

# Effect of Fibrin Glue on Intra-Operative Bleeding

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**Abstract:** *Introduction:* Effective management of bleeding is critical for promoting positive outcomes in the surgical patient. When the natural process of blood clotting does not occur or is adversely affected by surgery, other methods of achieving and maintaining surgical hemostasis are often indicated. Fibrin sealant, or fibrin "glue," is a unique surgical hemostatic/adhesive material that is being utilized with increasing frequency in a variety of surgical situations. There is a relative lack of studies from our country regarding the efficacy of fibrin glue in achieving haemostasis in open and laparoscopic surgeries. The present study was thus planned to fill this lacuna in Indian literature. *Methodology & Results:* A tertiary care centre based prospective observational study was carried out for twenty-four months. Patient of both sexes admitted in Sassoon Hospital with age group between 18-75 years undergoing open and laparoscopic surgeries having intraoperative bleeding in whom alternative methods have failed to control bleeding were considered. The quantitative data is represented as their mean  $\pm$  SD. The significance threshold of p-value was taken as  $<0.05$ . Out of 60 patients, 37 were males, and 23 females with mean age of the study subjects were 58.32 years. The mean operative time in the present study was 122.9 min. while mean blood loss was 212.2 ml. Using fibrin glue, mean time required for hemostasis was 4.12 minutes. Only 6.7% needed more than 10 minutes for hemostasis. Control of bleeding was achieved in 95% cases with fibrin glue with Blood transfusion required for 10% of the study cases. *Discussion & Conclusion:* Operative blood loss remains a significant problem affecting the prognosis of patients undergoing major surgeries. Fibrin sealant has been used to control bleeding in a variety of surgical applications (bleeding from suture hole, raw surfaces). The use of fibrin sealants appears to reduce the need for transfusion. In many studies, it was observed that fibrin sealant systems were useful for controlling bleeding foci, diffuse oozing, bleeding from needle puncture sites, lymphatic leaks, serous fluid collections, and diffuse parenchymal organ haemorrhage. Fibrin sealant is safe and effective for achieving predictable and rapid hemostasis in a broader range of surgical procedures with no post-operative complications.

**Keywords:** Fibrin sealant, fibrin glue, hemostasis, diffuse oozing, lymphatic leaks, diffuse parenchymal organ haemorrhage.

## 1. Introduction

Effective management of bleeding is critical for promoting positive outcomes in the surgical patient. Throughout a surgical procedure, bleeding must be controlled not only to provide the best view of the operative site, but also to prevent the adverse physiologic effects associated with blood loss. When the natural process of blood clotting does not occur or is adversely affected by surgery, other methods of achieving and maintaining surgical hemostasis are often indicated. The introduction of new surgical adhesives and hemostats will allow surgeons to perform operations using smaller and smaller incisions with less tissue trauma. Fibrin sealant or fibrin glue is a unique surgical hemostatic/adhesive material that is being utilized with increasing frequency in a variety of surgical situations. In practice, it is a two-component system in which a solution of concentrated fibrinogen and factor XIII are combined with a solution of thrombin and calcium to form a coagulum, simulating the final stage of the clotting cascade. Once the thrombin/calcium is combined with the fibrinogen/factor XIII, a fibrin clot forms in seconds, or somewhat slower if a more dilute form of thrombin is used. In some preparations, or in selected indications, an antifibrinolytic agent is included, presumably to prevent lysis of the clot [1,2] Fibrin sealant has been used in a wide variety of clinical applications. There are specific on-label indications for the use of commercial fibrin sealants. The on-label Indications for fibrin sealant are hemostatic in cardiac, liver, and splenic procedures and sealing colonic anastomoses. There is also extensive literature supporting the use of fibrin sealant in a wide variety of off-label applications [3]. There is a relative lack of studies from our country regarding the efficacy of fibrin glue in achieving haemostasis in open and laparoscopic surgeries.

## Aim and Objectives

- 1) To study the effect of fibrin glue on decrease in post operative haemoglobin level.
- 2) To study effect of fibrin glue on post operative bleeding.
- 3) To study, the time elapsed since application of fibrin glue as an index to assess the efficacy till complete haemostasis is achieved.

## 2. Material and Methods

A hospital-based prospective observational study involving patients undergoing open and laparoscopic surgeries at Sassoon hospital. The study was carried out from Nov 2015 - Oct 2017 and the sample size was 60 cases.

### Inclusion Criteria

Patient of both sexes admitted in Sassoon Hospital with age group between 18-75 years from the date of approval till October 2017, undergoing open and laparoscopic surgeries and having intraoperative bleeding where alternative methods have failed to control bleeding.

### Exclusion Criteria

- 1) Patient with a coagulation disorder
- 2) The patient is on anticoagulation
- 3) A patient who is medically unfit for surgery
- 4) Patient with systemic diseases such as diabetes mellitus and hypertension

All the subjects fulfilling the eligibility criteria were taken for study after written informed consent. Fibrin glue is a delivery system for applying to treatment site a tissue adhesive having a pair of the component, which must be kept separate from each other until they reach the treatment site. The delivery system comprised of: A first syringe body for storing a first tissue adhesive component and a second syringe body for separately storing a second tissue adhesive

component. A separate piston type plunger, having an elongated shaft, a head and push flange, associated with each of said syringe bodies for expelling from each of said syringe bodies its associated tissue component. A hypodermic needle, having an elongated portion related to each of said syringe bodies. Means for connecting said syringe bodies to said hypodermic needle so that each of said tissue adhesive component is afforded an independent flow path from its syringe body through said connecting means and through its hypodermic needle preventing the comingling of said first and second tissue adhesive component before they reach the treatment site. A hollow sleeve surrounding the elongated portions of said hypodermic needles retaining said elongated portions in parallel registration concerning each other and formed a structure, which permits the needles to be bent simultaneously into the desired shape.

Both syringes have a colour code. First one is yellow in colour and the second is red. Then there is two vial which also has the same colour code. Yellow bottle contain Component1: Human clottable protein 50-90 mg/ml (1ml human fibrinogen solution). The red vial contains Component2: Human thrombin 800-1200 IU/ml (1ml human thrombin solution).

Respective component fitted into the same syringes. After preparing the fibrin glue, it is ready to use and is applied to the bleeding site by pushing both the piston simultaneously of the syringes. As the component of both the syringes come in contact with the tissue, its action starts, and the coagulation process begins when thrombin converts fibrinogen to fibrin at the contact site. The site was observed for 15 minutes following application of fibrin glue to see for the achievement of complete hemostasis.

**Statistical Analysis**

The quantitative data will be represented as their mean ± SD. Categorical and nominal data will be expressed in percentage. All analysis will be carried out by using SPSS software version 21.

**3. Results**

**Table 1:** Distribution of subjects based on age group

Age group (years)	N	%
21-40	7	11.7%
41-60	33	55.0%
> 60	29	48.3%
Total	60	100.0%
Mean age - 58.32 +/- 10.16 years		

Mean age of the study subjects was 58.32 years with 55% and 48.3% cases between 41-60 years and > 60 years of age.

**Table 2:** Distribution of subjects based on Gender

Gender	N	%
Female	23	38.3%
Male	37	61.7%
Total	60	100.0%

Male predominance was seen among study cases with 61.7% males to 38.3% females.

**Table 3:** Distribution of subjects based on ASA grade

ASA Grade	N	%
<b>I</b>	45	75.0%
<b>II</b>	15	25.0%
<b>Total</b>	60	100.0%

Most of the cases (75%) were in ASA grade I while 25% were in ASA grade II.

**Table 4:** Distribution of subjects based on BMI levels

BMI	N	%
<= 25	37	61.7%
25.1-30	17	28.3%
> 30	6	10.0%
Total	60	100.0%
Mean BMI - 22.32 +/- 4.31 Kg/ m <sup>2</sup>		

Mean BMI of the study cases was 22.32 Kg/ m<sup>2</sup> with prevalence of obesity being 10% among study cases.

**Table 5:** Mean operative time and blood loss among study subjects

Variables	Mean	SD
Operative Time (min.)	122.90	41.45
Blood Loss (ml)	212.20	67.80

Mean operative time in present study was 122.9 min. while mean blood loss was 212.2 min.

**Table 6:** Distribution of subjects based on Time for hemostasis

Time for Hemostasis	Mean	SD
< 5 min	39	65.0%
5- 10 min	14	23.3%
> 10 min	4	6.7%
NA	3	5.0%
Total	60	100.0%
Mean- 4.12 +/- 1.16 mins		

Mean time required for hemostasis was 4.12 minutes. A total of 65% cases achieved hemostasis within 5 minutes while 23.3% and 6.7% required 5-10 and > 10 minutes for hemostasis.

**Table 7:** Mean pre- and post-op haemoglobin and creatinine levels

Variables	Time	N	Mean	SD	p- value
Hemoglobin	Pre-op	60	12.90	1.45	0.11
	Post-op	60	10.80	1.19	
S. creatinine	Pre-op	60	0.77	0.11	0.27
	Post-op	60	0.93	0.13	

A slight decrease was observed in pre and post-op haemoglobin among study cases (12.9 vs 10.8 gm%; p- 0.11), the difference was however non-significant. Similarly mean pre and post-op creatinine levels was also comparable (0.77 vs 0.93 mg%).

**Table 8:** Distribution of subjects based on control of bleeding

Control of Bleeding	N	%
Yes	57	95.0%
No	3	5.0%
Total	60	100.0%

Control of bleeding was achieved in 95% cases with fibrin glue.

**Table 9:** Distribution of subjects based on Requirement of blood transfusion

Requirement of Blood Transfusion	N	%
Yes	6	10.0%
No	54	90.0%
Total	60	100.0%

Blood transfusion was required for 10% of the study cases.

#### 4. Discussion

Advances in surgical technique have reduced the occurrence of postoperative complications. However, operative blood loss remains a major problem affecting the prognosis of patients undergoing major surgeries. Topical fibrin sealants have been used in Europe for more than 2 decades to promote hemostasis during a variety of surgical procedures [4]. The first fibrin sealant marketed in the United States was Tisseel (Baxter Healthcare, Deerfield, Ill), which was approved by the US Food and Drug Administration (FDA) in February 2000 [5].

There is a relative lacuna of studies using fibrin glue from the Indian subcontinent. The aim of the present study was thus to assess the efficacy of Fibrin Glue in open and laparoscopic surgeries for hemostasis. The present study included a total of 60 cases undergoing open and laparoscopic surgeries, where alternative methods have failed to control bleeding were included in the study. Mean age of the study subjects was 58.32 years with 55% and 48.3% cases between 41-60 years and > 60 years of age. Male predominance was seen among study cases with 61.7% males to 38.3% females.

Control of bleeding with fibrin glue was achieved in 95% cases with the mean time required for hemostasis was 4.12 minutes. Only 6.7% needed more than 10 minutes for hemostasis. Mean blood loss was 212.2 min. while blood transfusion was required for 10% of the study cases. A slight decrease was observed in pre and post-op haemoglobin among study cases (12.9 vs 10.8 gm%; p=0.11), the difference was however non-significant.

TISSEEL contains two components, Sealer Protein Solution and Thrombin Solution. The Sealer Protein Solution contains fibrinogen as the main active ingredient, the active ingredient of the Thrombin Solution is human Thrombin. Fibrinogen, which provides the adhesive and hemostatic capabilities of fibrin sealant, is the most important component. The tensile or adhesive strength of the sealant correlates directly with the fibrinogen concentration. However, the rapidity of the clot formation and the tensile strength of the fibrin seal are related to the concentration of thrombin.

Much of the literature generated during the past 30 years for the efficacy of fibrin sealant has come from Europe, but later studies have also been performed in the United States as well as Asia. Although many studies, like ours, lack a control group, it was observed that fibrin sealant systems

were effective for controlling slowly bleeding foci, diffuse oozing, bleeding from needle puncture sites, lymphatic leaks, serous fluid collections, and diffuse parenchymal organ haemorrhage [6,7].

Fibrin sealant has been used to control bleeding in a variety of surgical applications (bleeding from suture hole, raw surfaces). The use of fibrin sealants appears to reduce the need for transfusion, though the effect varies widely depending upon the type of surgery. In a systematic review, the proportion of patients receiving transfusion was reduced (relative risk 0.40, 95% CI 0.26-0.61; five trials with 275 subjects), as was overall blood loss (weighted mean difference [WMD] -151.68 mL, 95% CI -251.91 to -51.46; seven trials with 391 subjects) and the number of units of blood transfused (WMD -0.56, 95% CI -0.84 to -0.29) [8]. Schwartz M et al. [9] in their study on liver resection cases, observed mean time to hemostasis was 282 seconds with Crosseal, compared with 468 seconds with standard agents. Hemostasis was achieved within 10 minutes in 53 patients (91.4%) treated with the study fibrin sealant and in 44 control patients (69.8%; p<0.05).

Schips et al. [10] studied the efficacy of autologous fibrin glue for hemostasis in nephrectomy cases. Ten patients underwent laparoscopic partial nephrectomy were included in the study. Haemostasis was immediate in all cases after application of the sealant for 1 to 2 minutes to the resection site; no additional haemostatic measures were required. Mean blood loss was 90 cc (range, 20–200). Pre-operative and post-operative serum haemoglobin did not differ significantly (mean, 14.9 vs 12.6 g/dl). Mean operative time was 136 minutes (range, 60–180). No postoperative bleeding or other complications occurred.

Emir et al. [11] studied the efficacy of fibrin glue to control bleeding from the gallbladder bed during laparoscopic cholecystectomy. Bleeding from the gallbladder bed occurred in 14 of 382 patients who underwent laparoscopic cholecystectomy. Fibrin glue was applied to these 14 patients because of bleeding. The bleeding was under control in 13 patients, and in 1 patient it had to be converted to open surgery due to continued bleeding and hemostasis was achieved in this way. The mean time spent on bleeding control to achieve hemostasis was 23.9 minutes (15–35). Two patients required blood transfusion with their haemoglobin values decreasing below 8 mg/dL.

Mark R et al. [12] studied the hemostatic efficacy of a fibrin sealant-based topical agent in a femoral artery injury model including 6 cases. Blood loss (mean ± SEM) was significantly less from the arteriotomy treated with the fibrin-based dressing compared with the control dressing (4.9 ± 4.0 ml versus 82.3 ± 11.1 ml; p = 0.0005). Complete hemostasis was achieved at the first 15-minute interval in five of six arteriotomies treated with fibrin sealant and in none of the six control arteriotomies during 1 hour of assessment (p = 0.03).

David Albala M et al. [13] studied the efficacy of fibrin glue for hemostasis during urologic Surgery. A greater percentage of patients who received fibrin sealant achieved the primary endpoint of hemostasis at 10 minutes compared

with patients who received absorbable hemostat (96.4% vs 72%;  $p < 0.05$ ). Thus, based on the findings of present study and observations made by various other authors, we conclude that fibrin sealant is safe and effective for achieving predictable and rapid hemostasis in a wider range of surgical procedures with no post-operative complications.

## 5. Summary

A hospital-based observational study was conducted at Department of General Surgery, B. J. Medical College & Sassoon General Hospital, Pune. The aim was to assess the efficacy of Fibrin Glue in open and laparoscopic surgeries for hemostasis. A total of 60 cases undergoing open and laparoscopic surgeries, where alternative methods have failed to control bleeding were included in the study. Following observations were made during the study:

- 1) Mean age of the study subjects was 58.32 years with 55% and 48.3% cases between 41-60 years and > 60 years of age.
- 2) Male predominance was seen among study cases with 61.7% males to 38.3% females.
- 3) Most of the cases (75%) were in ASA grade I while 25% were in ASA grade II.
- 4) Mean BMI of the study cases was 22.32 Kg/ m<sup>2</sup> with the prevalence of obesity being 10% among study cases.
- 5) Mean operative time in the present study was 122.9 min. while mean blood loss was 212.2 min.
- 6) The mean time required for hemostasis was 4.12 minutes. A total of 65% cases achieved hemostasis within 5 minutes while 23.3% and 6.7% required 5-10 and > 10 minutes for hemostasis.
- 7) A slight decrease was observed in pre and post-op haemoglobin among study cases (12.9 vs 10.8 gm%;  $p = 0.11$ ), the difference was however non-significant. Similarly, mean pre and post-op creatinine levels were also comparable (0.77 vs 0.93 mg%).
- 8) Control of bleeding was achieved in 95% cases with fibrin glue.
- 9) Blood transfusion was required for 10% of the study cases.

## 6. Conclusion

Results of the present study demonstrated that fibrin glue is very useful in achieving hemostasis in open & laparoscopic surgeries, where alternative methods have failed to control bleeding. Patients treated with fibrin sealant also experienced no postoperative complications showing that no safety concerns were associated with the use of fibrin glue. We thus concluded that initial experience with fibrin glue in open and laparoscopic surgeries in our setup has been encouraging and further trials are required to recommend this as first-line hemostatic agent.

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