

# Fibrin Glue Injection in the Treatment of Fistula-in-Ano: A Non-Invasive Alternative Technique

## Anal Fistül Tedavisinde Fibrin Yapıştırıcı Enjeksiyonu: İnvazif Olmayan Alternatif Bir Teknik

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### Abstract

The goal of the study was to demonstrate whether injection of commercially available fibrin glue would be effective as an alternative treatment in closing the tract of the fistula-in-ano. Twenty-one patients with anal fistula were included to the study. There were 4 simple, 7 trans-sphincteric, and 10 inter-sphincteric fistulas. Ten of 21 patients had recurrent fistula. Fibrin glue was injected until it seen overflowed from the primary opening which then secured with two or three absorbable suture material. Follow-up visits were scheduled at one week, 1,3,6, and 12 months. All patients were followed-up at least 12 months. A complete healing was achieved in 14 patients in the first injection. Of the recurred seven patients 2 also had complete closure after second attempt; as a result, overall in 16 patients (76.2%) fibrin glue injection was found to be effective. Failure was observed in 5 patients (23.8%). There was no association between fistula types and recurrence; furthermore, the success rate of fibrin sealant was not affected either by sex, or by previous recurrent fistula ( $p>0.05$ ). Fibrin glue can be used safely in the treatment of anal fistulas, especially in recurrent and difficult cases. We recommend this technique, as a first choice of treatment in the patients with complex fistula and in whom the surgeon suggested the anal functions would be compromised when conventional surgery carried out.

**Key Words:** Fibrin glue, Tissue adhesive, Fistula-in-ano, Treatment, Technique

### Özet

Çalışmanın amacı; anal fistül traktlarının kapatılmasında ticari fibrin yapıştırıcıların enjeksiyonu, alternatif bir tedavi yöntemi olarak etkili olup olmadığını araştırmaktır. Anal fistülü olan 21 hasta çalışmaya alındı. Fistüllerin 4'ü basit, 7'si transsfinktenk ve 10'u intersfinktenk tipteydi. Yirmibir hastanın 10'unda nüks fistül vardı. Primer ağızdan taşana kadar fibrin yapıştırıcı enjekte edildi, daha sonra 2 ya da 3 emilebilen sütür ile kapatıldı. Takip süreleri 1. hafta, 1,3,6 ve 12. ay olarak belirlendi. Tüm hastalar en az 12 ay takip edildiler. On dört hastada ilk enjeksiyonda tam iyileşme sağlandı. Nüks eden 7 hastanın 2'sinde de, 2. denemeden sonra tam iyileşme sağlandı. Sonuç olarak toplam 16 (%76.2) hastada fibrin glue enjeksiyonunun etkili olduğu saptandı. Beş (%23.8) hastada iyileşme sağlanamadı. Fistül tipi ile nüks arasında bir ilişkiye rastlanmadı. Ayrıca cinsiyet veya fistül nüksünün fibrin yapıştırıcının başarısını etkilemediği saptandı ( $p>0.05$ ). Fibrin yapıştırıcı, özellikle nüks etmiş ve zor fistüllerin tedavisinde güvenle kullanılabilir. Kompleks fistülü olan hastalarda ve klasik cerrahi uygulandığında anal işlevlerin bozulabileceği düşünülen vakalarda bu yöntemin kullanılmasını öneriyoruz.

**Anahtar Kelimeler:** Fibrin yapıştırıcı, Doku yapıştırıcı, Anüs fistülü, Tedavi, Teknik

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## INTRODUCTION

Fistula-in-ano is a common disease. There are three main goals in the treatment; the first is to eliminate the fistula tract as a source of chronic infection, discharge, and sepsis; the second to prevent recurrence; and the third to preserve anal functions (1). Several techniques have been described up to now to achieving these purposes; such as insertion of a seton, fistulotomy, fistulectomy, excision of crypts and anal glands, cauterization of tract, implantation of an antibiotic chain, and more recently anal or rectal advancement flap (1-3).

Nevertheless, the results are still not satisfactory especially in complex and difficult fistulas; thus, surgeons have still been investigating an alternative better technique.

One of the proposed alternatives is the use of fibrin sealants, acts as surgical tissue adhesive, in fistula-in-ano. Fibrin sealant has gained a widespread use in almost every medical field for its ability to achieve three major clinical goals: reducing hemorrhage, allowing drug delivery and increasing tissue adherence. Considering its ability for tissue adherence, fibrin glue was first tried in early 1980's to close fistulas and sinuses (4,5).

The aim of the study is to show whether or not the fibrin sealants can be used in the definitive treatment of the patients with fistula-in-ano.

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## PATIENTS AND METHODS

The study complies with the Declaration of Helsinki and was approved by the local research ethics board and by Gazi University Medical School Ethics Committee. Of the patients admitted to Av.Cengiz Gökçek Gaziantep State Hospital Surgical Department because of fistula-in-ano between September 2004 and July 2005 overall 21 patients, who given informed consent, were included to the prospective and non-randomized study. There were 16 male (76.2%) and 5 female (23.8%) patients with a mean age of  $33.9 \pm 5.96$  (ranged between 27 and 46). According to the Parks classification (6) four fistula were simple, 7 transsphincteric, and remaining 10 intersphincteric in type. Ten patients had previously been treated surgically by various techniques elsewhere were recurrence (Table 1). Of these 21 patients one had had ulcerative colitis for more than 10 years, one Crohn's disease for 5 years, and two type I diabetes mellitus.

In all patients a complete physical examination, the routine basic laboratory tests and ano-rectal examinations were performed. Moreover, ano-rectal complaints and sphincter functions were carefully noted and compared with the findings after operation.

### Technique

A distal enema was applied and appropriate prophylactic antibiotic was administered to all patients. Following spinal or caudal anesthesia, the patients were prone positioned. The primary and secondary openings of the fistula tract were found by conventional methods; meanwhile a great care was taken to avoid creating a false tract. A tape was passed through the fistula tract by the guidance of a blunt tip stile.

The tract was then curettaged until the debris and epithelial layer of the fistula were completely removed.

A little bit of both primary and secondary fibrotic openings were excised to accelerate the later healing. At the site of primary opening, two or three absorbable sutures were placed through the mucosa and submucosa without tying. After cleansing of the tract with saline solution, the tape was taken out. Commercially available fibrin sealant (Tisseel VH Kit, Baxter) was prepared as recommended and applied freshly into the secondary opening until it was seen overflowing from primary opening.

After waiting a few minutes for the fibrin sealant to become solid, the sutures were gently tied over to further secure the primary opening. Only the secondary opening was loosely dressed and the patient was discharged within the day of operation.

The gluing was done once in 14 and twice in seven patients. A second injection was applied to the patients who had developed recurrences after the first injection. All patients were asked to come to the follow up visit at the end of the first week, 1st, 3rd, 6th and 12th months after operation.

### Statistical Analysis

Means and standard deviations (SD) of the data were calculated. Comparisons were made using the Mann-Whitney U test and chi-squared test when necessary, and p values of less than 0.05 were accepted as statistically significant.

**Table 1.** Demographics and overall results of the patients

	Overall	Complete closure	Failure	P value
No. of patients	21	16 (76.2%)	5 (23.8%)	
Male/female	16/5	12/4	4/1	>0.05
Age*	$33.9 \pm 5.96$ (27-46)	$32.31 \pm 5.5$ (27-45)	$39 \pm 5.5$ (34-46)	>0.05
Follow-up*	$15.14 \pm 2.26$ (12-19)	$14.87 \pm 2.15$ (12-19)	$16 \pm 2.64$ (12-19)	>0.05
Recurrent disease	10	6	4	>0.05
Simple	4	4	0	>0.05
Transsphincteric	7	5	2	>0.05
Intersphincteric	10	7	3	>0.05
Result of first injection**	21	14 (66.7%)	7	<0.001
Result of second injection**	7	2 (28.6%)	5	=0.001

\*Using Mann-Whitney U test made comparisons.

\*\*Compared by chi-squared test and p value was found to be <0.001

## RESULTS

All patients were followed-up at least 12 months with a mean duration of  $15.14 \pm 2.26$  (range between 12-19) months. In this period of time, a complete healing was achieved in 14 patients (66.7%) in the first attempt. Because of the recurrence, a second injection of fibrin glue was carried out in remaining seven patients, of whom two were going to have complete closure; as a result, injection of fibrin glue was successful in overall 16 patients (76.2%). Despite the second injection, the procedure was failed in 5 patients (23.8%). There was no statistically significant difference among different types of fistulas in terms of healing ( $p > 0.05$ ). Four simple, five transsphincteric and seven intersphincteric fistulas were healed completely whereas 0, 2, and 3 were failed respectively (Table 1). Consequently, success rate of fibrin sealant was not affected either by sex, or by recurrent fistula ( $p > 0.05$ ). However, the mean age was found to be statistically different when healed and unhealed patients were compared ( $32.31 \pm 5.5$  vs.  $39 \pm 5.5$  respectively,  $p < 0.05$ ).

Furthermore, seven patients in whom the first attempt of fibrin glue injection failed, the success chance of the second injection were also significantly reduced when compared with the success rate of the first attempt (healing in 2 of 7 patients with two attempts vs. 14 of 21,  $p < 0.001$ ).

There were 10 patients (47.6%) who already had recurrent disease before their admission. Of them 7 (70%) were treated successfully, whereas 3 failed. One of these three patients was already known to have ulcerative colitis; however, two patients with diabetes mellitus and a patient with Crohn's disease were found to be still well more than 13 months after operation. The interval between fibrin glue injections and recurrences after both first and second attempts was ranged between 1 and 10 months (mean  $5.16 \pm 2.55$  months).

The recurrences after the first injections occurred slightly earlier than the recurrences after second ones; however, this difference was not found to be statistically significant (mean duration of  $4.14 \pm 2.27$  vs.  $6.6 \pm 2.41$  for the first and second attempts, respectively;  $p > 0.05$ ).

During the follow-up period, neither was there any change in the sphincter functions nor any side effect attributed to the material used occurred.

## DISCUSSION

The best treatment is the easiest one that gives at least the same result with the others, thus every effort has been targeted on this purpose. When a surgeon comes face to face with an anal fistula patient, he or she always stressed by the possible risk of anal incontinence that may occur after surgery. In our opinion one of the most important reasons for the fibrin glue application in the treatment of fistula-in-ano is the guaranteed preservation of the sphincters. Like others (7, 8), we also didn't observe any change in anal functions until the end of the follow up period after gluing in any of the patients.

Although very successful studies have been reported previously (7, 9-11), we have not expected such a high success rate of 76.2%, especially in those series of patients that majority had complex fistula, of them ten had recurrent disease, two had inflammatory bowel disease, and two had diabetes. Furthermore, a patient with Crohn's disease who had been formerly operated on two times for anal fistula also healed even in the first attempt. This patient was still well 19 months after operation, which is consistent with the findings of some authors (12). Satisfactory closure of the fistulas, absence of side effects such as disturbance of anal functions, and easy application support the rational use of fibrin glue in the treatment of anal fistulas.

When the first attempt of fibrin glue injection failed, the success chance of the second injection was also significantly reduced ( $p < 0.001$ ). We do not exactly know what the factors that affect the success or failure of the gluing material are. Yet there is only a little knowledge about this topic. There was no association between fistula types and recurrence; furthermore, the success rate of fibrin sealant was not affected either by sex, or by previous recurrent fistula ( $p > 0.05$ ). However, there was a significant difference in regard of mean age between healed and failed patients, which suggested the more chronic disease and fibrosis might be a cause of recurrence in glued patients ( $p < 0.05$ ).

As a result, fibrin glue can be used safely in the treatment of anal fistulas, especially in recurrent and difficult cases. We recommend this technique, as a first choice of treatment in the patients in whom the surgeon suggested the anal functions would be compromised when desired surgery carried out. On the other hand, the quality of data to assess the efficacy of fibrin glue in the treatment of anal fistulae is still poor and further clinical trials are needed.

## REFERENCES

1. Duinslaeger M. Difficult fistulae. *Acta Chir Belg* 2000;100:118-122.
2. McLeod RS. Management of fistula-in-ano: 1990 Roussel Lecture. *Can J Surg* 1991;34:581-585.
3. Ross ST. Fistula in ano. *Surg Clin North Am* 1988;68:1417-1426.
4. Hedelin H, Nilson AE, Teger-Nilsson AC, Thorsen G, Petterson S. Fibrin occlusion of fistulas postoperatively. *Surg Gynecol Obstet* 1982;154:366-368.
5. Kirkegaard P, Madsen PV. Perineal sinus after removal of the rectum: occlusion with fibrin adhesive. *Am J Surg* 1983;145:791-794.

- 6.Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. Br J Surg 1976;63:1-12.
- 7.Maralcan G, Baskonus I, Aybasti N, Gokalp A. The use of fibrin glue in the treatment of fistula in ano: a prospective study. Surg Today 2006;36:166-170.
- 8.Park JJ, Cintron JR, Orsay CP, Pearl RK, Nelson RL, Sone, et al Repair of chronic ano-rectal fistulae using commercial fibrin sealant. Arch Surg 2000;135:166-169.
- 9.Cintron JR, Park JJ, Orsay CP, Pearl RK, Nelson RL, Abcarian H. Repair of fistulas-in-ano using autologous fibrin tissue adhesive. Dis Colon Rectum 1999;42:607-613.
- 10.Sentovich SM. Fibrin glue for all anal fistulas. J Gastrointest Surg 2001;5:158-161.
- 11.Venkatesh KS, Ramanujam P. Fibrin glue application in the treatment of recurrent anorectal fistulas. Dis Colon Rectum 1999;42:1136-1139.
- 12.Vitton V, Gazmi M, Barthet M, Desjeux A, Orsoni P, Grimaud JC. Long-term healing of Crohn's anal fistulas with fibrin glue injection. Aliment Pharmacol Ther 2005;21:1453-1457.