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Use of Fibrin Sealant for Split-Thickness Skin Grafts in Patients with Hand Burns: A Prospective Cohort Study

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ABSTRACT

OBJECTIVE: To evaluate the efficacy of fibrin sealant as a topical hemostatic agent and for graft fixation during skin grafting of hand burns.

METHODS: This prospective cohort study enrolled 40 patients with hand burns from January 2013 to December 2016. They were all treated with excision and split-thickness skin graft and divided into the fibrin sealant with tourniquet group (20 patients) and epinephrine tumescence group (20 patients).

MAIN OUTCOME MEASURES: Demographic and clinical data such as age, sex, burn characteristics, operation time, estimated blood loss, and take rate were collected from each patient.

MAIN RESULTS: The demographic and burn characteristics were not statistically different between the two groups. Estimated blood loss per cm² (0.30 vs 1.00; $P < .001$) was significantly lower and the graft take rate (99.2% vs 98.2%; $P = .032$) was significantly higher in the fibrin sealant with tourniquet group.

CONCLUSIONS: The use of fibrin sealants accompanied by tourniquets for hand burns exhibited superior results in terms of decreasing blood loss and had a better graft take rate compared with treatment with epinephrine tumescence.

KEYWORDS: epinephrine tumescence, fibrin sealant, fixation, hand burn, graft take rate, split-thickness skin graft, tourniquet

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and fibrin sealant have been proposed to address this important issue. Unfortunately, physicians have yet to reach a consensus as to which hemostatic technique is superior.

The use of tourniquets is essential in limiting blood loss resulting from tangential excision and grafting. While this method applies to limb exsanguinations and has been shown to reduce blood loss, the adequacy of excision has been questioned.⁵ Further, graft take can also be compromised by the hematoma derived from the excised wound itself.⁶

Epinephrine tumescence has been used extensively as a hemostatic agent through either topical application or infiltration. The tumescent technique of subdermal injection of diluted epinephrine solution prior to debridement and grafting has been used to decrease intraoperative blood loss associated with tangential excision and autografting.⁷

Although the use of tourniquets has been recently replaced by epinephrine tumescence in most types of hand surgery, this replacement technique is still associated with a risk of finger loss depending on epinephrine dose.⁸

The use of sutures or staples is a standard method for skin fixation. However, the use of fibrin glue has also been suggested. Fibrin sealants were used as adhesive agents as early as 1909, and first used for skin graft fixation in 1944.⁹ Fibrin sealants originally developed as hemostatic agents and have been widely used as adhesives in plastic and reconstructive surgery.^{10,11} The adhesive properties of fibrin sealants can reduce postoperative pain,¹² and it is a useful treatment for full-thickness burn wounds because of favorable effects on surgical outcomes such as decreased time to hemostasis and reduced blood loss and complications.^{13,14}

Recently, burn care has focused on long-term outcome measures such as minimizing pain, improving quality of life measures, and overall aesthetics.¹⁵ Fibrin sealant was selected as a technique in this study because it may help meet those goals. The hypothesis was that patients who received a tourniquet in combination with fibrin sealants during hand burn surgery would show decreased blood loss and postoperative pain without affecting graft take in comparison with the use of epinephrine tumescence.

INTRODUCTION

During the last few decades, burn treatment has significantly improved survival in addition to enhancing critical care. However, the current standard of surgical management of full-thickness burn wounds is still early excision and autografting,^{1,2} and the large blood loss associated with surgical intervention is a challenge in burn surgery.³ A bloodless operative field is very important in hand surgery in particular.⁴ As a result, various hemostatic techniques such as tourniquets, epinephrine tumescence, thrombin,

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METHODS

This prospective cohort study evaluated patients with hand burns undergoing skin graft procedures from January 2013 to December 2016. Forty patients who were admitted in Burn Center, Hangang Sacred Heart Hospital, Hallym University, Seoul, Korea, were recruited consecutively for this study. Inclusion criteria were (1) patients with no more than 20% total body surface area (TBSA) burned, (2) patients who had third-degree hand burns involving at least three fingers, and (3) patients who were scheduled to undergo excision and split-thickness skin graft (STSG). Patients who were younger than 18 years; had an inhalation injury; were pregnant; or who had underlying diseases such as diabetes mellitus, acute kidney injury, and cardiac problems were excluded.

The patients were divided into the fibrin sealant with tourniquet (FT) group ($n = 20$, experimental treatment) and the epinephrine tumescent (ET) group ($n = 20$, conventional treatment) alternatively in order. At least two burn surgeons confirmed the study protocol to decrease selection bias.

This study design conformed to the Strengthening the Reporting of Observational Studies in Epidemiology guideline.¹⁶ Study protocols were approved by the Hangang Sacred Heart Hospital, Hallym University Ethics Committee. The authors obtained written informed consent from all patients. If the patients could not give consent, consent was obtained from the patient's spouse, parent, or child (if younger than 18 years), in that order. The operation method for the FT group was as follows: a tourniquet with 250 mm Hg of pressure was applied to the proximal side of the injured upper extremity. Involved hands were excised tangentially under such conditions. After excision, fibrin sealant (Greenplast Q; Green Cross Corporation, Yongin, South Korea) 400 IU/mL was administered topically using the TISSOMAT spray device (Baxter Healthcare Corporation, Westlake Village, California) on wound beds. Wet gauze dressing and elastic bandage compression were placed over all excised areas. Next, the tourniquets were deflated. After 10 minutes of elastic bandage compression, gauze was removed and the wound was reexamined. Focal hemostasis was completed using electrocautery if needed.

In the interim, a donor harvest was usually completed, followed by sheet-type STSG. Fixation of STSG was done through a dilution procedure.¹⁷ Fibrin containing 400 IU/mL of thrombin is typically used for hemostasis. However, when fibrin is used to facilitate skin grafting, clotting occurs before the STSG can be manipulated because of its short coagulation time. Accordingly, it becomes difficult to insert the graft into the wound bed. Therefore, in this study, graft fixation was performed by extending the coagulation time of fibrin sealant by 30 to 60 seconds via dilution of the thrombin component of the fibrin sealant. Grafts were affixed with a few sutures for anchoring, and thin adhesive strips (Nexcare Steri-Strip Skin Closure; 3M, Maplewood, Minnesota) were used as reinforcement.

The operation method for the ET group was as follows: a tumescent solution with a ratio of 1:400,000 epinephrine-to-saline solution was injected on the wound beds before excision. After excision, focal hemostasis was completed using electrocautery, and then a donor harvest was completed. The grafts were affixed using a stapler. Because the fibrin sealant is adhesive, this was not necessary in the FT group. The rest of the procedure was the same as in the FT group.

In both groups, wound dressings were changed every 2 days after surgery. Removal of staples and anchoring sutures was performed 6 to 7 days after autograft application in both groups. Postoperative pain was subjectively measured using a numeric rating scale (0- to 10-point scale)¹⁵ at day 6 or 7 after surgery both before and after the staple and suture removal.

Demographic data (age and sex), burn data (burn cause, TBSA, and the body percentage of full-thickness burns), and clinical data (operation area, operation time, estimated blood loss [EBL], unit of transfusion, and take rate) were collected from each patient. Graft take was assessed using Image J software (National Institutes of Health, Bethesda, Maryland). The EBL was determined intraoperatively by subjective measurement by two qualified observers (a surgeon and an anesthesiologist), and the estimates were compared with sponge count and total sponge weight.

All continuous variables were expressed as means \pm SD, and the frequencies of categorical variables were expressed as percentages. Continuous variables were analyzed with the independent t test for normal distributions and with the Mann-Whitney U test for nonnormal distribution. Categorical variables were assessed using the χ^2 test. $P < .05$ was considered to be statistically significant. Statistical analyses were performed using SPSS version 24.0 (IBM Corporation, Armonk, New York).

RESULTS

A total of 40 patients (34 males and 6 females) participated in the clinical study. Twenty patients were included in the FT group, and 20 patients were included in the ET group. Demographic characteristics (average age, 41.5 vs 46.5 years [$P = .293$]; male sex, 90% vs 80% [$P = .658$]) and burn characteristics (burn caused by flame, 90% vs 85% [$P = 1.000$]; TBSA of the burn, 16.4% vs 16.4% [$P = .849$]; and TBSA of full-thickness burn, 8.8% vs 9.3% [$P = .839$]) were not statistically different between the two groups (Table 1).

Further, differences in operation characteristics were not statistically significant between the two groups (operation area, 5% vs 4.7% [$P = .572$]; operation size, 923.5 vs 842.5 cm² [$P = .360$]; operation length, 112.5 vs 116.5 minutes [$P = .564$]). The EBL (287.5 vs 812.5 mL; $P < .001$), EBL per cm² (0.30 vs 1.0 mL/cm²; $P < .001$), and amount of transfusion (0.2 vs 1.9 units; $P < .001$) were significantly lower in the FT group. Graft take rate was also better (99.2% vs 98.2%; $P = .032$). Postoperative pain was lower in the FT group. Fewer complications such as hematoma and seroma

and no infection were observed in the FT group (10% vs 35%), but the difference was not statistically significant ($P = .130$; Table 2).

DISCUSSION

Full-thickness hand burns have always presented great challenges for burn surgeons. Regaining hand function after severe burn depends on various factors that include surgical factors; skin graft fixation is one of the most important.

Skin graft fixation using fibrin sealant has been widely performed since the late 2000s. It has also recently become a novel autograft fixation method.¹⁰ Fibrin sealants are human-derived factors that are designed to reproduce the final steps of the physiologic coagulation cascade of a stable clot. The substance's physical attributes make it suitable for affixing skin grafts to recipient wound beds; it creates an ultrafine matrix structure to diffuse nutrients and cytokines, promote neovascularization, and facilitate growth of fibroblasts and capillary endothelial cells by serving as a scaffold. This structure promotes phagocytosis and blocks sources of infection.⁹

When compared with fibrin sealant, epinephrine tumescence is a good modality to reduce blood loss and is also widely used, but this technique carries a risk for tissue necrosis resulting from vasoconstriction, especially when used on the fingers.^{3,7,8}

Study authors chose to work with patients with hand burns because hand surgery necessitates a bloodless operative field and meticulous techniques. Further, two modalities for reducing blood loss were compared. It is therefore difficult to compare this study directly with other studies^{6,7,18} because the blood loss measurement and the operation sites differ.

Foster et al¹⁸ reported on the efficacy and safety of a fibrin sealant for adherence of skin graft to burn wounds, stating that

fibrin sealant is safe and effective for attachment of skin grafts, with outcomes better than staple fixation.¹⁸ Notably, EBL per cm² was much lower in the FT group (0.30 mL/cm²) than the ET group (1.0 mL/cm²) in the present study, although electrocautery was rarely used. These results suggest that epinephrine tumescence alone is not as effective as fibrin sealant with tourniquet use.

To ensure skin graft take, it is important to prevent hematoma and seroma development and the resulting inhibition of blood vessel in-growth in the graft, which plays a critical role in graft failure. This study showed that the FT group had lower hematoma and seroma rates even though there were no statistically significant differences because of the small group of subjects, further recommending this modality. No infections were observed in either group.

Staple removal can cause significant pain and anxiety in patients and often requires intravenous analgesia or general anesthesia. Staples cause severe complications if left in situ for long periods of time.^{19,20} In this study, a few sutures and thin adhesive strips in the FT group and staples in the ET group were used as anchoring materials. Pain scores before and after the removal of anchoring materials were recorded and significantly increased pain scores were reported in the ET group. Increased pain scores (2.10 to 5.25) were reported in the ET group, subsequently requiring additional pain medication or sedation during staple removal. This finding is consistent with other studies that show severe pain during staple removal, despite additional pain control,^{19,21} and again recommends the FT method over the ET method.

Prior to this study, there have been very few, if any, reports examining the operating methods to address burned extremities using hemostatic methods (notably, the tourniquet) for burn care. Desai et al²² indicated that blood loss could be reduced to 0.49 to 1.19 mL/cm² after early excision and tourniquet control. Although

Table 1.

PATIENT DEMOGRAPHICS

Variable	Total (N = 40)	FT Group (n = 20)	ET Group (n = 20)	P
Age, y	44.0 ± 15.2	41.5 ± 15.1	46.5 ± 15.1	.293
Median	46.0	41.5	48.5	
Range	10–75	10–75	16–69	
Sex, n (%)				.658
Male	34 (85.0)	18 (90.0)	16 (80.0)	
Female	6 (15.0)	2 (10.0)	4 (20.0)	
Burn cause, n (%)				1.000
Flames	35 (87.5)	18 (90.0)	17 (85.0)	
Scalds	5 (12.5)	2 (10.0)	3 (15.0)	
TBSA burned, %	16.4 ± 10.1	16.4 ± 10.9	16.4 ± 9.5	.976
Median	13.5	13.5	13.5	
Range	4–46	4–46	5–45	
TBSA of full-thickness burn, %	9.0 ± 8.4	8.8 ± 8.3	9.3 ± 8.7	.839
Median	6.0	5.0	6.0	
Range	4–40	4–30	4–40	

Abbreviations: ET, epinephrine tumescent; FT, fibrin sealant with tourniquet; TBSA, total body surface area. Values are expressed as mean ± SD.

Table 2.

OUTCOMES SUMMARY

Variable	Total (N = 40)	FT Group (n = 20)	ET Group (n = 20)	P
Operation area, %	4.8 ± 1.4	5.0 ± 1.3	4.7 ± 1.5	.572
Median	4.0	4.51	4.0	
Range	2–8	4–8	2–8	
Operation area, cm ²	883.0 ± 275.4	923.5 ± 278.8	842.5 ± 273.0	.360
Median	808.5	857.0	790.0	
Range	318–1680	624–1680	318–1544	
Operation time, min	114.5 ± 21.5	112.5 ± 27.5	116.5 ± 13.5	.564
Median	110.0	110.0	110.0	
Range	85–190	95–140	85–190	
EBL, mL	550.0 ± 357.5	287.5 ± 176.1	812.5 ± 293.7	<.001
Median	450.0	250.0	775.0	
Range	100–1500	100–750	350–1500	
EBL/operation area, %	116.6 ± 73.2	56.7 ± 25.9	176.5 ± 52.8	<.001
Median	92.7	56.3	181.3	
Range	25–287.5	25–93.8	87.5–287.5	
EBL/cm ²	0.6 ± 0.4	0.3 ± 0.1	1.0 ± 0.3	<.001
Median	0.5	0.3	1.0	
Range	0.1–1.6	0.1–0.5	0.5–1.6	
Amount of transfusion, unit	1.1 ± 1.0	0.2 ± 0.4	1.9 ± 0.7	<.001
Median	1.0	0.0	2.0	
Range	0–3	0–1	1–3	
Postoperative pain before anchor material removal	2.1 ± 0.9	2.1 ± 0.9	2.1 ± 1.0	.869
Median	2.0	2.0	2.0	
Range	1–4	1–4	1–4	
Postoperative pain after anchor material removal	4.8 ± 1.3	5.2 ± 1.4	4.4 ± 1.0	.040
Median	4.0	3.5	5.0	
Range	3–8	2–6	3–8	
Graft take rate, %	98.8 ± 1.5	99.2 ± 1.0	98.2 ± 1.7	.032
Median	99.0	99.5	99.0	
Range	94–100	96–100	94–100	
Complications, n (%)	9 (22.5)	2 (10.0)	7 (35.0)	.130
Hematoma/seroma				

Abbreviation: EBL, estimated blood loss; ET, epinephrine tumescent; FT, fibrin sealant with tourniquet. Values are expressed as mean ± SD.

many methods for reducing blood loss are similar, the combined use of tourniquets and fibrin sealants specifically have not been examined and reported prior to this study. These data show that blood loss per centimeter excised was less in the FT group (0.30 ± 0.1 mL/cm²) versus the ET group (1.00 ± 0.3 mL/cm²) and these patients experienced reduced pain after the removal of the FT procedure's respective anchoring materials (3.60 vs 5.25, $P = .001$).

Further, these data show similar graft takes between the two groups (99.2% vs 98.2%). Essentially, the FT group showed superior results compared with the ET group.

Limitations

This single-center study comprised a relatively small sample. However, most patients who experience major burns are transferred to this center from across the nation. Therefore, this patient sample was representative of Korean patients with burns.

Second, because the patients were not randomly assigned, there may have been a selection bias. To reduce this possible

source of bias, only patients with hand burns were enrolled. Moreover, all burn surgeons who performed the study procedures were experts and accordingly there was little to no treatment difference attributable to the surgeons.

CONCLUSIONS

Although fibrin sealant has proven to be effective in skin graft fixation and graft take, it is less widely used than sutures and staplers. Limitations notwithstanding, these data showed that there are favorable results that accompany the use of a tourniquet and fibrin sealants. There was also a marked reduction in blood loss in the FT group, which minimized the need for blood transfusion. Further, patients experienced less pain during the removal of anchoring materials compared with the removal of staples in the ET group. The authors believe that this technique deserves clinician attention and that these results may be generalizable to other populations. Further randomized controlled trials should be performed to verify these results. ●

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