reconstructions were either anastomoses or patch angioplasties and were performed using PTFE vascular prostheses. Results. The mean time to haemostasis of suture hole bleeding in the haemostyptic group (326.0 sec) was significantly shorter compared to the control group (514.3 sec) ($p=0.006$). The median intraoperative blood loss was 24.5 g in the treatment group and 57.3 g in the control group ($p=0.045$). Conclusions. It was shown that collagen patches coated with components of fibrin glue significantly reduce the time to haemostasis as well as blood loss at the operation site in patients undergoing vascular reconstruction with PTFE grafts.

Antifibrinolyfic additives to fibrin glue for laparoscopic wound closure in urinary tract.

Authors: Beduschi R., Beduschi M.C., Wojno K.J., Jhung M., Williams A.L., Wolf Jr. J.S.

Publication Date: 1999

Abstract:

Background and Objectives: Fibrinolytic activity of urine may rapidly degrade fibrin glue used in the urinary tract, thereby limiting tissue adhesion. The goals of this study were to verify the ability of antifibrinolytic agents to delay the degradation of fibrin glue in the urinary tract and to assess the results of this delay on subsequent wound healing. Materials and Methods: In 25 domestic pigs, a 3.5-cm incision in the urinary bladder was left open (N = 6) or closed laparoscopically with fibrin glue alone (N = 6), fibrin glue containing aprotinin 5000 KIU/mL (N = 6), or fibrin glue containing aprotinin 2500 KIU/mL with (N = 4) or without (N = 3) aminocaproic acid 12.5 mg/mL. At harvest 7 days later, the bladder was tested for leakage. Histologic features were scored by a pathologist blinded to the closure method. Results: There were no significant differences among the groups in the amount of leakage at harvest. Significant fibrin glue material in the wound was noted more often in the pigs treated with fibrin glue plus aprotinin (7 of 13) than in the fibrin glue-only group (0 of 6; P = 0.04). The presence of significant fibrin material in the wound correlated well with absence of granulation tissue (P < 0.001), such that granulation tissue bridging the wound edges was found more often in the fibrin glue-only group (6 of 6) than in the groups treated with fibrin glue plus aprotinin (4 of 13; P = 0.01). Conclusions: Although aprotinin +/- aminocaproic acid did delay the degradation of fibrin glue used to close a bladder wound, it was associated with inhibition of granulation tissue in the glued wound. These findings suggest that aprotinin alone and aprotinin plus aminocaproic acid are not useful additives to fibrin glue used for wound closure in the urinary tract.

Perioperative blood transfusions: Indications and options.

Authors: McFarland J.G.

Publication Date: 1999

Abstract:

A reevaluation of the indications for and alternatives to transfusion of allogeneic blood was precipitated by transfusion-induced HIV. The transfusion trigger has shifted from an optimal hemoglobin level and hematocrit (10/30) to that level of hemoglobin necessary to meet the patient's tissue oxygen demands. This critical level can best be determined by physiologic measurements. A number of autologous blood options can reduce the patient's allogeneic blood needs. Pharmacologic measures to increase hemoglobin levels (erythropoietin) and to decrease blood loss at surgery are discussed as are the potential contributions of blood substitutes to transfusion support of the surgical patient.

Comparative study of different biological glues in an experimental model of surgical bleeding in anesthetized rats: Platelet-rich and -poor plasma- based glue with and without aprotinin versus commercial fibrinogen-based glue.

Authors: Sirieix D., Chemla E., Castier Y., Massonnet-Castel S., Fabiani J.-N., Baron J.-F.

Publication Date: 1998

Abstract:

The use of fibrin glue in cardiovascular surgery has been associated with decreased operative time, effective control of localized bleeding, and reduced postoperative blood loss. All preparations of fibrin glue mimic the final common pathway of the coagulation cascade in which fibrinogen is converted to fibrin in the presence of thrombin and calcium. The goal of the study was to compare five different types of fibrin glue, with or without aprotinin, on a surgical bleeding model in the rat. In 70 anesthetized Wistar rats, after laparotomy, a 3 cm liver incision was performed. After randomization, seven groups were studied. In the first group, Biocol was used as a pinpoint application to the bleeding site. Four groups received a fibrin glue obtained from a single human donor plasma using Cell Saver V (Haemonetics). The sealant was applied as a two-component system. The first component of the glue was either platelet-rich-plasma (PRP) or platelet-poor-plasma (PPP). The second component consisted of a mixture of 0.5 ml CaCl 10% with 1000 U of human thrombin, with or without 400KUI of aprotinin (AP). The last two groups, control and aprotinin were treated using saline solution or topical aprotinin respectively. Hemoglobin and hematocrit were measured before surgery and 30 min after application of the glue. The decrease in hemoglobin (Hb) and hematocrit (Hct) was the primary efficacy variable. Before surgery, there was no difference regarding Hb and Hct values between groups. Thirty min after the application of the glue, the decrease in hemoglobin expressed as percent of the control values is only significantly

lower in the Biocol group when compared to control. No significant difference was observed with the other groups in comparison to control. The commercial fibrin glue (Biocol) is more efficient than other preparations. This efficacy is likely due to a higher fibrinogen concentration.

Optimal dose of basic fibroblast growth factor for long-segment orthotopic tracheal autografts.

Authors: Nakanishi R., Nagaya N., Yoshimatsu T., Hanagiri T., Yasumoto K.

Publication Date: 1997

Abstract:

When a primary anastomosis of the trachea is not feasible, extensive grafting is required. However, despite the use of omental wrapping for revascularization, long-segment tracheal grafts frequently do not maintain structural integrity because of insufficient blood supply. We examined the use of basic fibroblast growth factor for preservation of long-segment tracheal autografts after orthotopic transplantation with omental wrapping in 23 dogs. All animals received orthotopic tracheal transplantation, with 14- ring autografts that occupied a major part of the thoracic trachea, and omental wrapping. The 23 animals were classified randomly into six groups as follows: no treatment (group 1, n = 3), topical administration of fibrin glue alone (group II, n = 4), fibrin glue enriched with 1 mug/cm² basic fibroblast growth factor (group III, n = 4), fibrin glue enriched with 5 mug/cm² basic fibroblast growth factor (group IV, n = 4), and fibrin glue enriched with 10 mug/cm² basic fibroblast growth factor (groups V and VI, each n = 4). The omentum that was used to wrap the autografts was fed by the right gastroepiploic artery in groups I to V and by both the right gastroepiploic artery and splenic artery in group VI. All autografts in groups I and II showed dissolution. Ten of 12 autografts in groups III, V, and VI did not maintain long-term structural integrity. By contrast, all autografts in group IV showed long-term viability, as demonstrated by graft patency, epithelialization, cartilage morphology, and vascularity. We conclude that treatment with fibrin glue enriched with 5 mug/cm² basic fibroblast growth factor in combination with omental wrapping may prolong the viability of long-segment tracheal autografts.

Arthroscopic meniscal repair using fibrin glue. Part I: Experimental study.

Authors: Ishimura M., Ohgushi H., Habata T., Tamai S., Fujisawa Y.

Publication Date: 1997

Abstract:

An experimental study of rabbit menisci was carried our to evaluate the healing-promoting properties of fibrin glue and fibrin glue-containing marrow cells. A full-thickness defect, 1.5 mm in diameter, was made within the avascular portion of the meniscus and left empty in 20 menisci (C group), filled with fibrin glue in 20 menisci (F group), and filled with fibrin glue- containing marrow cells in 20 menisci (M group). Measurements of the remaining defects and histological examinations were performed 1, 3, 6, and 12 weeks after each procedure. Overall, the remaining defects in the F group and, particularly, in the M group were significantly smaller than those in the C group at the various time points. Furthermore, the results of histological study showed earlier mature healing of the defects in the M group than of those in the F group. Our results suggest that fibrin glue, especially in a preparation containing marrow cells, may enhance meniscal healing.

Fibrin glue: An alternative method of wound closure in glaucoma surgery.

Authors: O'Sullivan F., Dalton R., Rostron C.K.

Publication Date: 1996

Abstract:

Purpose and Methods: A commercially available tissue glue has been used to effect conjunctival wound closure after trabeculectomy. In four cases it was used in conjunction with sutures and in two cases alone to achieve watertight closure of the conjunctiva. A small transient leak was noted postoperatively in one case, and no case of flat anterior chamber occurred. Results and Conclusion: Intraocular pressure was controlled in all cases 3 months postoperatively. Tissue glue can be an effective method of achieving conjunctival wound closure in glaucoma surgery.

Autologous fibrin glue for tympanoplasty.

Authors: Park M.S.

Publication Date: 1994

Abstract:

To produce autologous fibrin glue (AFG) of improved quality, the concentration and amount of materials for AFG were modified. The quality of AFG was assessed through determination of fibrinogen level in plasma, observation of product during production, and testing for bonding strength before application. The AFG produced under these conditions was used successfully as a helpful adjunct in middle ear surgery.

Effect of Tisseel on healing after periodontal flap surgery.

Authors: Warrer K., Karring T.

Publication Date: 1992

Abstract:

Not Available

Obstruction of pancreatic ducts with a fibrin sealant. Study after segmentary autotransplantation in dog. [French]

Authors: Houvenaeghel G., Orsoni P., Delpero J.R., Monges G., Picaud R., Guerinel G.

Publication Date: 1991

Abstract:

The effects of the main pancreatic duct with a fibrin sealant have been investigated on an experimental model of segmental pancreatic transplantation in the dog. Fourteen segmental pancreatic transplantations were performed. A cephalic pancreactectomy was performed during the same operating time. The main duct was obstructed with a fibrin sealant (Tissucol modified by addition of a solution of aprotinine concentrated at 10,000 KUI per mL). Biological follow-up consisted in: 1) Intravenous Glucose Tolerance Testing at Day 0 and Day 28 with glycaemia's integral calculus and K V Alues. 2) Measurements of glycaemia and serum amylase every three days from day 0 to day 28. Histological examination of the pancreatic tissue before and after transplantation involved a microscopy analysis reporting the degree of fibrosis and necrosis. The areas of the Langherans islets and of the fibrosis were calculated with informatic area analysis. The study was carried on non diabetic dogs at Day 28. The glycaemia's calculus of IVGTT were not significantly different before and after transplantation ($p = 0.291$). On the other hand, there was a significant difference of the K Values before and after transplantation ($p = 0.006$). Histology after transplantation revealed important lesions of fibrosis and normal or hypertropic Langherans islets in most cases. Pancreatic ducts presented with linings thickened with fibrosis. There was no fibrin sealant in the lumen. Obstruction of pancreatic ducts with a fibrin sealant induces an important fibrosis of the pancreatic exocrin tissue allowing the preservation of a satisfactory endocrine function. This technic may be used in clinical practice during the segmental pancreatic transplantations or after cephalic pancreatico-duodenectomy.

Fibrin glue improves the healing of irradiated bowel anastomoses.

Authors: Saclarides T.J., Woodard D.O., Bapna M., Economou S.G.

Publication Date: 1992

Abstract:

Many surgeons are reluctant to construct a bowel anastomosis with irradiated intestine. Previous studies have demonstrated diminished tensile strength of rat small bowel anastomoses that have been irradiated intraoperatively. To determine whether fibrin glue, a known tissue adhesive, improves the healing of these anastomoses, 69 male Sprague-Dawley rats were randomized into three anastomotic groups: Group 1, sutured ileal anastomosis without radiation or fibrin glue; Group 2, irradiated sutured ileal anastomosis without fibrin glue; and Group 3, irradiated ileal anastomosis with fibrin glue added to the suture line. Groups 2 and 3 received a single dose of 2,000 R intraoperatively. At seven days, the rats were sacrificed and the anastomotic segment was tested for breaking (tensile) strength. Anastomotic collagen content was evaluated using a hydroxyproline assay. Tensile strength results demonstrated that Group 2 was significantly weaker than Groups 1 and 3 ($P = 0.001$) and that the hydroxyproline content of Group 3 was significantly greater than that of Group 2 ($P = 0.015$). These results show that the addition of fibrin glue to an intraoperatively irradiated small bowel anastomosis improves healing, as demonstrated by both tensile strength and hydroxyproline content studies.

Experience in Lille with use of a fibrin adhesive in plastic and reconstructive surgery. [French]

Authors: Pellerin P., Huart J.J., Galizia J.P., Dhellemmes P.

Publication Date: 1987

Abstract:

Not Available

Fibrin glue in nasal septal surgery.

Authors: Hayward P.J., Mackay I.S.

Publication Date: 1987

Abstract:

We have successfully used fibrin glue to avoid operative nasal packing in 30 cases of septal surgery. Avoiding a nasal pack is not only more acceptable to the patient but may also reduce hospital stay. Analysis of our results showed some minor short-term complications but initial post-operative septal deviation tended to resolve spontaneously. Transient oedema and hyperaemia occurred in 37 per cent of cases and may represent an allergic response despite few classical allergic reactions having been reported.

Salpingotransplantation with use of a tissue adhesive. [German]

Authors: Osada H., Inthraphuvasak J., Takagi S.

Publication Date: 1986

Abstract:

Not Available

Life salvage with fibrin glue in three cases of exsanguinating hemorrhage.

Authors: Errett L., Walsh G.

Publication Date: 1986

Abstract:

Fibrin glue, although widely used in Europe for a decade, has not been commercially available in North America because its fibrinogen component is obtained from multiple, pooled, human blood donors with the subsequent increased risk of blood transmissible diseases. Techniques developed recently to isolate fibrinogen from single-donor plasma will circumvent these potential hazards. In Canada the use of fibrin glue has not been widespread even though biologic fibrin glue can be made from components readily available within most hospitals. Equal amounts of cryoprecipitate from fresh frozen plasma and bovine thrombin will combine within 2 minutes to form the fibrin glue. Simultaneous injections of each component at bleeding sites form a film of the glue that will effectively control even small arterial bleeding. The authors present three case reports to illustrate how use of the glue can save lives in cases of exsanguinating hemorrhage. They discuss the multiple applications of the fibrin glue which they believe will soon be part of the armamentarium of all Canadian surgeons.

Comparison of two fibrin adhesives. Influence of ionic additives on the structure of the fibrin meshwork and its effect on the proliferation of human fibroblasts. [German]

Authors: Redl H., Schlag G., Dinges H.P.

Publication Date: 1985

Abstract:

Not Available

Fibrin seal: The state of the art.

Authors: Matras H.

Publication Date: 1985

Abstract:

Not Available

Tracheal repair with fibrin glue.

Authors: Kram H.B., Shoemaker W.C., Hino S.T.

Publication Date: 1985

Abstract:

Not Available

Reanastomosis of the rabbit oviduct with fibrin glue. [German]

Authors: Riss P., Spernol R., Beck A., Schindler K.

Publication Date: 1984

Abstract:

In order to investigate the use of fibrin glue in reconstructive surgery of the oviduct, tubal reanastomosis was performed with homologous fibrinogen concentrate in 26 rabbits. The contralateral tube was clamped. The pregnancy rate was 25%. No adhesions were seen in the area of the anastomosis on examination of the abdomen 3 months after operation.

Vesico-perineal fistula. Obliteration by fibrin glue. [German]

Authors: Grumbt H., Kurz W., Knoth H.-J.

Publication Date: 1984

Abstract:

Not Available

Clinical use of fibrin glue in plastic surgery. [Japanese]

Authors: Sawada Y., Nakajima H., Fujino T.

Publication Date: 1984

Abstract:

This report is on clinical experience with the use of biological fibrin glue. This system consists of highly concentrated human fibrinogen, thrombin, CaCl<inf>2</inf> and aplotinin. Satisfactory results were obtained in these clinical trials of 20 cases of skin graft and flap operations for the purposes of adhesion, hemostasis and temporary covering of wounds. In our series, post-operative hemorrhage, hematoma, infection and dead space formation were not seen. No immunological side effects or post-operative deterioration of the liver function were observed, although three patients received treatment with this system two times. It is suggested that fibrin glue is effective for extensive skin grafting. Moreover, hemostasis and suture procedures will be simplified technically, and blood loss and time of operation will be reduced. This system will also be effective for temporary covering of the raw surface.

Tissue sealing by local application of coagulation factors. [German]

Authors: Stemberger A., Blumel G.

Publication Date: 1983

Abstract:

Not Available

Intraluminal application of fibrinogen adhesive by the example of the endarterectomised pig aorta.

Authors: Rendl K.H., Waldstein N., Waclawiczek H.W.

Publication Date: 1983

Abstract:

In vascular surgery, the method of gluing of tissue with highly concentrated fibrinogen has been used up to now for sealing sutures, especially in clotting disorders, for anastomosis of arteries alone or in combination with sutures, especially in the microsurgical field, for sealing of prostheses, and for plugging fistulating lymphatic vessels with more or less success. The danger of thrombotic vascular occlusion in intravascular application has been pointed out. This is also clearly noted on the proprietary pack. However, experience with preclotting of Dacron prostheses indicates that specific application of a thin layer of fibrin glue should be possible. The possibility of intravascular glue application was investigated in animal experiments. Studied were moderately large arteries (diameter about 5 mm), the reconstruction of which occurs frequently in vascular surgery. The following questions were of interest: 1. Does intraluminal fibrin gluing lead to thrombotic vascular occlusion? 2. Does intraluminal fibrin gluing have an influence on the healing or intimal regeneration after limted endarterectomy?

Fibrin glue as a biological adhesive. Its use for skin grafting in animal experiment. [Japanese]

Authors: Sawada Y., Nakajima H., Fujino T.

Publication Date: 1983

Abstract:

Experimental autologous skin grafting was performed using human fibrin glue in pigs, during the course of which all skin grafts showed good takes. Although the adhesive effect was very weak compared to the conventional suture method, fibrin glue showed a hemostatic effect against capillary oozing from the wound. In the histologic examination, a thin fibrin layer was observed on the recipient bed 2 days after surgery, but disappeared on day 7. The fibrosis tissue between the graft and the recipient bed with fibrin glue was thinner than with the conventional suture method a week postoperatively, but 2 and 4 weeks postoperatively, fibrosis tissue was slightly thicker in the former. No rejecting reactions were observed.

Fibrin adhesive for colon anastomoses. [German]

Authors: Nociti V., Erba L., Alderi G., Brivio F.

Publication Date: 1983

Abstract:

Not Available

Experience with a fibrin adhesive. [Spanish]

Authors: Mallea I., Ochandio J.L., Almagro J.L., Marco J.

Publication Date: 1983

Abstract:

Not Available

Osteochondritis dissecans of the knee: Experimental studies and preliminary note on surgical technique. [Italian]

Authors: Leonardi M., Marinoni E.C., Torri G., Dalla Pria A.

Publication Date: 1982

Abstract:

Not Available

Fibrin glue in dermatosurgery. [German]

Authors: Staindl O.

Publication Date: 1982

Abstract:

Highly concentrated human fibrinogen as a biological tissue-adhesive-system was successful in a variety of clinical applications during the last few years. The adhesive-technique imitates the second phase of blood-coagulation, i.e. the tranformation of fibrinogen to fibrin by addition of a thrombin solution. The advantages of fibrin glue in operative dermatology are based on the possibility of flat tissue adhesion as well as the local sealing of small and medium sized vessels. Three groups of indications are reported: 1. Local blood-coagulation, demonstrated in our surgical management of rhinophyma. 2. The flat tissue adhesion without surgical suture, mainly used in fixation of skin transplants. 3. In cases of extended regional flap-transpositions or tissue transplantation using microvascular anastomoses a combined suture- and adhesive-technique is described.

Hemostatic efficacy of latest-generation fibrin sealant after hepatic resection: a randomized controlled clinical study.

Authors: Bektas H, Nadalin S, Szabo I, Ploder B, Sharkhawy M, Schmidt J

Publication Date: 2014

Abstract:

PURPOSE: This randomized, controlled, single-blinded multicenter study evaluated the efficacy of latest-generation fibrin sealant containing synthetic aprotinin as fibrinolysis inhibitor as supportive treatment for hemostasis after elective partial hepatectomy.

METHODS: Adult subjects undergoing resection of at least one liver segment were assigned to treatment with fibrin sealant or manual compression with a surgical gauze swab if persistent oozing necessitated additional hemostatic measures after primary control of arterial and venous bleeding. The primary outcome measure was the proportion of subjects with intraoperative hemostasis at 4 min after start of randomized treatment application. Secondary efficacy outcome measures included intraoperative hemostasis at 6, 8, and 10 min, intra- and postoperative rebleedings, transfusion requirements, and drainage volume.

RESULTS: Seventy subjects were randomized. Hemostasis at 4 min was achieved in 29/35 (82.9 %) fibrin sealant subjects compared with 13/35 (37.1 %) control subjects ($p<0.001$). Significantly more fibrin sealant subjects achieved hemostasis at 6 ($p<0.001$), 8 ($p=0.028$), and 10 min ($p=0.017$). The number of rebleedings was low in both study arms. Transfusion requirements and 48-h drainage volumes were similar between the study arms. No adverse events related to study treatment were reported.

CONCLUSIONS: Fibrin sealant was shown to be safe and superior to manual compression in the control of parenchymal bleeding after hepatic resection. The use of synthetic aprotinin as fibrinolysis inhibitor further improves the safety margin of fibrin sealant by eliminating the risk of transmission of bovine spongiform encephalopathy and other bovine pathogens.

[The effect of fibrin gluing and its important components on fibrosis of nerve anastomoses]. [German]

Authors: Herter T, Anagnostopoulos-Schleep J, Bennefeld H

Publication Date: 1989

Abstract:

The fibrinous adhesion, although generally adopted and more and more successfully applied in many sectors of surgery, is not yet fully established in the anastomosis of separated nerves. Initially, the adhesion was expected to offer some essential advantages in this domain, especially in the prevention of suture granulomas. However, the blood clots dissolved too early, and this resulted in the formation of dehiscences. So antifibrinolytic substances had to be added to the adhesive, and this led to a frequent appearance of fibroses. The adhesion of nerves is still hampered by this fact. Now we have examined the fibrosis-inducing effect of different factors of the adhesive system. We found that aprotinin and the fibrin clot as an obstacle to supply had no additional fibrotic effect, whereas thrombin, factor XIII and fibronectin promoted the formation of fibroses.

Antifibrinolytic additives to fibrin glue for laparoscopic wound closure in urinary tract.

Authors: Beduschi R, Beduschi MC, Wojno KJ, Jhung M, Williams AL, Wolf JS Jr

Publication Date: 1999

Abstract:

BACKGROUND AND OBJECTIVES: Fibrinolytic activity of urine may rapidly degrade fibrin glue used in the urinary tract, thereby limiting tissue adhesion. The goals of this study were to verify the ability of antifibrinolytic agents to delay the degradation of fibrin glue in the urinary tract and to assess the results of this delay on subsequent wound healing.

MATERIALS AND METHODS: In 25 domestic pigs, a 3.5-cm incision in the urinary bladder was left open (N = 6) or closed laparoscopically with fibrin glue alone (N = 6), fibrin glue containing aprotinin 5000 KIU/mL (N = 6), or fibrin glue containing aprotinin 2500 KIU/mL with (N = 4) or without (N = 3) aminocaproic acid 12.5 mg/mL. At harvest 7 days later, the bladder was tested for leakage. Histologic features were scored by a pathologist blinded to the closure method.

RESULTS: There were no significant differences among the groups in the amount of leakage at harvest. Significant fibrin glue material in the wound was noted more often in the pigs treated with fibrin glue plus aprotinin (7 of 13) than in the fibrin glue-only group (0 of 6; P = 0.04). The presence of significant fibrin material in the wound correlated well with absence of granulation tissue (P < 0.001), such that granulation tissue bridging the wound edges was found more often in the fibrin glue-only group (6 of 6) than in the groups treated with fibrin glue plus aprotinin (4 of 13; P = 0.01).

CONCLUSIONS: Although aprotinin +/- aminocaproic acid did delay the degradation of fibrin glue

used to close a bladder wound, it was associated with inhibition of granulation tissue in the glued wound. These findings suggest that aprotinin alone and aprotinin plus aminocaproic acid are not useful additives to fibrin glue used for wound closure in the urinary tract.

Hypersensitivity to sub-Tenon's topotecan in fibrin adhesive in patients with retinoblastoma.

Authors: Astudillo P.P.P., Durairaj P., Chan H.S.L., Heon E., Gallie B.L.

Publication Date: 2015

Abstract:

Sub-Tenon's space delivery of topotecan in a fibrin sealant was used as an adjunct to laser therapy for small retinoblastoma tumors in 25 children (77 injections). We report serious hypersensitivity reactions in 2 children on their third sub-Tenon's injection of topotecan in fibrin sealant. One child subsequently had topotecan in an autologous blood clot with no allergic reaction. Although allergic reaction to topotecan has been reported in the literature, fibrin glue reactions are more common and are likely due to aprotinin hypersensitivity.

The Use of a Fibrin Glue with a Low Concentration of Thrombin Decreases Seroma Formation in Postbariatric Patients Undergoing Circular Abdominoplasty.

Authors: Pilone V., Vitiello A., Borriello C., Gargiulo S., Forestieri P.

Publication Date: 2014

Abstract:

Background: The serum collection under the abdominal flap is the most common complication after a lipo-abdominoplasty. The frequency of seroma increases further among obese patients, who have achieved massive weight loss after bariatric surgery. The purpose of this study is to demonstrate the effectiveness of fibrin glues with a low concentration of thrombin in reducing seroma formation after a lipo-abdominoplasty.Methods: Thirty patients, that had achieved a significant weight loss after an intervention of laparoscopic adjustable gastric banding (LAGB), underwent a circular lipo-abdominoplasty at our bariatric surgery department. Patients were divided into two groups of 15 subjects each: group A underwent traditional surgery; in group B, we applied a slow-clotting variant of fibrin glue (ARTISS, Baxter) under the abdominal flap. All subjects were evaluated clinically using an ultrasound device on postoperative day 15. We considered positive for seroma, those cases with a liquid collection greater than 20 cc.Results: The groups were homogeneous for age, BMI, male/female ratio, and diabetic or smoker patients. The mean hospital stay was significantly longer in group A than in group B. We found eight cases of serum collection >20 cc in group A and only one case in group B. Hematoma, umbilicus necrosis, and surgical site infection occurred in both groups, but overall complication rate was lower in group B.Conclusions: The use of a fibrin glue with a low concentration of thrombin could be useful during wound closure and may decrease seroma formation in postbariatric patients undergoing lipo-abdominoplasty.

The effect of fibrin sealant combined with fibrinolysis inhibitor on reducing the amount of lymphatic leakage after axillary evacuation in breast cancer: A prospective randomized clinical trial.

Authors: Mustonen P.K., Harma M.A., Eskelinen M.J.

Publication Date: 2004

Abstract:

Background and Aims: One third of women undergoing mastectomy with axillary evacuation for primary breast cancer suffer from postoperative seromas leading to unnecessary costs and complications such as infections and new operations. Different methods to prevent seroma formation have been tried without permanent success. The aim of this prospective randomised study was to examine the effect of fibrin sealant with fibrinolysis inhibitor firstly on the reduction of the amount of lymphatic leakage after axillary evacuation and secondly on the reduction of days with drains and postoperative seroma punctures. Methods: 40 patients with primary breast cancer were prospectively randomised to the treatment group (n = 19) getting fibrin clue combined with fibrinolysis inhibitor (aprotinin) sprayed into the axillary fossa and to the control group (n = 21). Results: There were no differences in the incidence of postoperative seromas between the groups. However, the seromas were easier to treat if fibrin clue was used. Total quantity (mean +/- SD) of lymphorrhea and total number of aspirations (mean +/- SD) were almost twice as high in the patients of the control group compared to those having fibrin sealant. In the treatment group seromas resolved after one or occasionally after two aspirations in 71% of patients, while in the control group 90% of patients needed three or more aspirations. Conclusion: Potentially, fibrin sealant combined with fibrinolysis inhibitor might be used for the treatment of post-axillary evacuation lymphorrhea and seroma.

Human fibrin sealant in pancreatic surgery: Is it useful in preventing fistulas? A prospective randomized study.

Authors: D'Andrea A.A., Costantino V., Sperti C., Pedrazzoli S.

Publication Date: 1994

Abstract:

Some authors have suggested the use of human fibrin sealants in pancreatic surgery to prevent fistulas. We performed a prospective randomized study including 97 patients (34 F, 63 M). Forty six were affected by pancreatic inflammatory diseases and 51 had pancreatic or peripancreatic neoplasms. All the patients were managed by the same surgical staff. Surgical treatment included 30 pancreaticoduodenectomies, 40 pancreatico-jejunostomies, 23 left pancreatic resections and 4 tumour excisions. The patients were randomized at the moment the surgical treatment was chosen and divided into 2 different groups: group A, including 43 subjects who had intraoperative fibrin sealing, and group R, including 54 patients who had no fibrin sealing during surgery. At the end of the trial, 6 patients in group A (13.9%) and 6 in group B (11.1%) developed a pancreatic fistula. No statistically significant difference was detected between the 2 groups. The highest incidence of fistulas was observed in the patients with pancreatic cancer in group A (18.7%) and in the patients who underwent pancreatico-duodenectomy in group A (25.0%).

Prospective study of using fibrin glue to prevent leak from esophagogastric anastomosis.

Authors: Hsu H.-K., Hsu W.-H., Huang M.-H.

Publication Date: 1992

Abstract:

Not Available

Pancreatic duct occlusion with fibrin sealant and pylorus preserving technique after duodenocephalopancreasectomy for periampullary carcinoma. [Italian]

Authors: Cavallini M., Tallerini A., Stipa F.

Publication Date: 1991

Abstract:

Dehiscence of pancreaticojejunostomy represent the main technical postoperative complication after duodenocephalopancreasectomy for periampullary carcinoma. The incidence of this complication is particularly high in cases of narrow duct and a tender pancreatic gland. In this case the authors suggest a technique of occlusion of the residual pancreatic stump using a fibrin sealant. This approach was utilized in 6 consecutive patients affected by resectable periampullary carcinoma. No postoperative mortality was observed. Pancreatic fistula developed in 5 cases and all of them resolved spontaneously in 1-4 months. The sixth patient underwent, at 3 months p-o, a CT-guided percutaneous aspiration of an intraabdominal fluid collection and with no further complications. 3 patients died at 3, 9 and 11 months because of liver metastases. Currently 3 patients are alive and apparently disease free at 25, 7 and 5 months. Pancreatic endocrine function was assessed in 5 patients at 3 months p-o. Blood glucose and insulin, glucagon and C-peptide plasma levels, all fasting and 1 our after a standard meal, revealed a normal glucose metabolism. The authors conclude that, since fibrin sealant avoids the pancreatic fibrosis which could be induced by non-absorbable polymers and the benign evolution of this type of pancreatic fistula, this method for handling the exocrine secretion is a safe and satisfactory approach which is particularly indicated in case of a pancreatic stump at risk for intestinal anastomoses.

Use of fibrin components from autogenous blood in the surgical treatment of malignant neoformations of the larynx. [Russian]

Authors: Veremeenko K.N., Opanashchenko G.A., Kizim A.I.

Publication Date: 1989

Abstract:

This paper describes the use of fibrin compositions derived from autogenous blood, contrykal, a fibrinolysis inhibitor, and thrombin combined with calcium chloride for fortifying sutures applied in the laryngoesophageal defect area at the final stage of laryngectomy.

Therapy of malignant pleural effusion by fibrin gluing. [German]

Authors: Kreuser E.D., Seifried E., Hartmann R.

Publication Date: 1984

Abstract:

Not Available

Laboratory indicators of the efficiency of fibrin glue in laparoscopic surgery.

Authors: Stanojkovic Z., Antic A., Stanojkovic M., Jelic M., Dencic S., Sokolovic D.

Publication Date: 2014

Abstract:

BACKGROUND: Fibrin glue (FG) is a blood-derived tissue adhesive that mimics the natural coagulation process. It consists of two basic components - fibrinogen and thrombin, where activation of fibrinogen and its transformation into fibrin under the action of thrombin is the third phase of blood coagulation. FG is used to promote wound healing, skin grafting, to provide hemostasis in microvascular surgery and parenchymal injury and to serve as a matrix for repair of bone defects. The aim of this study was to analyze laboratory indicators of the metabolic response to surgical trauma, when applying different means of hemostasis during laparoscopic cholecystectomy. METHODS: The study included a total of 40 experimental pigs in which was performed laparoscopic cholecystectomy and intraoperative artificially damage of gallbladder boxes, which was repaired using FG in animals of experimental group (EG) or using standard means in animals of the control group (CG). FG was homemade, prepared from two components, of which the first was prepared from the cryoprecipitate with the addition of antifibrinolytic agents (aprotinin). The second component was a commercial bovine thrombin with calcium chloride. During 30 days of follow-up we have taken blood samples for following biochemical tests: general laboratory tests (glucose, bilirubin, cholesterol, triglycerides), enzyme markers of hepato-biliary damage (AST, ALT, AP, GGT), parameters of synthetic liver function (total protein and albumin), electrolytes (Na, K). RESULTS: There is a statistically significant higher levels of AST and ALT in CG ($p<0,05$), while the level of GGT and AP is less in EG from the fifth to thirtieth day, but without statistical significance. The elevated values of AST and ALT in EG faster return to normal (day 5th in EG vs day 14th in

CG). Postoperative concentration of Na+ does not show a statistical difference between groups, while the concentration of K+ in CG is high statistical decreased until the 14th day (3,725+/-0,386 in CG vs 5,025+/-1,237 in EG, p<0,0001). CONCLUSIONS: Application of FG provides less parenchyma destruction and faster liver recovery and thus can be used as efficient hemostatic agent in laparoscopic surgery.

Fibrin sealant: A review of its use in surgery and endoscopy.

Authors: Dunn C.J., Goa K.L.

Publication Date: 1999

Abstract:

Fibrin sealant (fibrin adhesive; fibrin glue; Beriplast P) is a haemostatic and wound support product consisting of the blood coagulation factors fibrinogen, factor XIII and thrombin, the antifibrinolytic agent aprotinin and calcium chloride. Fibrin sealant has been used to good effect in a wide variety of surgical and endoscopic procedures. Suture support was provided in series of patients with oesophageal, gastric, colonic or rectal anastomoses, and fibrin sealant was as effective in haemostasis as microcrystalline collagen powder in hepatic surgery. It did not reduce postoperative peritoneal drainage after elective cholecystectomy, however. A 41% reduction ($p < 0.02$) in incidence of air leakage was achieved when fibrin sealant was added to sutures in patients undergoing pulmonary resection in a randomised single-blind study. A high rate of complete remission of malignant pleural effusion has been reported after intrapleural instillation of fibrin sealant, and successful sealing of CSF leaks after trauma or surgery has also been achieved. Attenuation of prolonged or excessive haemorrhage after dental extraction has been achieved in patients on anticoagulant therapy or with haemorrhagic disorders who received fibrin sealant with packing and suturing. Repeated endoscopic injection of fibrin sealant was superior to single injection sclerotherapy with polidocanol 1% in a randomised study in 805 patients with bleeding peptic ulcers. Other data suggest that endoscopic injection of fibrin sealant is associated with lower recurrence of bleeding and need for emergency surgery than thrombin with adrenaline (epinephrine) or hypertonic saline with adrenaline. Similar haemostatic efficacy to laser photocoagulation or sclerotherapy was reported in a retrospective comparison. A statistically significant reduction relative to suturing in the incidence of wound dehiscence was reported after the use of fibrin sealant in cataract surgery, and

benefit of the sealant has also been noted in patients receiving skin grafts and in those undergoing transurethral resection of the prostate gland. Conclusions: Although comparative studies would assist in the clarification of the place of the product discussed with respect to other haemostatic or wound support techniques and to other fibrin sealants, the formulation reviewed here has been shown overall to be effective and well tolerated in a variety of haemostatic and wound healing support roles in numerous types of surgery. Fibrin sealant has also been shown to be useful when administered endoscopically, with superiority over sclerotherapy being shown after repeated application in patients with peptic ulceration. Fibrin sealant can therefore be considered useful in a number of surgical and endoscopic settings.

Use of fibrin glue in hepatic trauma.

Authors: Kram H.B., Reuben B.I., Fleming A.W., Shoemaker W.C.

Publication Date: 1988

Abstract:

We evaluated the efficacy and safety of fibrin glue (FG) made with highly concentrated human fibrinogen and clotting factors in achieving hemostasis of superficial and deep hepatic injuries. Experimentally produced hepatic injuries were produced in 12 adult mongrel dogs and hemostatically sealed with FG. Half of the dogs each received two penetrating hepatic injuries consisting of a large laceration and a deep stab wound through the liver; the remaining dogs underwent resection of a large segment of the left lobe of the liver. Hemostasis was achieved by applying FG into and over the bleeding wounds; hepatic arterial occlusion was not used. Complete hemostasis was achieved in all animals before skin closure. One dog from each group was re-explored and the liver specimens harvested for gross and microscopic examination at postoperative intervals of 12 hours, 24 hours, and 2, 3, 6, and 8 weeks. There were no cases of intra-abdominal infection, abscess formation, or bile fistulae. Histologic examination demonstrated a thickened capsule containing fibrous connective tissue and neovascular proliferation; there were no signs of local or systemic toxicity. One dog died on postoperative day 1 from rebleeding from the hepatic injury; all other dogs survived without complications. We conclude that FG provides effective hemostasis of superficial and deep hepatic injuries, and has good systemic and local compatibility. Its use in surgery for hepatic trauma may lead to less intraoperative blood loss and transfusion requirements, as well as a reduced need for major hepatic resection to control hemorrhage.

Anaphylactic reaction after systemic application of aprotinin triggered by aprotinin-containing fibrin sealant.

Authors: Kober BJ, Scheule AM, Voth V, Deschner N, Schmid E, Ziemer G

Publication Date: 2008

Abstract:

We report a 67-yr-old male after multiple surgical procedures for treatment of arterial occlusive disease who suffered an anaphylactic reaction after administration of aprotinin (Trasylol) prior to urgent coronary artery bypass surgery. The patient had been treated with aprotinin-containing fibrin sealant in 2004 and in 2007, 2 wk before coronary artery bypass surgery. The postoperative serologic screening revealed positive results for qualitative aprotinin-specific IgG, highly elevated quantitative aprotinin-specific IgG and moderately elevated aprotinin-specific IgE antibodies.