THE ROLE OF TOPICAL THROMBIN IN SKIN GRAFTING

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A prospective study to evaluate the efficacy of thrombin as a hemostatic agent in burn patients was conducted on 24 patients undergoing debridement and skin grafting. All patients also acted as their own control. Results showed a 43.5% reduction in bleeding on the thrombin-treated sites compared with the control sites. There was no adverse effect on the rate of wound healing from the thrombin, and no difference in the nature of the scar seen at the thrombin-treated site compared with the control site. (*J Natl Med Assoc.* 1991;83:416-418.)

Key words • thrombin • skin graft • hemostasis • burn

Over 2 million cases of burns are reported in the United States each year. Of these, more than 10 000 require hospital treatment, with many requiring debridement and skin grafting. Robinson,[1] in a study of 35 patients in 1946, determined that about 46 mL of blood was lost from the donor site after taking a 20-cm × 10-cm split thickness skin graft. The thicker the graft, the more bleeding there was, and certain areas, such as the back and buttocks, bled more than others. In major burns, the blood loss from one debridement and grafting can be enormous. Such losses can result in cardiovascular derangements and even shock, especially in debilitated patients and small children. Also, the risks of blood transfusion add to the needed reduction of blood loss in burn patients.

The desire to reduce the amount of blood loss in burn patients prompted us, several years ago, to use thrombin as a hemostatic agent on the donor and recipient sites. The present study was designed to establish the efficacy of the thrombin treatment.

MATERIALS AND METHODS

A prospective study was carried out on 24 burn patients who underwent skin grafting procedures. The patients were of various races, sexes, and ages. All patients served as their own controls, and studies were conducted on identical parts of the body for each patient.

The objectives of the study were:

- to determine the efficacy of thrombin in decreasing bleeding from the donor site,
- to determine the effect of the thrombin on the rate of reepithelialization, and
- to compare the type of scar at the thrombin-treated site with the scar in the control area.

The harvesting of the skin graft was done primarily with a Brown electric dermatome. The thickness varied from .008 in to .016 in, but the thickness of the graft was the same for each control and thrombin-treated sites.

After harvesting the split thickness skin graft, the donor site was divided into two halves, the study and

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TABLE 1. BLOOD LOSS AT THROMBIN-TREATED GRAFT SITES VERSUS CONTROL SITES IN 24 BURN PATIENTS*

Patient	Blood Loss Thrombin (mL)	Blood Loss Control (mL)	Difference (mL)
1	8.8	19.2	10.4
2	15	21.8	6.8
3	18.6	28.8	10.2
4	9.8	22.2	12.4
5	7.4	20	12.6
6	7.5	22.5	15.5
7	8.6	20.6	12
8	33.4	46.6	13.2
9	12.5	23.8	11.4
10	2.46	5.2	2.8
11	36.6	61.4	25.8
12	15.2	30.4	15.2
13	4.2	5.2	1
14	4.4	5.2	.8
15	21.8	33.4	11.6
16	5.8	12	6.2
17	24.8	56.2	31.4
18	21.6	40	18.4
19	18.8	34.6	15.8
20	9.8	11.4	1.6
21	9.2	19	9.8
22	11	16.6	5.6
23	10.6	18.89	8.2
24	27.8	54.8	27

*Area of study = 20 cm × 10 cm.

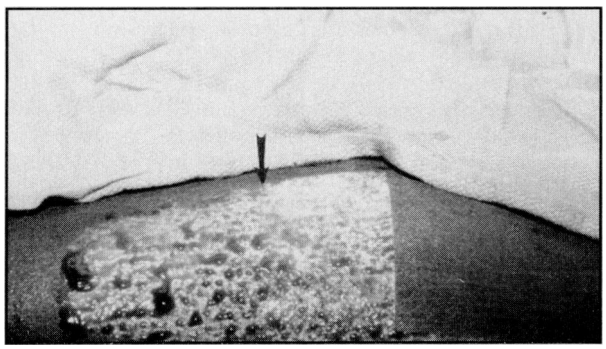

Figure 1. Donor site. The area to the left of the arrow is the control site and the area to the right of the arrow is the thrombin-treated site.

control sites. Topical thrombin solution containing 1000 units of thrombin bovine origin per cc was applied to the study site (half of the donor site), and an identical quantity of normal saline was applied to the control site (the second half of the donor site) in an identical manner.

The same number of dry, weighed gauze sponges were placed on each half. The sponges were removed at the end of 5 minutes and weighed to determine the blood loss. The area of each site was measured and the blood loss was determined for a 20-cm × 10-cm area for both the control and the thrombin-treated sites. The rate of reepthelialization was assessed for each area by the rate at which the xeroform dressing on the donor site lifted spontaneously, exposing a healed bed.

Four to 6 months after healing, the donor wounds were assessed for the quality of the scar in the control and thrombin-treated areas.

TABLE 2. MEAN, STANDARD DEVIATION, AND RANGE OF BLOOD LOSS AT THROMBIN-TREATED GRAFT SITES VERSUS CONTROL SITES IN 24 BURN PATIENTS

Donor Site	Mean Blood Loss (mL)	Standard Deviation	Range (mL)
Control	26.2	15.92	5.2-61.4
Thrombin	14.4	9.25	2.5-36.6
Difference	11.8	1.60	

RESULTS

The results showed a marked reduction in bleeding in the sites treated with thrombin compared to the control sites (Table 1 and Figure 1).

Statistical analysis showed that blood loss from the control site ranged from 5.2 mL to 61.4 mL (mean: 26.2 mL, $SD = 15.92$) (Table 2). Blood loss in the thrombin-treated sites ranged from 2.5 mL to 36.6 mL (mean: 14.4, $SD = 9.25$). The difference in mean blood loss between the control areas and thrombin-treated areas was 11.8 mL ($SD = 1.60$). No significant difference was noted in the rate of healing between the control and thrombin-treated areas in each patient. Both wounds healed between 7 and 14 days in almost all patients. The quality of the scar at 4 to 6 months was found to be no different at the control and thrombin-treated sites in each patient.

DISCUSSION

Thrombin is a protein substance produced through a conversion reaction where prothrombin is activated by tissue thromboplastin in the presence of calcium chloride:

CALCIUM CHLORIDE
PROTHROMBIN→THROMBIN
TISSUE THROMBOPLASTIN

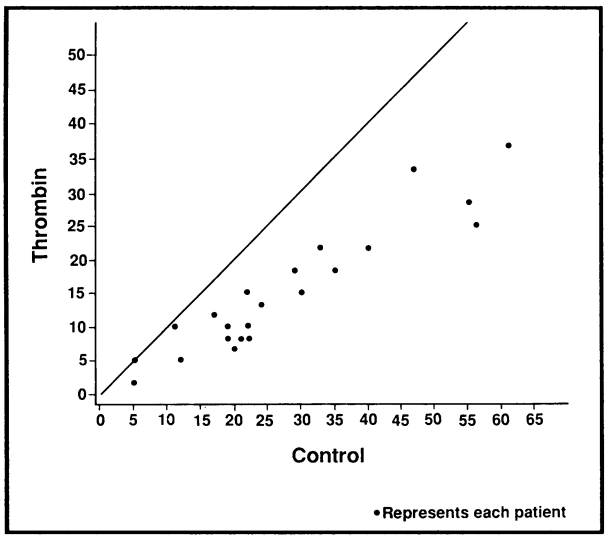

Figure 2. Graph depicting blood loss from the donor and thrombin-treated sites.

It acts in the final stage of blood coagulation to convert fibrinogen to fibrin in the presence of calcium:

THROMBIN
FIBRINOGEN→FIBRIN
CALCIUM

Thrombin is useful as an aid in hemostasis when oozing blood capillaries and small venules occur.[2] Thrombin has been used as a hemostatic agent in cardiac,[3] gynecological,[4] ophthalmologic,[5] visceral,[6] and maxillofacial[7] surgeries. It also has been used in burn debridement,[8] skin grafts, and surgery of heparinized patients.

This study demonstrates the significant hemostatic effect of thrombin on the donor site in burn patients.[9] There was an average reduction in bleeding of 43.5% on the thrombin-treated sites compared to the control sites, and decreased bleeding was noted in all 24 patients at the thrombin site (Figure 2).

Although there were considerable differences in individual blood loss as indicated by the standard deviations of 15.92 and 9.25, the standard deviation of 1.60 in the difference between the mean blood loss of the control and the thrombin-treated sites was a significant finding. It showed that most of the patients had comparable differences in blood loss between the thrombin and control sites. Using the paired *t*-test, the *P* value was statistically significant ($P<.001$).

The study also demonstrates that the use of thrombin has no deleterious effect on the healing of the donor site, and there is no long-term effect on the resulting scar.

As a result of this study, we believe that thrombin is useful as a hemostatic agent in burn patients undergoing debridement and skin grafting. We recommend its use, especially in patients who cannot tolerate significant blood losses.

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