Journal of Clinical and Investigative Surgery

https://doi.org/10.25083/2559-5555
https://proscholar.org/jcis/
ISSN: 2559-5555

Comparison of blood loss at the donor site & Acute cardiovascular effects by using adrenaline infiltration and topical adrenaline during skin graft harvest

Chethan L[1*], Harish Kumar P[2], Ramesh Kumar Sharma[3], Sandhya Yaddanapudi[4]

[1]*Department of Plastic Surgery, JSS Medical College and Hospital, Mysuru, Karnataka, India*
[2]*Department of Anaesthesia, JSS Medical College and Hospital, Mysore, Karnataka, India*
[3]*Department of Plastic Surgery, PGIMER, Chandigarh*
[4]*Department of Anaesthesia, PGIMER, Chandigarh*

ABSTRACT

Background. Burn surgery is associated with high blood loss to both the donor and recipient site. Although various techniques for reducing intraoperative blood loss have been described, topical adrenaline and adrenaline infiltration have significantly reduced blood loss. The present study compared blood loss to the donor site and acute cardiovascular effects (such as heart rate/ HR and blood pressure/ BP), by using adrenaline infiltration and topical adrenaline while harvesting the skin graft in the same patient, but in a different place. *Materials and Methods*. It is a prospective study that included 50 patients, all undergoing skin graft harvesting using method 1 and local adrenaline - method 2, in different locations. Blood loss and acute cardiovascular effects were assessed and compared between two methods. *Results*. Blood loss at the donor site is significantly lower in adrenaline infiltration compared to topical infiltration (4.7±0.6 ml vs 10.4±1.2 ml, $p<0.001$). Compared to baseline, the mean increase in HR and BP was significantly higher after adrenaline infiltration than topical adrenaline, but for a short period of time. Changes in HR values were larger than in BP. *Conclusions*. Our study showed that adrenaline infiltration was better than topical adrenaline in conserving blood loss, but acute cardiovascular effects (increased BP and HR) were greater after infiltration, being clinically insignificant and requiring no treatment.

Category: Original Research Paper

Received: February 03, 2022
Accepted: April 5, 2022
Published: May 15, 2022

Keywords:

blood loss, heart rate, blood pressure, donor site, topical adrenaline, adrenaline infiltration

*Corresponding author:

Chethan L,

Department of Plastic Surgery, JSS Medical College and Hospital, Mysuru, Karnataka, India 570015

E-mail: chethan.doctru@gmail.com

Introduction

A wide variety of techniques have been described to reduce intraoperative blood loss at both the recipient site and the donor site. These include the application of topical epinephrine with or without thrombin to excised wounds and/or donor sites, and subcutaneous infiltration of vasoconstrictors such as epinephrine [1,2]. Some studies have assessed topical epinephrine combined with subcutaneous epinephrine at only specific skin graft donor sites, such as the scalp [3]. Others have examined infiltration of epinephrine beneath all burn wounds and donor sites, but have not reported whether tourniquets were used adjunctively [4]. Still others have reported subcutaneous epinephrine infiltration without use of topical epinephrine application [5].

Historically, burn wound excision and skin graft closure have been associated with substantial intra-operative blood loss [6-9]. However, epinephrine tumescence of burn wounds and donor sites, combined with the use of topical epinephrine, has significantly reduced blood loss during burn surgery [4,10-13]. The acute systemic effects of the administered epinephrine (both subcutaneous and topical) are incompletely understood. Although the majority of investigators have reported no significant adverse cardiovascular effects [3,12,14-17], others have described episodes of tachycardia and/or hypertension related to the administration of epinephrine during burn surgery [18,19]. Unfortunately, interpretation of these studies is complicated by variability in the injected volumes and concentrations of the epinephrine solutions, by the anecdotal nature of many of the observations, and by the absence of detailed prospective monitoring of cardiovascular parameters during and after epinephrine administration. No prospective studies have specifically

To cite this article: Chethan L, Harish Kumar P, Ramesh Kumar Sharma, Sandhya Yaddanapudi. Comparison of blood loss at the donor site & Acute cardiovascular effects by using adrenaline infiltration and topical adrenaline during skin graft harvest. *J Clin Investig Surg*. 2022;7(1):56-61. doi: 10.25083/2559.5555/7.1.10

examined the cardiovascular responses to subcutaneous and topical epinephrine during burn surgery.

According to our data, there are still no studies comparing blood loss using adrenaline infiltration and topical adrenaline at the donor site in the same patient. The current study aims to compare the blood loss at the donor site and the changes in cardiovascular effects induced by the two methods, and to show which is superior in preserving blood loss during skin graft harvesting.

Materials and Methods

This prospective study was conducted at the Postgraduate Institute of Medical Education and Research [PGIMER], in the Departments of Plastic Surgery and Anaesthesia & Intensive Care, for a period of two years. Patients undergoing superficial skin graft surgery during this period were included in the study. All fifty patient underwent skin graft harvest using Adrenaline solution 1:5,00,000 (2 mL of 1:1,000 adrenaline in 1 liter of warm injectable normal saline). Area of skin graft taken was 50cm^2. Patients who are having skin diseases like pemphigus diseases, necrotizing fasciitis, cardiac diseases, hypertension (>150/90 mm of Hg) were excluded from study. Blood loss during skin grafting at the donor site and acute effects on cardiovascular system, such as BP and HR, have been noted in the two methods.

Method 1

Skin was prepared by painting and draping. Baseline blood pressure and heart rate were noted. 1:5,00,000 adrenaline solution (2mL of 1:1,000 adrenaline in 1 liter of warm injectable normal saline) infiltration has given at the donor site by using 10ml syringe attached to 18-gauge needle. The infusion was by hand pressure. The skin was infiltrated until it became firm (approximately 30ml). Blood pressure and heart rate was noted after 1minute, 2minutes, 3minutes, 4minutes, 5minutes, 10minutes and 15minutes of adrenaline infiltration. The skin graft was taken after 15 minutes of infiltration using the manual dermatome or Humby's knife. The excised donor site was covered by serial application of weighed saline soaked gauze pads for 15mins, and the weight of the blood-soaked gauze pads was noted in grams. Blood loss was estimated by subtracting the weight of saline soaked gauze pads from that of blood-soaked gauze pads.

Method 2

It was performed on the same patient 5 minutes after the completion of the above procedure. Skin was prepared by painting and draping for the second graft. Baseline blood pressure and heart rate was noted. Graft was taken from the donor site by using manual dermatome or Humby's knife. Excised donor site was covered by serial application of weighed gauze pads soaked in 1:5,00,000 adrenaline solution (2 ml of 1:1,000 adrenaline in 1 liter of warm injectable normal saline) for 15 minutes and weight of the blood-soaked gauze pads noted in grams. Blood loss and blood pressure, heart rate was noted as done in method 1.

Then, blood loss and acute effects on cardiovascular system, such as blood pressure and heart rate were compared between method-1 and method-2 by statistical analysis.

Statistical analysis

Data were expressed in mean ± SD and percentage. For analysis, percentage change (from the baseline) in blood pressure and heart rate were calculated using the following formula: Percentage change in BP or HR =

$$= \frac{\text{recorded BP or HR-Baseline BP or HR} \times 100}{\text{Baseline BP or HR}}$$

The data were compared between the two methods by using Student's paired t-test. P-value<0.05 was considered as statistically significant.

Results

Fifty patients were enrolled in this prospective study. Blood loss and acute cardiovascular effects, such as blood pressure (BP) and heart rate (HR), were noted after the two methods in all these 50 patients. The mean ± SD (range) age of the patients was 31.9±11.6 (15-50 years). Males were 40 (80%) and females were 10 (20%). In 23 patients (46%) graft was taken from the right thigh, while in the remaining 27 patients (54%) graft was taken from the left thigh (Table-1).

Table 1

Parameters		**Value (n=50)**
Age (mean±SD (range))		31.9±11.6 (15-50) years
Sex (number of patients)	Male	40 (80%)
	Female	10 (20%)
Site (number of patients)	Right thigh	23 (46%)
	Left thigh	27 (54%)

The mean blood loss was 4.7±0.6 grams in method-1 and 10.4±1.2 grams in method-2. A comparison of two methods shows that blood loss was significantly less in method-1, with a p-value <0.001 (Figure 1).

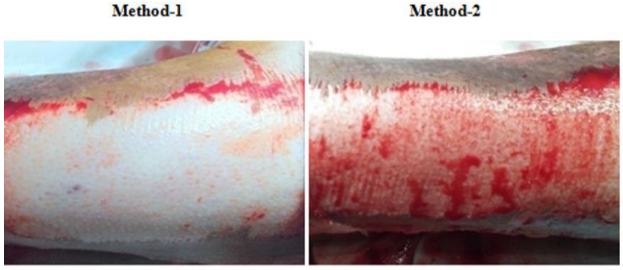

Figure 1. Appearance in the case of the two methods studied

BP and HR were noted at baseline and 1, 2, 3, 4, 5, 10 and 15 minutes after adrenaline infiltration or topical application. For analysis, the percentage change from baseline in blood pressure and heart rate was calculated using the formula presented above.

The maximum change in SBP occurred at 2nd minute with both infiltration and topical methods (5.0±4.5 vs 2.1±2.6 respectively). Change in SBP was statistically different at all measurement times (1 minute to 15 minutes) between the two methods (Table 2 and Figure 2).

Table 2

Time	Method-1 (n=50) mean SBP(% change)±SD	Method-2 (n=50) mean SBP(% change)±SD	p-value
1st minute	4.6±3.0	1.3±1.8	<0.001
2nd minute	5.0±4.5	2.1±2.6	<0.001
3rd minute	3.9±4.0	1.6±2.8	<0.001
4th minute	3.2±4.7	1.4±3.3	0.004
5th minute	2.2±3.6	0.9±3.5	0.023
10th minute	1.8±3.8	0.1±2.9	0.007
15th minute	2.5±3.5	0.2±2.6	0.002

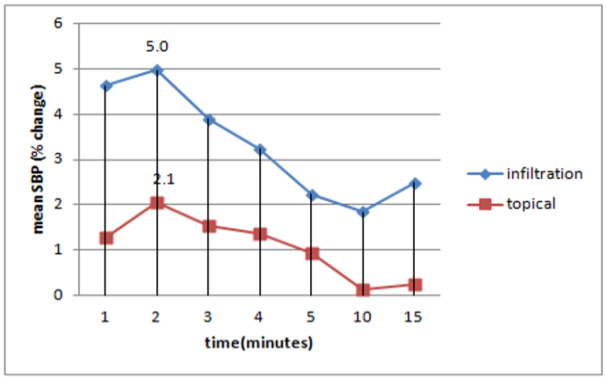

Figure 2, showing mean % change in SBP

An increase in SBP of >10% from baseline occurred in 3 of 50 patients with method-1 at the 2nd minute, compared to 1 with method-2 at the 5th minute. The maximum change in DBP occurred in the 2nd minute with both infiltration and topical methods (5.0±4.7 vs 2.4±3.7 respectively). The change in DBP was statistically different only for 1 to 3 minutes between the two methods and was more with the infiltration method (Table-3 and Figure 3).

Table 3

Time	Method-1 (n=50) mean DBP(% change)±SD	Method-2 (n=50) mean DBP(% change)±SD	p-value
1st minute	3.8±4.8	1.3±2.4	0.002
2nd minute	5.0±4.7	2.4±3.7	0.007
3rd minute	3.9±5.2	1.0±3.7	0.002
4th minute	2.9±6.2	1.0±4.7	0.078
5th minute	3.0±6.2	1.7±4.6	0.243
10th minute	3.0±5.4	1.5±3.1	0.061
15th minute	2.5±5.4	1.0±3.9	0.114

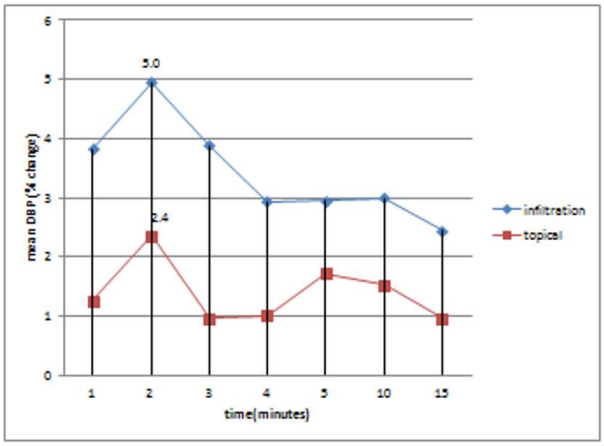

Figure 3, showing mean % change in DBP

An increase in DBP of >10% from baseline occurred in 8 of 50 patients with method-1 at the 2nd minute, compared to 2 with method-2 at the 4th minute. The maximum change in HR occurred at the 2nd minute with both infiltration and topical methods (9.0±6.0 vs 2.8±2.8 respectively). The change in HR was statistically different at all the measurement time points (1 minute to 15 minutes) between the two methods, with more change occurring after infiltration method (Table 4 and Figure 4). An increase in HR of >10% from baseline occurred in 21 of 50 patients with method-1 at the 2nd minute compared to 2 with method-2 at the 4th minute. No arrhythmias were found in this study.

Table 4

Time	Method-1 (n=50) mean HR(% change)±SD	Method-2 (n=50) mean HR(% change)±SD	p-value
1st minute	8.3±4.9	2.4±2.5	<0.001
2nd minute	9.0±6.0	2.8±2.8	<0.001
3rd minute	8.1±5.0	2.3±3.2	<0.001
4th minute	7.3±5.0	1.9±3.7	<0.001
5th minute	5.6±4.4	1.2±3.5	<0.001
10th minute	4.9±4.2	0.8±2.7	<0.001
15th minute	4.3±3.7	0.8±3.1	<0.001

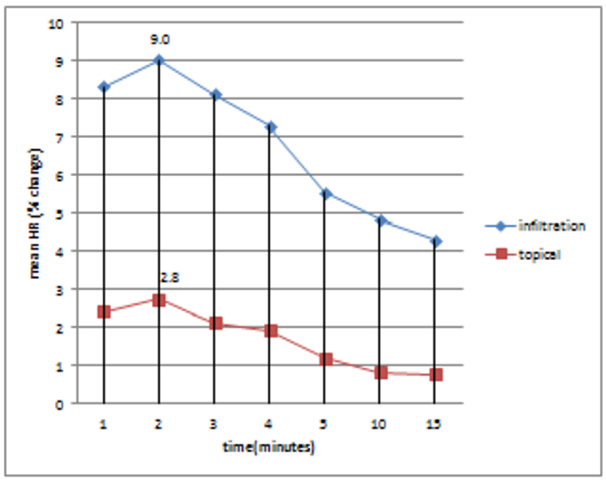

Figure 4, showing mean % change in HR

Discussion

Burns are associated with a large amount of blood loss. The surgical treatment of the burn wound can also cause substantial intra-operative blood loss (both from excised wounds and from donor sites), which can lead to increased blood transfusion requirements [20-23]. The surgeon has many techniques available to reduce intraoperative blood loss, including the use of hot laparotomy towels, pressure dressings, tourniquets, electrocautery, topical thrombin, topical epinephrine, and subcutaneous epinephrine injection [24-26]. Epinephrine tumescence of burn wounds and donor sites, combined with the use of topical epinephrine, significantly reduced blood loss during burn surgery [4,10-13]. The acute systemic effects of the epinephrine administration (both subcutaneous and topical) are incompletely understood. Although most investigators have reported no significant adverse cardiovascular effects [3,12,14,15-17], others have described episodes of tachycardia and/or hypertension related to the administration of epinephrine during burn surgery [18,19]. Unfortunately, the interpretation of these studies is difficult due to the variability of the injected volumes and the different concentrations of epinephrine solutions used.

The main findings of this study were as follows. (1) Total blood loss was small with both methods. However, it was significantly lower with adrenaline infiltration compared to topical adrenaline (10 ml vs. 5 ml). (2) In general, the increase in BP and HR after adrenaline was minimal. The maximum increase in BP compared to the initial value was on average 5%, and that of HR was 9%. (3) Hemodynamic changes were more frequent and occurred earlier after adrenaline infiltration than after topical adrenaline. (4) Changes in HR were more than those in BP. The hemodinamic changes lasted for a short time. In this study, both infiltration of adrenaline and topical adrenaline were used at different donor sites in the same patient, thus reducing the interpatient variability. The results of the study can therefore be considered valid despite a small sample size. Blood loss and acute cardiovascular effects depends on many factors, such as the area of excision of the graft, the concentration and volume of adrenaline injected or applied, the time between injection and excision.

Returning to previous studies, Cartotto et al. investigated in their prospective study blood loss, the need for transfusion, and wound infection in the first group compared to the second group; this study did not report separately the effect of adrenaline, topical adrenaline and the use of tourniquets [10]. The reduced blood loss in the first group was due to the combined effect of all three techniques. Gomez et al. showed in their retrospective study that the modified tumescent surgical technique significantly reduced the intra-operative and total blood transfusion requirements than the traditional surgical technique. They used compresses soaked in an adrenaline-thrombin solution. Also, this study did not report the effect of the individual technique (reporting only the effects on transfusion requirements) and no estimate of blood loss was made. Yet, this study does not assess the incidence of perioperative systemic cardiovascular adverse reactions (arrhythmias, tachycardia and hypertension) of topical application of saline-adrenaline solution (topical and subcutaneous injection) [27]. It should be noted that the transfusion rate is not an accurate measure of blood loss. Djurickovic et al. demonstrated that both tourniquets and epinephrine injected under the eschar during burn wound excision significantly reduced blood loss. In this study, blood loss was calculated by determining the difference between preoperative and postoperative hemoglobin values and the volume of whole blood administered between them, not taking into account the amount of blood lost intraoperatively [28].

There are conflicting data in the literature regarding the systemic effects of subcutaneous and topical epinephrine during burn surgery. Several studies suggest that there are no significant cardiovascular effects (being minimal, if any) associated with subcutaneous administration of epinephrine during the tumescent technique [3,12,13,15,28]. A major limitation common to all of these studies is the lack of specific and detailed cardiovascular monitoring during and after epinephrine infiltration. Only one study described how often observations of vital signs were made [15]. The method and frequency of cardiovascular monitoring were not disclosed in the others [3,12,13,28]. There were also substantial variations in the concentration and dose of epinephrine administered, as well as the type of wound that was infiltrated (i.e., donor site vs. burn wound).

In our study, the concentration and dose of adrenaline infiltration were constant in all patients and only the donor site was selected. There has been a significant increase in BP and HR in the infiltration method compared to the topical method, but clinically no intervention or treatment was required for this change.

Robertson et al, noted a statistically significant increase in the HR and MAP associated with epinephrine tumescence [19]. Although these changes were statistically significant, they were considered small and clinically irrelevant. Again, the technique and frequency of cardiovascular monitoring have not been described.

Cartotto et al. reported that in consecutive patients who received subcutaneous and topical epinephrine during burn surgery were monitored before epinephrine administration and then after epinephrine infiltration [29]. This monitoring period lasted up to 20 minutes; there was no significant increase in heart rate from baseline

and no arrhythmias occurred. Mean arterial pressure (MAP) increased acutely. The increase in MAP was not clinically significant, it did not require intervention. In the present study, there was a significant change in HR after infiltration compared to the local one, but clinically it does not require any intervention or treatment.

Lee et al. reported that a 26-year-old woman developed premature ventricular complexes and ventricular tachycardia during surgery when she was given an epinephrine-soaked application to the donor's skin and burnt wound sites to control bleeding [30]. The patient was resuscitated immediately and within 10 minutes the vital signs returned to normal. Caution is advised when applying soaked epinephrine to a large area of skin, especially a burnt wound.

In other study, Missavage et al. showed that the administration of either topical or clysed epinephrine during acute burn excision does not cause any side effects for safe anesthetic management; there were no detectable increased plasma levels of epinephrine or norepinephrine [15]. Epinephrine provides the burnt surgeon with two safe methods for controlling intraoperative blood loss.

Our study showed that adrenaline infiltration was better than topical adrenaline in preserving blood loss, but acute cardiovascular effects, such as increased BP and HR, were greater after infiltration. The changes in BP and HR were clinically insignificant and did not require any treatment or intervention.

Limitations of this study

The type of anesthesia (general or spinal anesthesia) and the anesthetic drugs used were not standardized and could have had an impact on the hemodynamic parameters.

The amount of adrenaline in the soaking was impossible to measure, a problem observed in the previous study [29].

The hemodynamic effects observed in the study depend on the amount of adrenaline used. These effects are expected to be different when using a higher volume of adrenaline for larger graft areas.

Conclusions

In conclusion, our study showed that adrenaline infiltration was superior to topical adrenaline in reducing the blood loss during skin graft harvesting. The increase in BP and HR was not clinically significant and did not require any intervention or treatment. The technique seems to be safe and has been easily adopted by surgeons.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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