Indian Journal of Basic and Applied Medical Research; September 2021: Vol.-10, Issue- 4, P. 180 - 189
DOI: 10.36848/IJBAMR/2020/29215.55695

Original article:

Comparison of the effect of 0.25% bupivacaine moistened versus normal saline moistened dressings on post operative pain relief in patients undergoing lower limb split thickness skin grafting (ssg) at donor site: A randomized, double blind, controlled, intervention study

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ABSTRACT

Introduction: Split thickness skin grafting is the most commonly used method of achieving skin for soft tissue defect.

Aim: To compare the effectiveness of bupivacaine-moistened dressing versus normal saline dressing in patient requiring split thickness skin graft for reconstruction of various defects.

Method: Hospital based, randomized, double blind, controlled, interventional study conducted on 60 patients fulfilling inclusion and exclusion criteria, randomly distributed 30 patients to group A in which donor site dressing was soaked by instilling an aqueous solution of 0.25% bupivacaine and 30 in group B donor site dressing was soaked by instilling normal saline in plastic surgery operation theatre, Department of Anaesthesiology at SMS Medical College and Attached Group of Hospitals, Jaipur with due permission from institutional ethics committee and Research Review Board and with written informed consent.

Results: All two groups were almost similar for age, sex, physical parameters and duration of surgery. we observed, no clinically significant change in hemodynamic parameters (heart rate, SBP, DBP, SpO_2) of the patients, signifying adequate pain control in both the groups (Table no. 12,13,14,15). In present study we did not observed any unwanted side effects. There was a significant difference in VAS scores in group A and B from 1st to 24th postoperative hours. VAS scores were significantly lower in group A as compared to group B, suggesting that postoperative pain was higher in group B in comparison to group A. The number of patients requiring rescue analgesia was lower in group A in comparison to group B and Time to first analgesic requirement was compared in both group and was found to be lower in group B. The total analgesic dose consumption was also higher in this group. The differences in time to first and second analgesic requirement was statistically significant and total analgesic consumption also was statistically significant ($p<0.05$).

Conclusion: 0.25% bupivacaine moistened dressing after split thickness skin grafting at donor sites provides better postoperative pain relief, reduces rescue analgesic requirement without any untoward side effects and thus is an effective method of reducing postoperative pain in patients undergoing split thickness skin grafting.

Keywords: skin grafting, bupivacaine.Donor site, Rescue analgesia, post operative pain.

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Introduction:

Split thickness skin grafting is the most commonly used method of achieving skin for soft tissue defect. Split thickness skin grafts are used in burns, reconstructive procedures and extensive wound management.[1] The grafting can reduce the duration of hospitalization and can improve the function and appearance of the area of body receiving skin graft.[2] The posterior-lateral part of thigh is most commonly used as a donor site of split thickness skin graft.[3] Pain at donor site is probably the most disturbing complication in the early post-operative period.[4] Pain at the split thickness skin graft donor site can be a real problem for most patients especially in first five post-operative days.[5] Typically, donor site is covered with non-adherent fine mashed gauze impregnated with different ointments.[6] Unfortunately this technique is usually painful and is one of its main drawbacks.[7] Moriarty sign says that if split thickness skin graft donor site is more painful post operatively than the recipient site then good graft take is likely.[8] The purpose of donor site management is to maintain an environment that promotes healing and prevent morbidity (pain, infection, and delayed healing). Reduction in post-operative morbidity and fast recovery of the donor site can be achieved by reducing this pain.[9] Different methods of reducing pain at donor site includes ice application at the donor site, fascia iliaca compartment block and a number of dressings. Bupivacaine is an anesthetic agent that blocks the nerve impulses that transmit pain sensation to brain. It is most commonly used for spinal blocks but can also be used for local infiltration anesthesia and peripheral nerve blocks.[10] So bupivacaine- soaked dressing is an applicable option for split thickness skin graft donor site for early postoperative analgesia.

Aim:

The aim of this study was to compare the effectiveness of bupivacaine- moistened dressing and conventional dressing in patients requiring split thickness skin graft for reconstruction of various defects.

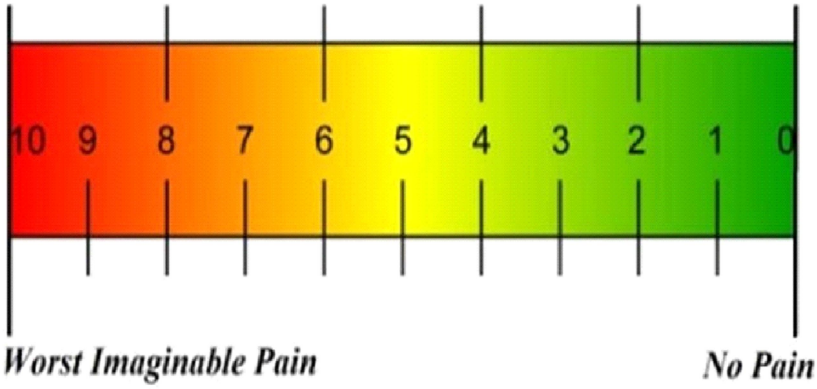
Method:

A hospital based, randomized, double blind, controlled, interventional study, conducted on Sample of 30 cases in each group calculated at 95% confidence interval and 80% power to verify the expected 89.3% cases in need of rescue analgesia dose in first 24 hours post-operative period in both groups in Plastic surgery operation theatre Department of Anaesthesiology at SMS Medical College and Attached Group of Hospitals, Jaipur with due permission from institutional ethics committee and Research Review Board and with written informed consent. Two groups were made Group A (0.25% bupivacaine Group): - The donor site dressing was soaked by instilling an aqueous solution of 0.25% bupivacaine (12ml/100cm² of the donor site wound) and Group B (normal saline Group): -– The donor site dressing was soaked by instilling normal saline (12mL/100cm² of the donor site wound). This trial was so planned that neither the doctor nor the patients were aware of the groups and the drug used. Patients of either sex, age group of 16 to 60 years with ASA grade I & II, undergoing elective split thickness skin grafting for reconstruction of various defect, in whom only thigh was used as split thickness skin graft donor site. Patient having bleeding disorders, ASA grade III & IV, history of allergy to any component of the dressings, Pregnant women, Immuno-compromised patients, Apprehensive / Psychiatric patients and Patient refusal were excluded from study. Pre-anaesthetic check-up was done a day before surgery which includes complete history of patient, local examination, general physical and systemic examination, routine investigations, were done. Visual analogue scale was explained to patient.

We informed to each patient about the study, the procedure and dressings and written consent was taken from each patient. In all patient's skin graft harvested from the proximal antero-medial and posterior-lateral aspect of

the thigh. After harvesting the graft donor site wound first covered with Jelonet (paraffin gauze) than a catheter of small diameter (epidural catheter with multiple hole) was placed on this layer of Jelonet, which was turn covered with sterilized gauges and finally covered with a sterilized bandage.

Visual analogue score: Postoperatively, the pain was assessed by using visual analogue pain scale (VAS) between 0 and 10 (0 = no pain, 10 = most severe pain).



In Group A, the donor site dressing soaked by instilling an aqueous solution of 0.25% bupivacaine and in Group B, the donor site dressing wi soaked by instilling normal saline. The amount instilled was depending on the size of graft taken. For every 100cm² of the donor site wound, 12 ml of 0.25% Bupivacaine in group A and normal saline in group B was instilled once immediately after the surgery and then repeated after 12 hours of the first instillation. At the time of drug instillation, the donor site was in horizontal position (on top) so the drug was evenly distributed. Pain assessed by Visual Analogue Scale (VAS). VAS score assessed at an interval of 0,1,2,6,12,24 hours after grafting. Patient who was complain of intense pain or in whom VAS score was ≥4 (i.e. need for analgesia), given intravenous rescue analgesics in the form of injection Tramadol with dose of 2 mg/kg (slow IV injection). We were observed time of administration of first and subsequent rescue analgesics, cumulative dose of rescue analgesics given. Vitals were recorded at an interval of 0,1,2,6,12,24 hours. Final conclusion of analgesia sparing effects of dressings and adverse effect if any, was made at 24 hours postoperatively. All the information was recorded on a proforma. The collected data was entered in Microsoft Excel and then was analysed and statistically evaluated using SPSS-PC-17 version. Quantitative data was expressed by mean, standard deviation and difference between comparable groups were tested by student's t-test (unpaired) or Mann Whitney 'U' test, while qualitative data was expressed in percentage. Difference between the proportions were tested by chi square test or Fisher's exact test. 'P' value less than 0.05 was considered statistically significant.

Results:

The patients ranged from 16 years to 60 years of age with mean age of Group A 33.86 ±11.07 years and Group B was 34.67 ± 14.87 year. Distribution of sex was similar in both groups, mean weight in the two groups is almost same and statistical comparison between the mean weight was non-significant. ASA grade distribution between two groups is non-significant. Duration of surgery and total volume in 24 Hrs. of bupivacaine (24.87 ± 8.77) or normal saline (27.20 ± 8.88) infused in the two groups was also similar ($p>0.05$). Comparison of mean

diastolic blood pressure and SPO2 in two groups at different time intervals showed that they were statistically non-significant.

Table 1: Socio Demographic Profile

	Group A		Group B		P value
AGE GROUP	**No.**	**%**	**No.**	**%**	
≤40	20	66.66	21	70.00	0.814
>40	10	33.33	9	30.00	
Mean ± SD	33.86±11.07		34.67±14.87		
SEX					
Male	23	76.67	24	80.00	1.00
Female	7	23.33	6	20.00	
WEIGHT					
	Mean	SD	Mean	SD	
Mean Weight	56.48	9.56	53.50	9.00	0.094 (NS)
Median	53		52		
ASA GRADE					
Grade 1	23	76.66	24	80.00	1.00
Grade 2	7	23.33	6	20.00	
DURATION OF SURGERY					
	Mean	SD	Mean	SD	
Mean	45.17	3.59	45.83	3.73	0.483
Median	45		45		

Table 2:

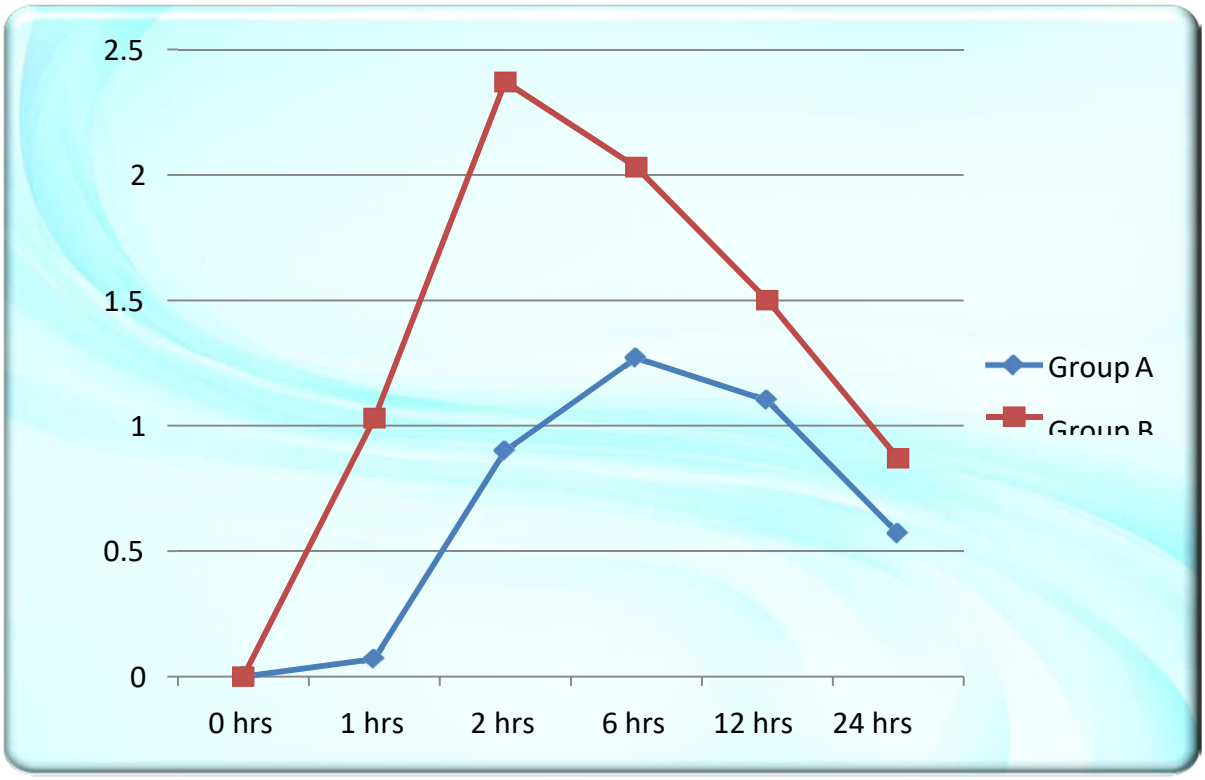
The time required for rescue analgesia was less in Group B than with Group A, which means Group A has longer action for relief of pain and was statistically significant. The number of patients receiving rescue analgesia was higher in group B (28) compared to group A (5), which was statistically significant. Rescue analgesia was given when VAS score was > 4. The total number of doses of rescue analgesia administered was lower in group A compared to group B, which was statistically significant. The total analgesic dose consumption is higher in group (B) as compare to group (A) ($p<0.001$).

Time to analgesic requirement (in min)	**Group A**		**Group B**		**p value**
	Mean	**SD**	**Mean**	**SD**	
First	273.00	57.62	193.21	31.69	<0.001
Second	597.50	74.25	490.50	63.61	0.048
Third	-	-	640.00	0.00	-
Patients requiring rescue analgesics					
	No.	%	No.	%	<0.001

Yes	5	16.66	28	93.33	
No	25	83.33	2	6.66	
Number of doses of rescue analgesia received					
1 doses	5	16.66	28	93.33	<0.001
2 doses	2	6.66	10	33.33	0.024
3 doses	0	0	1	3.33	
Mean analgesic dose consumption (in mg)					
	Mean	SD	Mean	SD	
in 24 hrs	24.48	54.41	140.20	76.49	<0.001

Fig. 1:

shows that there is a significant difference in VAS scores in group A and group B from 1ST to 24TH postoperative hour and VAS scores are higher in group B as compare to group A.



The comparison of mean systolic blood pressure in two groups at different intervals which showed that they were statistically significant ($p<0.05$) at 6th, 12th hours and the comparison of mean heart rate in two groups at different intervals which showed that they were statistically significant ($p<0.05$) at 2nd hours.

DISCUSSION:

The primary aim was to compare the use of bupivacaine-soaked dressing with conventional dressing for pain relief in split thickness skin graft donor site. The basis of this study was that with use of a local anaesthetic agent locally at the split thickness skin graft donor site there should be considerable pain relief in early postoperative

period due to blockage of nerve endings, which transmit pain signals to the nervous system. This study demonstrated that when the split thickness skin graft donor site dressing was kept moist through the instillation of 0.25% aqueous solution of bupivacaine hydrochloride with the help of a catheter placed in it, it produced considerably more pain relief. This considerably reduced the need for rescue analgesia compared to conventional dressing.

In the present study, a total of 60 patients were taken. Two study groups were made each consisting of 30 patients. In Group A the donor site dressing was soaked by instilling an aqueous solution of 0.25% bupivacaine (12ml/100cm² of the donor site wound) and Group B the donor site dressing was soaked by instilling normal saline (12mL/100cm² of the donor site wound). Both groups were almost similar for age, sex, physical parameters and duration of surgery.

Mean age in group A and B were 33.86±11.07, 34.67±14.87 respectively for two groups which was comparable and statistically insignificant (p = 0.814). The male and female patients were 23 and 7 respectively in group A as compared to 24 and 6 respectively in group B, which was comparable and statistically not significant (p = 1.00). ASA grades, weight in the two groups were statistically insignificant. Mean duration of surgery (min.) was 45.17±3.59, 45.83±3.73 in groups A and B respectively and statically non- significant. Also, the total volume of bupivacaine and normal saline used was comparable between the two groups (24.87±8.77 ml v/s 27.20±8.88 ml, p=0.309) and statically non-significant in the present study. It has been universally accepted that moist dressing at split thickness skin grafting donor site has better results over dry dressing both in terms of healing and pain management. In the present study moist dressing was used in both groups to ensure that the analgesic effect was due to local anesthetic effect and was not due to moist nature of dressing.[11]

In Our study postoperative pain score was assessed by VAS immediate postoperative period was 0 in both the groups. The mean VAS score readings were lower in Group A in comparison to Group B and were statistically significant from 1st to 24th hours. The results of our study are comparable with observations of Muhammad Sheraz Raza et al[11] who observed that Bupivacaine 0.25% moistened dressing (Group A) at split thickness skin graft, donor site significantly lower VAS as compared with patient receiving normal saline (Group B) moistened dressing. Jenwitheesuk K et al[12] also noted that the pain relief score defined as the difference between pain score before and after dressing was statistically significantly higher in Bupivacaine group A during the first five postoperative days compared to control group B in patients undergoing skin thickness skin grafting of lower limb. Zohar E et al[13] noted in their study on evaluating the analgesic effect of bupivacaine wound instillation after total abdominal hysterectomy with bilateral salpingo-oophorectomy that during the first 4 hours of the surgery the pain scores after coughing and leg raise were significantly lower in the Bupivacaine group as compared to control group (p=0.006and p=0.009, respectively). However, they also observed the pain score at the rest were similar between the two groups. Chester JF et al[14], found that in patients undergoing cholecystectomy, wound perfusion with 0.5% bupivacaine (Group A) had significantly lower linear analogue pain score as compared with patient undergoing wound perfusion with normal saline (Group B) on day 1st (44 v/s 82 mm, p<0.001) and day 2nd (32 v/s 78 mm, p<0.001). Fredman et al,[15] showed that the pain score (VAS) generated after coughing and leg raise were significantly (p < 0.04) lower in the Ropivacaine Group when compared with the control group in patients undergoing cesarean section delivery.

In the present study, the time of administration of first dose of rescue analgesia (duration of analgesia calculated from time of instillation of 0.25% bupivacaine/ normal saline to the time when patient complains of pain) was

statistically significantly higher in bupivacaine group A (273.00±57.62 min) compared to normal saline group B (193.21±31.69 min) ($p<0.001$), and the time of second dose of rescue analgesia was also statistically significantly higher in bupivacaine group A (597.50±74.25 min) compared to normal saline group B (490.50±63.61 min) ($p=0.048$). To ensure that adequate effect of bupivacaine was achieved before the effect of subarachnoid block weans off, the drug was instilled at donor site while the patient was still under the effect of spinal anesthesia. Similar to our study, Jenwitheesuk K et al,[12] noted in their study that during the first five postoperative days, the pain relief duration in bupivacaine moistened dressing (Group A) was much prolonged as compared to control group (Group B) (8 v/s 1 hour on day 1st, 9 v/s 1 hour on day 2nd, 11 v/s 2 hour on day 3rd & 4th, 11 v/s 3 hour on day 5th in group A and group B respectively).

Local anaesthetic primarily act by inhibiting the nociceptive transmission from the surgical wound by blocking the voltage-gated sodium channels expressed on small-diameter neurons.[16] It is possible that local anaesthetics may also have anti- inflammatory properties which may contribute to the analgesic effect.[17] Local anaesthetics may also produce analgesia by absorption into the systemic circulation. It has been shown that even low doses of intravenous local anaesthetic reduce the development of central hyperalgesia.[18] It's possible that local anaesthetic wound instillation decreases injury induced C fiber activity with consequent attenuation of peripheral and central sensitivity.[19]

In our study, the number of patients requiring rescue analgesia was lower in group A in comparison to group B. Only 5 (16.66%) patients of bupivacaine group demanded rescue analgesic doses compared to 28 (93.33%) patients in normal saline group B and this difference was statistically significant, $p<0.001$. Our findings are supported by a study on evaluating the effectiveness of bupivacaine moistened dressing on split thickness skin grafting donor site by Raza et al,[11] in which only 5 out of 75 (6.67%) patients required rescueanalgesic doses compared to 72 out of 75 (96%) patients in control group B. Jenwitheesuk K et al.[12] in their study on use of bupivacaine moistened dressing at donor site for split thickness skin grafting, also noted that a fewer number of patients in Bupivacaine group A required intravenous pethidine as rescue analgesic for pain relief postoperatively as compared to control group B (6 v/s 16 on day 1st, 4 v/s 13 on day 2nd). In the present study, the total number of doses of intravenous tramadol as rescue analgesic received by patients in bupivacaine group A were significantly lesser compared to normal saline group B (7 v/s 39). Our result are supported by a study done by Chester JF et al,[14] in which they observed that on 1st and 2nd postoperative day patients perfused with saline demanded more than 3 and 5 times respectively, the number of doses of intravenous pethidine as rescue analgesics through PCAD (Patient Controlled Analgesic Device), compared with those receiving bupivacaine for wound perfusion following elective cholecystectomy. Also, the actual number of doses of pethidine delivered to patients were lower in patients receiving bupivacaine compared to those receiving normal saline (9 v/s 18 on day 1st, 6 v/s 17 on day 2nd). In another study by Zohar E et al[13] they also noted that the number of pump infusion (doses) delivered for postoperative rescue analgesic were significantly lower in bupivacaine group as compared to control group (10±5 v/s 14±4 respectively) in patient undergoing total abdominal hysterectomy with bilateral salpingo-oophorectomy.

In our study the total analgesic dose consumption was also higher in group B, the total dose of intravenous tramadol as rescue analgesic received by patients in group A (bupivacaine group) was significantly lesser compared to normal saline group B (24.48±54.41 mg v/s 140.20±76.49 mg, $p<0.001$). Zohar E et al[13] in their study noted that during the first 6 hour after the operation, the total rescue morphine administered was 6 ± 4 mg

vs 12 ± 6 mg ($p < 0.001$) for the Bupivacaine and Control groups, respectively. The total rescue meperidine administered during the next 18 h after surgery was 29 ± 37 mg vs 95 ± 36 mg ($p < 0.001$) for the Bupivacaine and Control groups, respectively. Their findings supports our results. In another study by Fredman et al[20], they noted that the total rescue morphine administered through patient controlled elastometric pump during the first 6 postoperative hours was 2 ± 3 mg v/s 10 ± 5 mg ($p<0.01$) for the ropivacaine and control group respectively in patients undergoing cesarean section. Topical bupivacaine applied to split thickness skin graft donor site produces an analgesic effect that reduces requirement of opiates. The benefits of this technique are decreased adverse effect of opiates and early mobilization of patients.[12]

In present study we observed, no clinically significant change in hemodynamic parameters (heart rate, SBP, DBP, SpO_2) of the patients, signifying adequate pain control in both the groups. In present study we did not observed any unwanted side effects. Local anaesthetic wound instillation has been shown to be associated with catheter related infection, delayed wound healing and local anaesthetic induced myotoxicity. Care must be taken while administering through catheter to prevent wound infection. In clinical setting, local anaesthetic induced myotoxicity seems to be rare because local anesthetic-induced analgesia and anesthesia is achieved at a dosage insufficient to produce clinically recognizable myotoxicity.[21] In our study, myotoxicity was not specifically assessed. However, considering our study design, this complication is unlikely because the local anesthetic was not injected directly into muscle or subcutaneous tissue.

Some authors[22,23] postulate that wound infiltration with local anesthetic may interfere with wound closure and normal wound healing; however, there are no definitive data on mature wound strength after wound infusion analgesia. This hypothesis seems to be more important in damaged and infected tissues in which the inflammatory cascade is crucial to wound healing. Conversely, it is possible that partial blockade of the inflammatory response in the first phase of wound closure may be beneficial and may result in less fibroblast hyperplasia and therefore a decreased risk of hypertrophic scar formation. Our results showed no difference between groups regarding wound healing and risk of infection. However, a larger number of patients would be needed to study this issue further. The limitations of this study were Analgesic effect was assessed for a period of 24 hours only. However, this study aimed at evaluating the analgesic efficacy of bupivacaine in wound instillation during immediate post-operative period only. Despite our favourable results, the efficacy of local anaesthetics wound instillation requires further investigation. Instillation volume and drug concentration may influence the success of this technique. The optimal concentration and amount of bupivacaine needed for postoperative pain relief was not determined in our study. Further studies using different concentration and volume of bupivacaine are needed to determine the optimal concentration and amount of bupivacaine.

This study concludes that Bupivacaine-soaked dressing provides effective postoperative analgesia and reducing the requirement of rescue analgesia in the early postoperative period, at split thickness skin graft donor site, compared to the conventional dressing.

CONCLUSION

In our study we compared the effectiveness of bupivacaine-moistened dressing and conventional dressing in patients requiring split-thickness skin grafting for reconstruction of various defects. The groups were comparable with respect to demographic data, ASA and hemodynamic parameter. The pain scores were significantly lower in bupivacaine group as compared to normal saline group. Mean analgesic dose consumption of rescue analgesia postoperatively was less in the bupivacaine groups (24.48 ± 54.41) as compared with normal

saline groups (140.20 ± 76.49) in milligram. We conclude that 0.25% bupivacaine moistened dressing after split thickness skin grafting at donor sites provides better postoperative pain relief, reduces rescue analgesic requirement without any untoward side effects and thus is an effective method of reducing postoperative pain in patients undergoing split thickness skin grafting.

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