Use of Fibrin Glue in Reconstructive Plastic Surgery

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Abstract

Human fibrin glue (Tissucol) is a plasma-derived compound endowed with adhesive and hemostatic properties and possessing a specific local anti-infection function mediated through activation of nonspecific immune elements. The aim of this randomized clinical study was to show that in patients who have undergone prolonged reconstructive plastic interventions after ablative cancer surgery following cancer resection, Tissucol decreases infectious complications. Between June 1985 and February 1992, 102 subjects were treated with fibrin glue during reconstruction operations. Analysis of the results showed that in the Tissucol group a statistically significant reduction was verified regarding both immediate complications, such as partial separation of the surgical wound and inflammation, and delayed complications, such as cicatricial hyperthrophy. In conclusion, patients treated with Tissucol showed a better quality of surgical wound, a more rapid postoperative functional recovery and, consequently, a decrease in the duration of hospitalization as compared to a control group of 112 patients.

Introduction

Fibrin seal is a compound containing a high concentration of plasma proteins such as coagulation proteins and their plasma activator. When blended, these give rise to an insoluble and stable fibrin clot, which exhibits both a hemostatic and an adhesive action combined with a biostimulating property promoting tissue repair [1–3]. A resistance to infections is achieved naturally by specific and nonspecific mechanisms since lymphocytes and antibodies as well as polymorphonuclear leukocytes (PMNs), macrophages, and plasma factors, such as complement and betalysins [4–7], are found.

The nonspecific factors come into play at a very early stage; postoperative septic complications begin in the first few hours after surgery. This is also true for depression of the reticuloendothelial system, which normally occurs after severe injury, burns, hemorrhage, and lengthy operations. The demonstration that have a precise chemotactic property, exercised by means of the fibrinogen-fibrin system, can be taken as conclusive evidence that fibrin glue possesses a

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Table 1. Controlled clinical trial June 1985–February 1992: criteria for eligibility

Extensive ablations for cancer and immediate reconstructions
Negative anamnesis and laboratory tests for hepatitis B and non-A/non-B hepatitis
Informed consent

specific local anti-infection function, mediated by activation of the nonspecific immune elements. Thus, it may be concluded that in the presence of fibrin glue PMNs are mobilized in large numbers to perform their particular defensive function [8, 9].

Oncologic surgery is often characterized by extremely destructive operations which require complex reconstruction. Postoperatively, there is considerable serohematic loss. Accumulation of fluid in and around the surgical wound not only leads to flap separation and wound dehiscence, but also provides an excellent bacterical culture medium. Problems of this kind result in lengthening of the hospital stay but, much worse, may cause significant local and systemic infections [10, 11].

In order to attempt to reduce such complications, it was decided to use fibrin glue. The aim of the study was to assess the efficacy of reconstructive surgery after ablative cancer surgery. Efficacy was defined as a decrease in serohematic and infectious complications compared to a group of patients who underwent the same type of operations without the application of fibrin glue [12] (Table 1).

Material and Methods

From June 1985 to February 1992, 102 patients with various oncologic pathologies whose plastic repair involved use of human fibrin glue (Tissucol) were treated at the Istituto Nazionale Tumori in Milan (Table 2). Of these patients, 60 were male and 42 female. The age range was between 18 and 82, with an average of 50.3 years old and a median of 45 years old. Before being entered into the study, patients underwent hematology examinations testing for biohumoral hepatitis B and non-A/non-B hepatitis markers. Furthermore, each patient was subjected to the immediate hypersensitivity test by means of a subcutaneous injection of 50 μl of the Tissucol preparation, to ascertain if there was an allergic reaction. All these tests gave negative results [13, 14].

Table 2. Reconstructive plastic surgery in which fibrin glue was utilized: eligible oncological operations

Breast reconstruction with myocutaneous flaps
Head and neck reconstructions
Reconstruction of inguinal-iliac region
Composite plastic reconstructions
Reconstruction of the vulva

The total quantity of Tissucol utilized was 161.5 ml, with an average of 2.08 ml per application. The material was applied using the spray-set system; no particular postoperative antibiotic regime was performed and suction drainage was applied when indicated.

Prothombin time (PT) and partial thromboplastin time (PTT) were performed to ascertain any change in intrinsic or extrinsic coagulation which might be linked to use of human fibrin glue. These tests were performed the day before surgery, 15 days afterwards and then every 6 months.

The control group consisted of a total of 112 patients, 67 males and 45 females, whose ages ranged from 30 to 70 years, with an average age of 48 and a median of 44 years. Figure 1 illustrates the subdivision of cases in the two arms of the study by site of surgical intervention.

This study is also being conducted in the Division of Plastic Surgery, S. Anna General Hospital, Como, Italy. A total of 11 patients were recruited (Tissucol: six patients; controls: five patients), but currently their follow-up does not allow any valid conclusions.

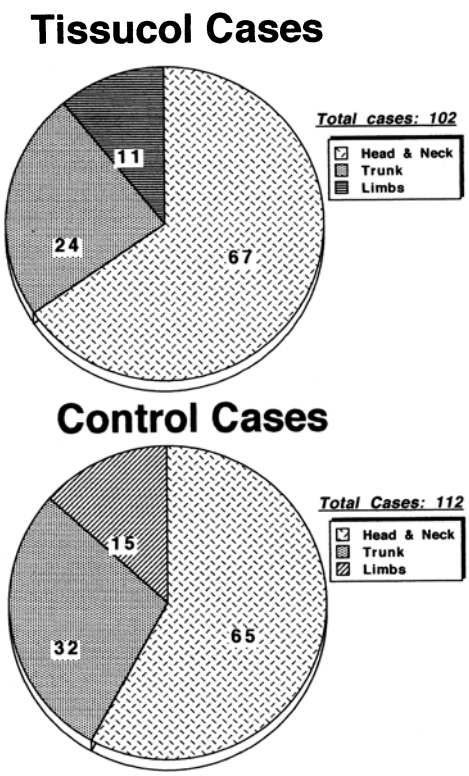

Fig. 1. Distribution of the two arms of the study according to the site of surgical operation

Results

Table 3 lists the patients treated with Tissucol and those from the control sample on the basis of the ablative and reconstructive procedures used. Resection is always followed by reconstruction, the effect of which is to produce extensive wound areas leading to considerable loss of serohematic fluid. This results in the formation of serohematic "pockets", which frequently provoke a variety of complications. This fluid is an excellent culture medium for several bacterial strains, especially gram-positive and anaerobic bacteria, which may result in wound infection, wound dehiscence, skin and fat necrosis. Additional complications are lymph collection and seromas. These complications can prolong the period of hospitalization. In our hospitals a patient with inguinal-iliac lymph node dissection requires an average postoperative hospital stay of 39 days, and wound disruption occurs in 40 %–60 % of patients.

It was decided to use Tissucol to achieve hemostasis, reduce serohematic fluid loss, seal tissues and reinforce sutures. Since Tissucol is a human plasma derivative, the possibility that viral disease such as hepatitis B or non-A/non-B hepatitis might be transmitted was evaluated. This risk can be ruled out for the following reasons: careful donor and plasma selection, product-specific heat treatment, and the clinical experience in over one million cases all over the world [15–17]. At the present time, there is no evidence of transmission of HTLV III virus in patients treated with Tissucol; also, the virus is known to be substantially unstable when exposed to heat [16, 18].

Figure 2 illustrates the main complications which can be associated with use of this product, such as those affecting coagulation, and implications resulting from the operation itself subdivided in the two arms of the study.

Hemocoagulation performed according to the study protocol consistently produced normal hematologic values, both in patients treated with Tissucol and in the control group.

Table 3. Distribution of Milan cases into the Tissucol-treated and the control groups, broken down into the type of reconstructive surgery and ablative surgery that were performed

Type of reconstruction	Type of demolition surgery	Tissucol	Controls
Head and neck reconstruction with pedicled myocutaneous flaps or free flaps	Wide demolitions and lateral cervical lymphnode dissection	67	65
Composite plastic reconstructions	Extensive ablation for malignant soft tissue tumors	20	25
Reconstruction of the inguinal-iliac with sliding cutaneous flaps	Inguinal-iliac lymphnode dissection	9	13
Breast reconstruction with latissimus dorsi myocutaneous flap	Halsted radical mastectomy	4	7
Reconstruction of the vulva with a gracilis myocutaneous flap	Total vulvectomy	2	2
Total		102	112

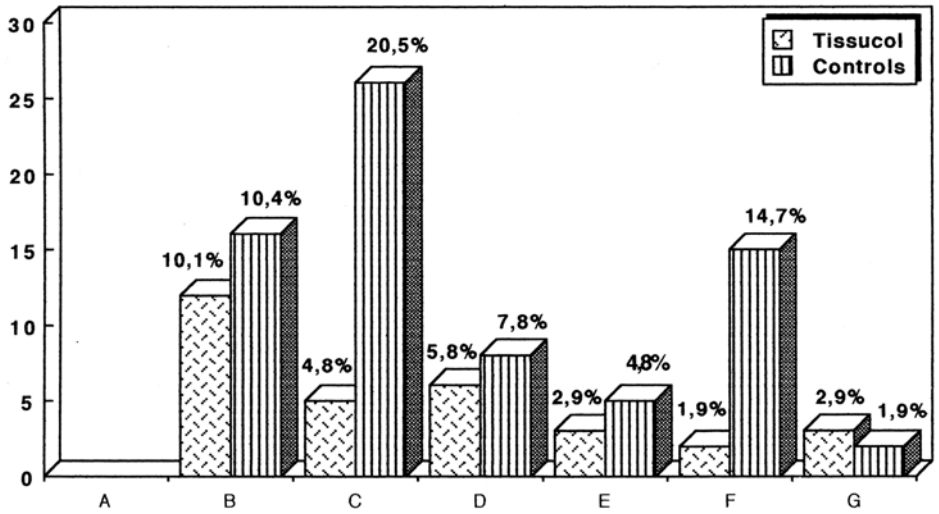

Fig. 2. Statistically relevant differences in immediate complications, such as partial separation of the surgical wound or inflammation, in the Tissucol arm vs the control arm. *A* Disorders of the intrinsic or extrinsic coagulation process; *B* serohematic fluid accumulation; *C* partial separation of the surgical wound; *D* partial necrosis of the wound; *E* hematoma; *F* inflammation; *G* lymph cysts

These data show no statistically significant differences in the incidence of seromas, lymph cysts, partial skin necrosis and hematoma between the study group and the control group. Wound dehiscence and wound inflammation show a different pattern, with a greater frequency in the control group.

Length of postoperative hospital stay ranged between 3 and 50 days for the study group, with an average of 10.5 days. In the control group the range was between 7 and 75 days, with an average of 25 days (Fig. 3).

After discharge from hospital, both groups received the same type of follow-up. A careful clinical examination to detect any delayed clinical complications was performed every 3 months during the first year following discharge, every 4 months during the second year and every 6 months from the third year on. Furthermore, every 6 months after discharge patients treated with Tissucol have undergone hematologic tests to check for the presence of the markers of hepatitis B and non-A/non-B hepatitis and to evaluate PT and PTT, checking for any coagulation disorders.

At the present stage of the follow-up, which ranges between 9 and 82 months, with an average of 44 months, tests for hepatitis B and non-A/non-B hepatitis in Tissucol treated patients have been consistently negative and the hemocoagulation values have been within the normal range.

Figure 4 illustrates the differences observed between the two groups regarding onset of delayed complications which arose during the observation period. The data show that no statistically remarkable differences can be found between the study group and the control group regarding cutaneous fistulae and lymph cysts, whereas in the onset of scar hypertrophy, statistically signifi-

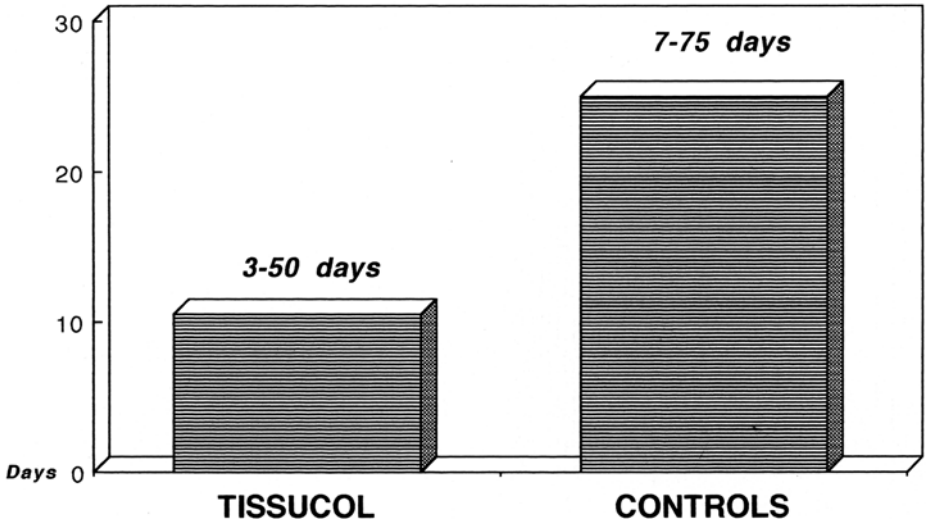

Fig. 3. Relevant differences between the Tissucol and control groups regarding post-operative hospitalization

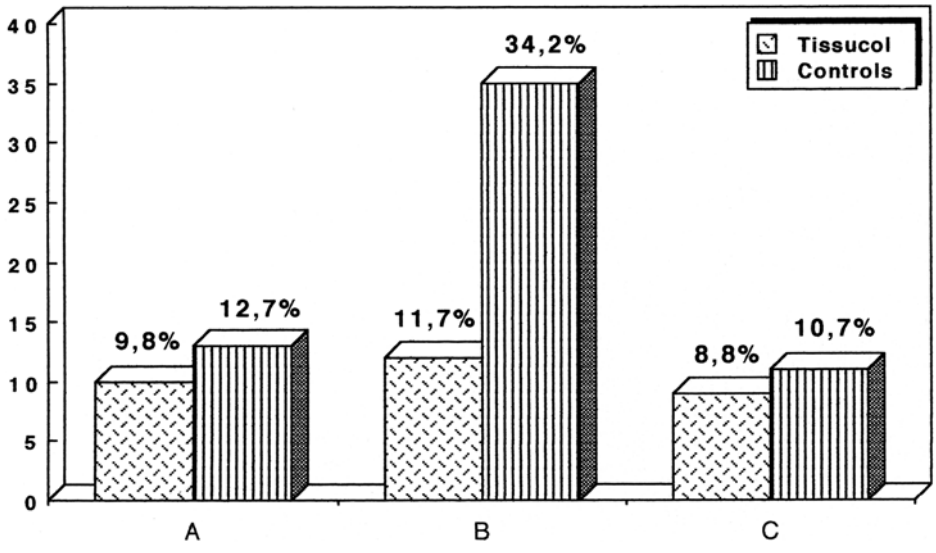

Fig. 4. Delayed complications. *A* Lymph cysts; *B* cicatricial hypertrophy; *C* cutaneous fistulae. A statistical difference was observed between the two groups for cicatricial hypertrophy

cant differences exist: 11.7% in the Tissucol group vs 34.2% in the control group.

Conclusions

The above observations on the frequency of immediate and delayed complications are consistent with a specific anti-infection function of fibrin glue, mediated through activation of PMNs. By reducing the frequency of inflammatory processes, there is a corresponding reduction in the risk of tissue inflammation and thus disruption of the surgical wound. Moreover, a decrease in the frequency of inflammation also reduces the delayed risk of hypertrophic scars.

Another favorable situation with the Tissucol group was the decrease in immediate complications, resulting in a reduction of postoperative hospital stay: 10.5 days vs 25 days in the control group. There was no substantial difference in the frequency of seromas between the two groups of patients.

Thus, Tissucol, when selectively used, reduces the frequency of onset of inflammatory processes as well as their associated immediate and delayed consequences. A better quality of surgical wound results in a more rapid postoperative functional recovery, a shorter hospital stay and therefore lower health care cost 3 (Figs. 3, 4).

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