

Original research-Orijinal araştırma

Histopathological effects of fibrin glue in maxillary sinus mucosa: An experimental study

Maksiller sinüs mukozasında doku yapıştırıcılarının histopatolojik etkisi: Deneysel çalışma

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Abstract

Aim. Fibrin glue is used as a tissue adhesive and local haemostatic agent during intranasal surgeries and it also causes mechanical fastening of tissue repairing procedure. Fibrin glue is generally considered highly biocompatible and adhesive to tissue surfaces, but it has very low cohesive strength. The aim of this study was to assess the histopathological effects of fibrin glue in maxillary sinus mucosa in the animal model. **Method.** Ten Wistar albino rats were used. The fibrin glue used for the present study was a fibrinogen-based compound with double sealant components. Ten rats were anaesthetized with ketamine HCl, then the fibrin glue was applied in the left maxillary sinus, and sterile saline solution was injected in the right maxillary sinus. On postoperative day 21, the animals were euthanatized and maxillary sinus mucosa was resected for histopathological examination. Fibroblast proliferation, vascular proliferation, fibrosis, and inflammatory cell infiltration were scored from zero to three and the ratios of edema and necrosis were reported. **Results.** There were no significant differences in fibroblast proliferation, vascular proliferation, fibrosis, and inflammatory cell infiltration scores and the ratios of edema and necrosis between the saline and fibrin glue groups. **Conclusions.** Our findings support the use of fibrin glue for sinus surgery. But the surgeon should be aware of the fact that it has a potential to cause inflammatory changes.

Keywords: Fibrin glue, maxillary sinus mucosa, histopathological findings, animal model, surgical material.

Özet

Giriş. İntranazal cerrahilerde fibrin glue doku yapıştırıcısı ve lokal hemostatik ajan ve doku yenilenmesini mekanik olarak hızlandıran bir ajan olarak kullanılmaktadır. Fibrin glue'nun biyouyumluluğu genellikle yüksek olarak kabul edilir ve doku yüzeyleri için yapışkan olmakla birlikte yapışkan gücü çok düşüktür. Bu çalışmada fibrin glue'nun maksiller sinüs mukozası üzerindeki histopatolojik etkisinin rat modelinde gösterilmesi amaçlanmıştır. **Yöntem.** Bu çalışmada 10 Wistar albino rat kullanılmıştır. Fibrin glue bu çalışmada bir fibrinogen tabanlı çift bileşimli dolgu materyali olarak kullanıldı. Ratlara ketamin HCl ile genel anestezi uygulandıktan sonra sol maksiller sinüslerine fibrine glue ve sağ maksiller sinüslerine steril salin solusyonu enjekte edildi. Postoperatif 21. günde ratlara ötenazi uygulandıktan sonra maksiller sinüs mukozası histopatolojik inceleme için cerrahi olarak çıkartıldı. Fibroblast proliferasyonu, fibrozis, vasküler proliferasyon ve inflamatuvar hücre infiltrasyonu 0-3 arasında skorlanırken ödem ve nekrozis yüzde olarak tespit edildi. **Bulgular.** Fibrin glue ve saline uygulanan iki grup arasında fibroblast proliferasyonu, vasküler proliferasyon, fibrozis ve enflamatuvar hücre infiltrasyonu skorları ve ödem ve nekrozis oranları arasında istatistiksel olarak anlamlı bir fark saptanmadı. **Sonuçlar.** Elde ettiğimiz bulgular maksiller sinüs cerrahinde fibrine glue'nun güvenli bir şekilde kullanılabileceğini desteklemekle birlikte bu maddenin mukozal yüzeylerde inflamatuvar değişikliklere neden olan bir potansiyelinin olabileceğini hekimlerin daima akılda tutması gerektiği kanısındayız.

Anahtar sözcükler: Fibrin glue, maksiller sinüs mukozası, histopatolojik bulgular, hayvan deneyleri, cerrahi materyal

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Introduction

The human body is able to repair soft and hard tissue wounds in many cases. Often this repairing procedure is achieved by mechanical fastening of tissues by sutures or staples methods. The basic technique of suturing is difficult for sinus mucosa perforations because of limited access to and friability of the membrane, therefore liquid tissue adhesives are used for the repair of perforations. Three tissue adhesives are most frequently used: cyanoacrylates, gelatin resorcinol and fibrin-based glues. Gelatin resorcinol and cyanoacrylates are known to have cytotoxic effects; on the other hand, the fibrin glues, are generally considered highly biocompatible and adhesive to tissue surfaces but have very low cohesive strength [1]. Iatrogenic injuries during functional endoscopic sinus surgery (FESS) are more frequently seen in anterior ethmoid region that is directly neighboring the lamina cribrosa. Lamina cribrosa are very fragile. Bony defects or dehiscences can occur in other regions, such as the tectal insertion of the middle turbinate, the canals of the anterior and posterior ethmoidal artery. When these iatrogenic injuries lead to the cerebrospinal fluid (CSF) leak; a lot of techniques and materials such as a muscle, fascias (lata, temporalis), bone wax, bony pate, mucochondral flaps, dural flaps, tissue adhesives, and fat can be used for closure of fistulas [1-3].

The aim of this study was to assess the histopathological effects of fibrin glue in maxillary sinus mucosa and to compare the results by using sterile saline solution which is known as non cytotoxic material in rat model.

Material and methods

Animals

The experimental procedures were approved by the Animal Ethics Committee of Cumhuriyet University, and the study was conducted following accepted guidelines for the care and use of laboratory animals for research. Ten Wistar albino rats (Cumhuriyet University Animal Laboratory, Sivas, Turkey), weighing 200-250 g were used. All the animals were fed by a standard laboratory diet and drinking water was available ad libitum during the experiment. They were kept in a room where the temperature (22°C ± 2°C), humidity (50%-70%), and 12-h day-night cycle were controlled. All rats were observed for several days to ascertain health before operations and controlled for their microbiological status.

Fibrin glue

The fibrin glue used for the present study was a fibrinogen-based compound with double sealant components (Beriplast® P Combi- Set, Behring GmbH AG, Marburg, Germany). The 3 mL Beriplast® P set contains:

Vial 1: Fibrinogen concentrate consisting of 270 mg dry substance, containing human plasma protein fraction with a factor XIII activity of 180 U.

Vial 2: Aprotinin solution consisting of 3 mL solution containing 3000 KIU of bovine lung aprotinin.

Vial 3: Thrombin containing a human plasma protein fraction with a thrombin activity of 1500 IU.

Vial 4: Calcium chloride solution consisting of 3 mL solution containing 17.7 mg calcium

chloride-dihydrate.

Before application, the two sealant elements were prepared separately by transferring the aprotinin solution to the fibrinogen concentrate and transferring the calcium chloride solution to the trombin. To apply the fibrin glue, a tuberculin syringe was filled with each sealant element. By pushing the two syringe plungers simultaneously, a coagulating glue forms between the tips.

Study protocol and surgical procedure

Ten rats were anaesthetized with ketamine HCl 75 mg/kg Implus xylazine 6 mg/kg IM. The surgical site was scrubbed with povidone iodine three times. The incision was extended from the left side of the mouth to the right side and was marked just above the apex of the buccogingival sulcus. The soft tissues were elevated superiorly in the subperiosteal plane to expose the fossa which is localized just above the teeth. Then the fibrin glue was applied to the left maxillary sinus, and sterile saline solution was injected in the right maxillary sinus with a tuberculin syringe. Finally, the periosteum and mucosal flap were replaced and sutured. On postoperative day 21, the animals were euthanatized with pentothal sodium 200 mg/kg given as an intraperitoneal injection. Then rat's maxillary sinus mucosa was resected for histopathological examination. The extent and severity of fibrosis, fibroblast proliferation, vascular proliferation, inflammation, edema score and necrosis rate in the both maxillary sinus mucosa were categorized as follows: no: 0, mild: 1; moderate: 2; significant: 3. The presence of edema and necrosis were recorded.

Histopathological evaluation

Histological analysis was performed by a single pathologist who was also blinded to the identity of samples. The specimens were fixed in 10% formalin for 12 hours and embedded in paraffin. The sections, 5 µm in thickness, were stained with hematoxylin-eosin and examined by light microscopy (Nikon, Eclipse E 600, Japan). The extent and severity of fibroblast proliferation, fibrosis, vascular proliferation, inflammatory cell infiltration, edema, and necrosis were evaluated in the maxillary sinus mucosa of the both the groups. Fibrin glue and sterile saline solutions were applied into the left and right maxillary sinuses, respectively. Fibroblast proliferation, fibrosis, vascular proliferation, and inflammatory cell infiltration were determined by a semi-quantitative scoring and categorized as follows: no: 0, mild: 1; moderate: 2; significant: 3. The presence of necrosis and edema were recorded.

Statistical analyses

Data were expressed as the mean ± SD, median (min-max), and percentage. The fibrosis, fibroblast proliferation, vascular proliferation scores were analyzed by t test. The inflammatory cell infiltration scores were analyzed by Mann-Whitney test. The level of significance was set at $p < 0.05$.

Results

Table 1 presents the fibroblast proliferation, vascular proliferation, fibrosis and inflammatory cell infiltration scores and ratio of edema and necrosis of the saline and fibrin glue groups. There were no significant differences in fibroblast proliferation, vascular proliferation, and fibrosis scores between the study groups ($p > 0.05$). We found no significant difference between the study groups with regard to the inflammatory cell infiltration scores ($p > 0.05$). There was no significant difference between the study groups with regard to the ratio of edema and necrosis ($p > 0.05$) (Figure 1).

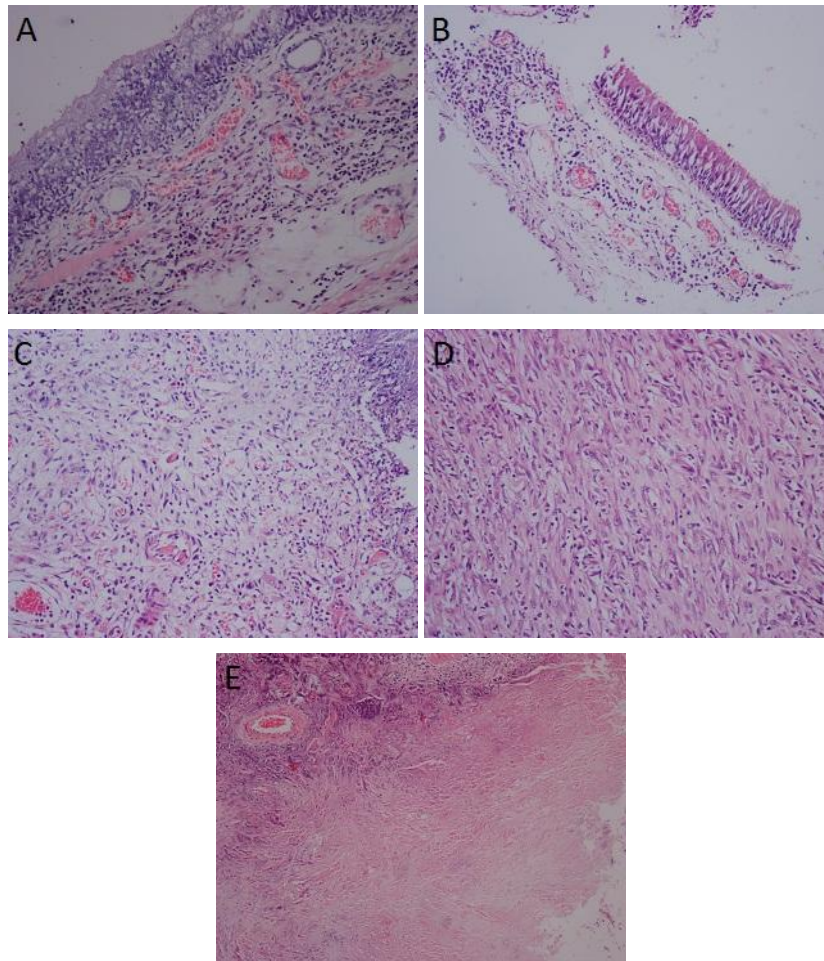


Figure 1. Representative image of histological appearance of maxillary sinus mucosa (H&E). A-B. Dense mixed cellular inflammatory cell infiltration and edema under epithelium (x50). C. Capillary vessel proliferation and dispersed inflammatory cell (x50). D. Prominent fibroblastic activity (x20). E. Necrosis (x10).

Table 1. Fibrosis, fibroblast proliferation, vascular proliferation and inflammatory cell infiltration scores, and ratio of edema and necrosis of saline and fibrin glue groups.

	Group 1 Fibrin glue	Group 2 Sterile saline solution
Fibrosis	2±0,8	1,4±1,0
Fibroblast proliferation	2,3±0,7	1,2±1,2
Vascular proliferation	2,1±1,0	1,7±1,2
Inflammatory cell infiltration	2,5(0-3)	3(2-3)
Edema	10(100%)	7(70%)
Necrosis	4(40%)	4(40%)

Discussion

In this study, we compared the effect of saline and fibrin glue with regard to the fibroblast proliferation, vascular proliferation, fibrosis and inflammatory cell infiltration scores and ratio of edema and necrosis after intranasal surgery in a rat model.

Several studies have investigated the effect of fibrin glue during its use as an adhesive agent of CSF, closing sinus membrane perforation, in human or animal studies [2-4]. Fibrin glues were first used to establish homeostasis. Young and Medawar [4] produced the first biologic adhesive, which was used in microsurgery for peripheral nerve sutures in 1940. A significant improvement in the development of fibrin glues was made when

industrial plasma fractionation methods were implemented, which made it possible to develop concentrated fibrinogen preparations. Thus, the fibrin glue currently available offers the significant, additional benefit of accelerating postoperative wound healing, which is a function of the high concentrations of growth factors in platelets [2]. Fibrin glue is used to facilitate homeostasis and reduce operative and postoperative bleeding and oozing during surgical procedures. The amount of fibrin sealant required depends on the area of tissue to be treated. In endonasal operations, the amount is usually small [5, 8].

Farrag et al. [6] used fibrin sealant in closing mucocutaneous fistulas following head and neck cancer surgery and found that there was no clear correlation between risk profile and the affectivity of fibrin sealant. On the other hand, this study shows that the use of fibrin sealant may decrease the need for dressing changes and home care nursing visits, and appeared to decrease total time needed for fistula healing. Consequently this study showed that fibrin sealant may be useful as a conservative measure to enhance the healing of mucocutaneous fistulas following head and neck surgery. Postsurgical lymphatic leaks and fistulae are uncommon but potentially life-threatening complication following different head and neck surgical procedures. Measures like drainage, pressure dressings, and total parenteral nutrition and diet modifications are not always successful. Fistulae may lead to prolonged hospitalization and surgical reinterventions. Vaiman and Eviatar [7] show that fibrin sealant might be an effective and time-saving treatment of lymphatic fistulae after neck dissection; in addition to other conservative methods.

In summary in the literature, fibrin glue is used for the treatment of many different diseases and for homeostasis. The fibrin glue has contained a high concentration of fibrinogen and growth factors, which induce rapid healing of the sinus membrane. So fibrin glue is used for the treatment of fistula that is a complication of sinus surgery. Our findings show that fibrin glue causes inflammation and necrosis in the maxillary sinus mucosa as much as sterile saline solution. This suggests that fibrin glue does not produce harmful effects in maxillary sinus mucosa. Our findings support the use of fibrin glue in the intranasal surgeries but it has a potential to cause inflammatory changes; so the surgeon should be aware of this situation.

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