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Original Article

Comparative Analysis of Effect of Lidocaine and Adrenaline Soaked Gauze Versus Normal Saline Soaked Gauze at Skin Graft Donor Site of Thigh: A Randomized Control Trial

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ABSTRACT

Objective: To compare the hemostatic effect of Lidocaine and Adrenaline soaked gauze with normal saline soaked gauze at skin graft donor site of thigh.

Study Design: Randomized control trial (Trial ID: NCT04344483).

Place and Duration of Study: Plastic & Reconstructive Surgery Department, Dow University of Health Sciences Dr. Ruth K.M. Pfau Civil Hospital, Karachi Pakistan, from Jun to Oct 2020.

Methodology: A randomized controlled trial was carried out on 60 Patients under treatment in burn surgery unit. Patients were randomly assigned to 2 groups. Patients in both groups at donor sites received subcutaneous infiltration for 10 minutes, either with 2% Lidocaine and 1:100,000 Adrenaline soaked gauze or with normal saline soaked gauze. Outcomes included intraoperative bleeding, number of dressings required in first 24 hours after surgery, post-operative pain in first 24 hours, systemic analgesia requirement after surgery within 24 hours and donor-site epithelization at 14th post-operatively. Statistical Package for Social Sciences version 25 was used to analyze the data.

Results: out of 60 patients, the mean age was estimated as 36.58±12.42 years and 44(73.3%) patients were males while 16(26.7%) were females. Statistically significant difference was observed in number of dressings (p=0.001), mean pain score in first 24 hours (p=0.001), intra-operative bleeding (p=0.001) and systemic analgesia requirement in 24 hours of surgery (p=0.001) between both groups.

Conclusion: In comparison to normal saline soaked gauze, the Lidocaine and Adrenaline soaked gauze was effective in terms of number of dressings, pain in first 24 hours, intra-operative bleeding and systemic analgesia requirement after burn surgery at skin graft donor site of thigh.

Keywords: Adrenaline, Burn surgery, Donor site, Hemostatic effect, Lidocaine, Normal saline, Skin graft.

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INTRODUCTION

Third-degree burns and other wounds such as road rash, pressure ulcers, wounds from necrotizing tissue infections and crush injury wounds may need to undergo excision and skin grafting.[1] Many surgical specialists commonly use procedure of split-skin grafting (SSG).[2] Split-thickness skin grafting (STSG) frequently used as a rehabilitation technique to replace missing or broken skin which is caused by chronic wounds, trauma and burns.[3] They are also used to resurface line cavities, close donor sites of flaps, and resurface muscle flaps and mucosal deficits. Split-thickness skin graft provides effective and quick way for closure and healing of acute and chronic wounds.[4] The formation of second wound (donor site) takes place in SSG. Epidermis and part of the dermis is being excised in a procedure of split thickness or partial thickness skin graft. Split-thickness skin graft is frequently used technique in clinical practice for the management of postoperative, post-burn and post-traumatic wounds. SPTSG is still considered as gold-standard to cover deep skin defects.[5]

The donor site treatment following the split-thickness skin graft is a concern in clinical practice because more pain at donor site is usually reported by patients as compared to the graft recipient site.[6] Bleeding is a routine complication of SPTSG specifically at donor site from where skin is harvested. SPTSG donor site may bleed extensively specially in patients with massive burning of total body surface area (TBSA).[6] Rapid and effective hemostasis causes more promising outcome, short time in operation theatre and a healing process free from any adverse event.[7] The local management of donor site wounds should be aimed to provide surroundings that permit uneventful and speedy re-epithelialization with reduction in discomfort, hospital length of stay and pain. Pain may be reduced by adequate control of blood loss during and after surgery that, lessen the

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surgical time, intervention becomes easier and harmless, shorten the period of re-epithelialization at donor-site and economically beneficial as availability of operating room increases for others. The classic split thickness skin graft dressing should be hemostatic, fast in epidermal healing and antibacterial.[2,8,9]

Regrettably, hemostasis is a subject in the field of surgery which is understudy and on-going practice is based on habits and beliefs instead of evidence. In simple words, there is no such gold-standard for topical hemostasis.[7] There is no consensus developed for the management of donor-site in a specific way for rapid healing, increased patient comfort and decreased pain.[9] However, various techniques have been suggested for improved control on bleeding such as subcutaneous, systemic and topical treatments. The use of subcutaneous or topical vasoconstrictors like Adrenaline is proven beneficial to restrict the blood loss.[8] While it has been found in various studies that injectable Adrenaline under donor-site skin reduces bleeding in burn surgery, it is currently not largely known practice.[1] Nevertheless topical Adrenaline gauze, tourniquet and electrocautery is still used by many surgeons. There is variation in literature regarding the information on systemic and local effects of epinephrine. Some authors believe that effects are transient and minimal whereas others report that the effect on graft and healing of donor skin is adverse.[10] Therefore, the study aims to investigate the hemostatic effect of Lidocaine and Adrenaline soaked gauze v/s normal saline soaked gauze to further study the role of Adrenaline in control of blood loss of donor-site.

METHODOLOGY

It was a randomized control trial (Trial ID: NCT04344483) conducted at Plastic & Reconstructive Surgery Department, DUHS Dr. Ruth K.M. Pfau Civil Hospital, Karachi from Jun to Oct 2020. Sample size of 33 patients per group was calculated by using PASS 11 sample size calculator by taking proportion of patients who bleed less than normal for Lidocaine and Adrenaline soaked gauze as 0.36,[11] by considering 35% difference in controls, power of test as 80% and 95% confidence level. The patients were recruited through non-probability purposive sampling technique.

Inclusion criteria: Patients undergoing burn surgery of age more than 15 years of either gender with thigh as a donor-site were included in the study.

Exclusion criteria: Patients with bleeding disorder, concomitant injuries, donor site other than thigh, previously harvested donor-site and patients on anti-platelet medications were excluded from the study.

Study was conducted after obtaining approval from hospital Ethics Committee and Dow Institutional Review Board (IRB-1506/DUHS/Approval/2020). The purpose of study and associated risks and benefits of the procedure were explained to patients or their attendants to get their consent to become the part of the study. Patients were recruited after obtaining informed consent. Confidentiality of the study participants was assured by tagging patients' medical record number with other serial number. The patients were randomly assigned to two groups, 30 patients were assigned to Group-A while 30 patients were assigned to Group-B. Closed envelop technique was used for random assignment of the patients. Group-A was treated with Lidocaine, Adrenaline soaked gauze and Group-B was treated with normal saline soaked gauze. After admission of the patients, they Split thickness skin graft was harvested from donor site using Humby's knife. Humby's knife was adjusted to the thickness of graft. It was placed at the settings of 0.011 to 0.015 inch (0.25-0.4 mm). Due to unreliability of these settings we ensured the proper thickness of the graft by adjusting the opening of the blade so that it could be snuggled fit the beveled edge of a number 10 blade into the opening. Down blade for the knife was kept at 1.5 mark for both the groups. After harvesting skin from donor-site, the soaked gauze was applied to the donor-site for ten minutes. The procedure was performed by consultant surgeon under general anesthesia. Group-A received 2% Lidocaine and 1:100,000 Adrenaline soaked gauze while Group-B received normal saline soaked gauze at donor-site for ten minutes. After removal of the soaked gauze Sufratul dressing was applied to donor-site of the patients of both the groups. Dressing on donor-site was opened on 14th post-operative day or in some cases before as was necessary due to exudate or bleeding. Graft viability was assessed on 5th post-operative day. Moisturizing creams was applied to donor sites after complete epithelialization. Post-operative pain was monitored in first 24hrs after surgery. The primary end point of study was intraoperative bleeding. The secondary end points of study include number of dressings required in first 24 hours after surgery, donor-site epithelization at 14th post-operative day, post-operative pain in first 24 hours along with systemic analgesia requirement after surgery.

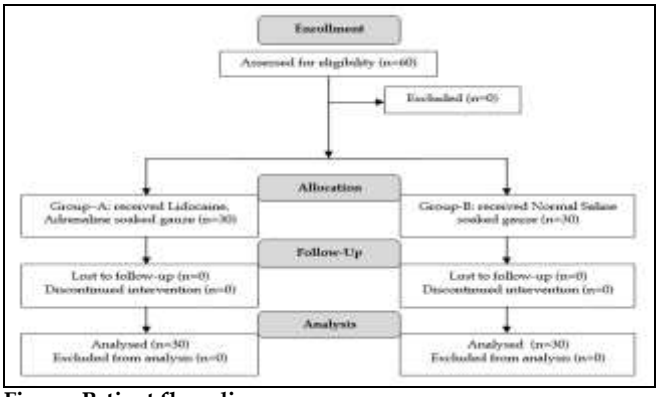

Figure: Patient flow diagram

SPSS version 22 was used to analyze data. Quantitative variables like age and post-operative pain in 24 hours of surgery were expressed as Mean and SD. Median and interquartile range was estimated for number of dressings required. Qualitative variables such as gender, intra-operative bleeding, systemic analgesia requirement in 24 hours after surgery and donor-site epithelialization were expressed as frequency with percentage. Mean rank of number of dressings was compared between both groups using Mann-whitney U test. Independent samples t-test was used to compare post-operative pain in first 24 hours and Fisher-exact test was to compare intraoperative bleeding, donor-site epithelization at 14th post-operative day and systemic analgesia requirement after surgery between both groups. The outcomes which were significant between both groups i.e. number of dressings, post-operative pain in first 24 hours, intraoperative bleeding and systemic analgesia requirement after surgery were stratified with respect to age and gender. The *p*-value ≤0.05 was taken as statistically significant.

RESULTS

The mean age was estimated as 36.58±12.42 years and most of the patients were of age >35 years (n=38, 63.3%). Out of 60 patients, 44 were males (73.3%) and 16 were females (26.7%).

The median number of dressing was 0 (Inter-quartile range: 0-1). Overall, mean pain score in first 24 hours was 4.70±2.09. Out of 60 patients, 17(28.3%) patients had abundant intra-operative bleeding, 37(61.7%) patients had less than normal bleeding and 6(10.0%) patients had normal bleeding. Of 60 patients, 27(45%) patients had required systemic analgesia after surgery and 59(98.3%) patients had donor-site epithelization at 14th post-operative day respectively.

The mean rank of number of dressings was significantly higher in Group-B than Group-A, which indicates that patients in Group-B required more dressings than Group-A (*p*=0.001). The mean pain score in Group-B was 5.56±2.11 which was higher than Group-A (3.83±1.70), the difference between both groups was statistically significant (*p*=0.001). In Group-A, none of the patients had abundant intra-operative bleeding whereas in Group-B more than half of the patients abundant intra-operative bleeding (56.7%), the relationship was statistically significant between groups and intra-operative bleeding (*p*=0.001). In Group-A, only 20% of the patients required systemic analgesia in 24 hours of surgery whereas in Group-B 70% of the patients required systemic analgesia in 24 hours of surgery. There was statistically significant relationship between systemic analgesia requirement in 24 and both groups (*p*=0.001). (Table-I)

Table-I: Comparison of Outcomes Between both Groups (N=60)

Outcomes	Group-A	Group-B	*p*-value
Pain in first 24 hours (Mean±SD)	3.83±1.70	5.56±2.11	0.001
Intra-operative bleeding [n(%)]			
Abundant	0	17(56.7)	0.001
Less than Normal	27(90.0)	10(33.3)	
Normal	3(10.0)	3(10.0)	
Systemic analgesia requirement in 24 hours [n(%)]			
No	24(80.0)	9(30.0)	0.001
Yes	6(20.0)	21(70.0)	
Donor **site epithelialization at 14th post-op day [n(%)]**			
No	0	1(3.3)	0.999
Yes	30(100.0)	29(96.7)	

Table-II: Association of Number of Dressings and Pain in First 24 Hours with Respect to Age and Gender

	Groups		*p*-value
	Group-A	Group-B	
No of dressings (Mean Rank)			
Age groups			
≤ 35 years	13.54	9.05	0.107
>35 years	24.44	15.05	0.001
Gender			
Male	5.36	10.94	0.012
Female	18.74	26.62	0.017
Pain in first 24 hours (Mean±SD)			
Age groups			
≤ 35 years	5.00±1.75	4.70±1.76	0.695
>35 years	5.94±2.28	3.40±1.53	0.001
Gender			
Male	3.82±1.64	5.42±2.18	0.067
Female	3.85±2.03	5.88±2.02	0.001

In age group >35 years, the mean rank of number of dressings was higher in Group-A than Group-B (p=0.001). Similarly, in both gender i.e. male and female, the mean rank of number of dressings was significantly higher in Group-B than Group-A (p=0.012 and p=0.017). In age group >35 years, mean pain in first 24 hours of surgery significantly higher in Group-A than Group-B (p=0.001). With respect to gender, in males no statistically significant difference was observed between Group-A and Group-B for mean pain in first 24 hours of surgery (p=0.067), whereas in females statistically significant difference was observed between Group-A and g=Group-B for mean pain in first 24 hours of surgery (p=0.001). (Table-II)

With respect to age groups i.e. ≤35 years and >35 years statistically significant difference was observed in proportions of intra-operative bleeding (p=0.001 and p=0.001) whereas for systemic analgesia requirement significant difference was observed in age>35 years (p=0.001) between both groups. With respect to gender i.e. female and male statistically significant difference was observed in proportions of intra-operative bleeding (p=0.048 and p=0.001) and systemic analgesia requirement (p=0.024 and p=0.003) between both groups. (Table-III)

Table-III: Association of Intra-Operative Bleeding and Systemic Analgesia Requirement with Respect to Age and Gender (n=60)

	Groups	Intra-operative bleeding			*p*-value	Systemic analgesia requirement in 24 hours		*p*-value
		Abundant	Less than Normal	Normal		No	Yes	
Age groups								
≤ 35 years	Group A	8(66.7%)	3(25.0%)	1(8.3%)	0.001	4(33.3%)	8(66.7%)	0.09
	Group B	0	8(80.0%)	2(20.0%)		7(70.0%)	3(30.0%)	
>35 years	Group A	9(50%)	7(38.9%)	2(11.1%)	0.001	5(27.8%)	17(72.2%)	0.001
	Group B	0	19(95.0%)	1(5.0%)		17(85.0%)	3(15.0%)	
Gender								
Female	Group A	0	7(100.0%)	0	0.048	5(71.4%)	2(28.6%)	0.024
	Group B	4(44.4%)	4(44.4%)	1(11.2%)		1(11.1%)	8(88.9%)	
Male	Group A	0	20(87.0%)	3(13.0%)	0.001	19(82.6%)	4(17.4%)	0.003
	Group B	13(61.9%)	6(28.6%)	2(9.5%)		8(38.1%)	13(61.9%)	

DISCUSSION

The skin grafting in burn surgery are significantly correlated with morbidity such as pain and blood loss.[12] Adrenaline, introduced by Braun in 1902, has been used as a vasoconstrictor.[11] Later on, multiple applications of Adrenaline, comprising of tropical application of Adrenaline-soaked swabs and subcutaneous Adrenaline solution infusion, were describe to help prevent blood loss in burn surgery.[2] Appropriate monitoring is necessary while using these methods, as cardiac arrhythmias can occur, especially when Adrenaline is used in conjunction with inhalational anesthesia.[11,13] In burn surgery, previous research found that subcutaneous injection of Adrenaline solution at concentrations up to 1:50,000 had strong outcomes, and even higher concentrations were successfully used in other types of surgery.[14] However, even with promising results, some recent comparative studies have been published to disregard these results.[1,11] To best of our knowledge, there is no such study being conducted in Pakistan to assess intra-operative bleeding, the number of dressings needed on donor site, post-operative pain in first 24 hours along with systemic analgesia requirement after surgery or percentage of donor-site epithelization at 14th post-operative day. Therefore, in this research we have evaluated the effect of 2% Lidocaine and 1:100,000 Adrenaline soaked gauze as compared to normal saline soaked gauze at donor-site of thigh for ten minutes in burn surgery.

In the present research, we found that intra-operative blood loss was less than normal-to-normal in 100% of the patients who had 2% Lidocaine and 1:100,000 Adrenaline soaked gauze. Whereas in normal saline soaked gauze group, more than 50% of the patients had abundant blood loss. Cartotto R *et al.* measured the impact of an intraoperative blood saving technique containing donor site and excised wound topical Adrenaline, donor site and burn wound Adrenaline tumescence and limb tourniquets relative to a historical test group, where only topical Adrenaline and thrombin is added to donor sites and excised wounds. Results of the study revealed that mean blood loss decreased from 211 mL per percentage of excised and grafted body surface area in the historical control group to 123 mL in the

conservation strategy group (p=0.02) and concluded that conservative strategy resulted in profound results.[15] Brezel *et al*. in their research found that less bleeding was observed in epinephrine treated sites versus thrombin treated sides (29 vs 0) with relative risk as 59 (RR 95% CI 3.76-925.91).[16] In another research by Gacto *et al*. also observed statistically significant difference in blood loss "less than normal" in epinephrine treated donor site versus cases treated with saline (Relative risk=2.60).[11]

In our study, we observed a substantial difference between two groups in intra-operative blood loss, and additionally we found a significant difference between both groups in the number of dressings. There were less hydrocolloid dressings for patients in the Lidocaine and Adrenaline saturated gauze group than for patients in the usual saline group. It is one of the benefits of subcutaneous Adrenaline penetration to mitigate the oozing into the hydrocolloid dressing following surgery, which stays dry and clean and does not need to be changed and decreases pain associated with those manoeuvres as well.[17,18] Zhang J *et al*.,[19] investigated the effect of 2% Lidocaine and 5% sodium bicarbonate mixture spray on wound dressing in burn surgery. They found SpO2 during dressing in the alkalized Lidocaine group was significantly higher than the control group (p=0.001). Further alkalized Lidocaine group showed lower pain than control group (p<0.001), and the pain scores during and post debridement and dressing in the alkalized Lidocaine group were significantly lower than control group (p=0.001). Hence, they concluded Lidocaine has significant analgesic effect and may help in reducing post-operative pain. In the present study, we have also found significant lower post-operative pain in intervention than control group.

As the addition of local anesthesia to injected solution help in reducing postoperative pain, similarly it may also help in reducing the requirement of systemic analgesia.[20] The present study also revealed that patients in Lidocaine group required less systemic analgesia in 24 hours of surgery than patients in control group (20% versus 70%). Hence, hemostatic agents are important patients undergoing for skin grafting for burn surgery or for any other procedure where minimization of blood loss, post-operative pain and dressings are desired.[2] Further multi-center with larger sample size studies are required in order to increase the generalizability of the findings. Also the area of graft should be considered and compare with post-operative pain and analgesia requirement as it could be a confounding factor.

CONCLUSION

As compared to normal saline soaked gauze, the Lidocaine and Adrenaline soaked gauze was effective in terms of number of dressings requirement, post operative pain management in first 24 hours, intra-operative bleeding control and systemic analgesia requirement in 24 hours of burn surgery at skin graft donor site of thigh.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

ZZ & HA: Data acquisition, data analysis, critical review, approval of the final version to be published.

RMK & US: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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