Original article

Evaluation of amnion versus calcium alginate as split-thickness skin graft donor site dressing: A randomised controlled trial

Roeya E Rasul[1], Bushra Akram[1], Zain ul Abidin[1], Farrukh Aslam Khalid[2], Sheraz Raza[3], Kamran Khalid[4]

[1]Senior Registrar, Plastic Surgery, Jinnah Burn and Reconstructive Surgery Centre, Allama Iqbal Medical College, Lahore, [2]Assistant Professor, Plastic Surgery, Jinnah Burn and Reconstructive Surgery Centre, Allama Iqbal Medical College, Lahore, [3]Associate Professor, Plastic Surgery, Abu Umara Medical and Dental College, Lahore, [4]Professor, Plastic Surgery, Jinnah Burn and Reconstructive Surgery Centre

Correspondence to: Dr. Roeya-E-Rasul, Email: rerasul@yahoo.com

ABSTRACT

Background: Split-thickness skin graft (STSG) covers patient's primary wound, but, at the expense of a donor-wound which heals by secondary intention. This study evaluated the efficacy of amnion and calcium alginate dressings at STSG donor sites in terms of healing duration, patient comfort and incidence of infection.

Patients and methods: An open label randomised control trial was conducted during October 2018 to May 2019. Total 60 patients, aged 20-45 years, were randomly allocated to two equal groups. Amnion was applied to 30 donor sites in Group A and calcium alginate in 30 donor sites in Group B. Patients were phone-called on 1st, 3rd and 7th post-operative days and donor site pain scored using numerical rating scale. Donor site was opened on 10th postoperative day and signs of infection assessed. Lastly, the day on which donor site healed, revealing an epithelialized wound, was noted.

Results: Group A included 30 patients (11 females, 19 males) having mean age of 31.23 years and Group B included 30 patients (12 females, 11 males) having mean age of 31.30 years. Average pain scores on 1st, 3rd and 7th post-operative days were 7.6, 6.6 and 4.4 in Group A and it was 8.2, 6.5 and 4.4 in Group B. Two cases of amnion, 4 of calcium alginate got infected. Average healing duration was 11 days in Group A; and it was 14 days in Group B (p-value = 0.000).

Conclusion: Amnion shows quicker healing and better pain control than calcium alginate.

Keywords:

Amnion, Alginate, Split-thickness skin graft (STSG), Donor site dressing, Randomized control trial

INTRODUCTION

Split-thickness skin graft is an important tool in the armamentarium of a plastic surgeon. It is a commonly used reconstructive technique, but results in a donor site wound which heals by secondary intention and is often a source of discomfort for the patient. The need for quick and painless recovery of the graft's donor site cannot be overstated in burn patients, who have to endure the pain of this surgically created wound and might also need further grafts from the same site at a later date. Keeping in view the ease of patients, many studies have been carried out to determine the ideal donor site dressing but none has been agreed upon so far.[1-4]

Amnion (AM) has been advocated as an efficient donor site dressing.[1-5] Studies have shown that amnion and amniotic membrane products contain anti-inflammatory cytokines and growth factors which are implicated in healing and regeneration.[5] It is also said to have analgesic and antibacterial properties. Recent advances in amnion preservation have made it safer to use, without risks of transmitted infections.

Cryopreservation, gamma-irradiation, glycerol preservation and lyophilisation are commonly used preservation methods these days.[5] Calcium alginate is used as the routine dressing at graft donor sites by a majority of surgeons.[6,7] It is composed of calcium alginate and sodium alginate in a ratio of 4:1. The alginates have the ability to absorb fluid 15-20 times their weight.[6] Furthermore, their calcium is replaced by the body's sodium, thus activating the clotting cascade and giving it haemostatic properties.[6] Internationally, studies have been conducted comparing calcium alginate with the polyurethane dressing of graft donor sites and good results have been obtained with calcium alginate, due to its absorptive properties, causing early epithelialization and being very comfortable for the patient.[6,8]

The rationale of this study was to compare a biological dressing, amnion, with a commercially available calcium alginate dressing, to see which allows for quicker re-epithelialisation, better comfort for the patient and lessens rate of infection.

Conflict of interest: The authors declared no conflict of interest exists.

Citation: Rasul R, Akram B, Abidin Z, Khalid FA, Raza S, Khalid K. Evaluation of amnion versus calcium alginate as split-thickness skin graft donor site dressing: A randomised controlled trial. J Fatima Jinnah Med Univ. 2022; 16(1):7-11.

DOI: https://doi.org/10.37018/OUAN1021

PATIENTS AND METHODS

The study registered with the Australian New Zealand Clinical Trials Registry (ACTRN12618001632280) and was conducted from October 2018 to May 2019 at the Department of Plastic Surgery, Jinnah Burn and Reconstructive Surgery Centre, Lahore. The sample size was calculated with 95% confidence interval, 80% power of study. After approval from the Institutional Review Board, a total of 60 patients were included in this open label randomized control trial. Patients of either gender, aged 20 to 45 years, with wounds requiring STSG for coverage as a single sheet (up to 10 x 30 cm), were included. Patients with known allergies to any dressing product used in this study, those who were immunocompromised or had chronic diseases like diabetes, hypertension, ischemic heart disease, were excluded.

Random number table with allocation ratio 1:1 was used to divide the participants into two groups. Group A patients had their donor sites dressed with Amnion while Group B with Calcium Alginate.

For amnion preparation, healthy pregnant females scheduled for Caesarean section, with no co-morbidities or infections, having tested negative for HBV, HCV and HIV were enrolled and informed consent taken for the acquisition of amnion. Placenta contaminated with meconium was discarded. Placenta was removed from amnion and amnion was further cleaned of blood by washing with plenty of normal saline and dipping in it for an hour. Membrane tissue cultures were sent and the membranes shifted to a container with 70% glycerol. Glycerol has antibacterial and antiviral properties.[5] This was kept in the refrigerator at 4^0C. When the culture reports were received, membranes with any growth were discarded.[9]

A single sheet of STSG, measuring 4 inches by width, 30 cm in length, with thickness set at 0.010 inches, was harvested with Zimmer® dermatome. The donor site (Figure 1A) was then covered for 2 minutes with a gauze soaked in adrenaline (1:100,000) solution, for hemostasis. For Group A, already prepared Amnion was taken from the fridge and immersed in normal saline for 10 min to remove any traces of glycerol. It was then applied to the donor site, covered with tulle dressing, dry gauzes, roll of cotton and circumferential crepe. For Group B, calcium alginate dressing was applied after drying the donor site. Tulle dressing was placed on it, followed by sterile gauze, cotton roll and crepe.

Patients were discharged 1 day after the surgery. Telephonic contact was made with discharged patients and Numerical Rating Scale (NRS) (Table 1)[10] was used for pain evaluation on the 1st, 3rd and 7th post-operative days. Patients were asked to come for follow up in out-patient department on 10th post-operative day, their dressing was opened and all layers of gauze over the tulle dressing that could be easily separated were removed. In case of signs of donor site infection, including erythema or discharge, wound cultures were sent. The donor site was re-dressed with gauze and crepe. Daily dressings were then done and regular follow up maintained in out-patient department till the day the dressing in contact with the donor site spontaneously left it, revealing it to have healed and epithelialized. Confounding factors like age and gender were addressed through stratification of data.

Table 1: Numerical rating scale (adapted from Polomano et al, 2016[10])

Score	Denotes
0	No pain
1	Hardly noticeable pain
2	Notices pain, does not interfere with activities
3	Distracts at times
4	Distracts me, can do usual activities
5	Interrupts some activities
6	Hard to ignore, avoid usual activities
7	Focus of attention, prevents doing daily activities
8	Awful, hard to do anything
9	Can't bear the pain, unable to do anything
10	As bad as it could be, nothing else matters

All the data was recorded and analyzed in the data sheet and entered from there into SPSS version 21.0. Quantitative variables, like age, pain score and duration of healing are presented as mean and standard deviation. Qualitative variables (infection, gender) presented as frequencies and percentages. Data was further stratified for age and gender and T-test used to compare pain score and duration of healing between Group A and B. Chi-square test was used to compare frequencies and percentages of infection at the donor site. A p-value of <0.05 has been taken as statistically significant.

RESULTS

A total of 60 patients were included in this study, 30 in group A (amnion group) and 30 in group B (calcium alginate group). 11 patients (36.67%) were female and 19 (63.33%) were male in group A, whereas 12 patients (40%) were female and 18 (60%) were male in group B. All patients completed the study. The mean age of the participants in group A was 31.23 $\pm$ 7.30 years (range, 20 to 44 years). The mean age of the participants in group B was 31.30 $\pm$ 7.49 years (range, 21 to 45 years). Mean pain scores were significantly different on the

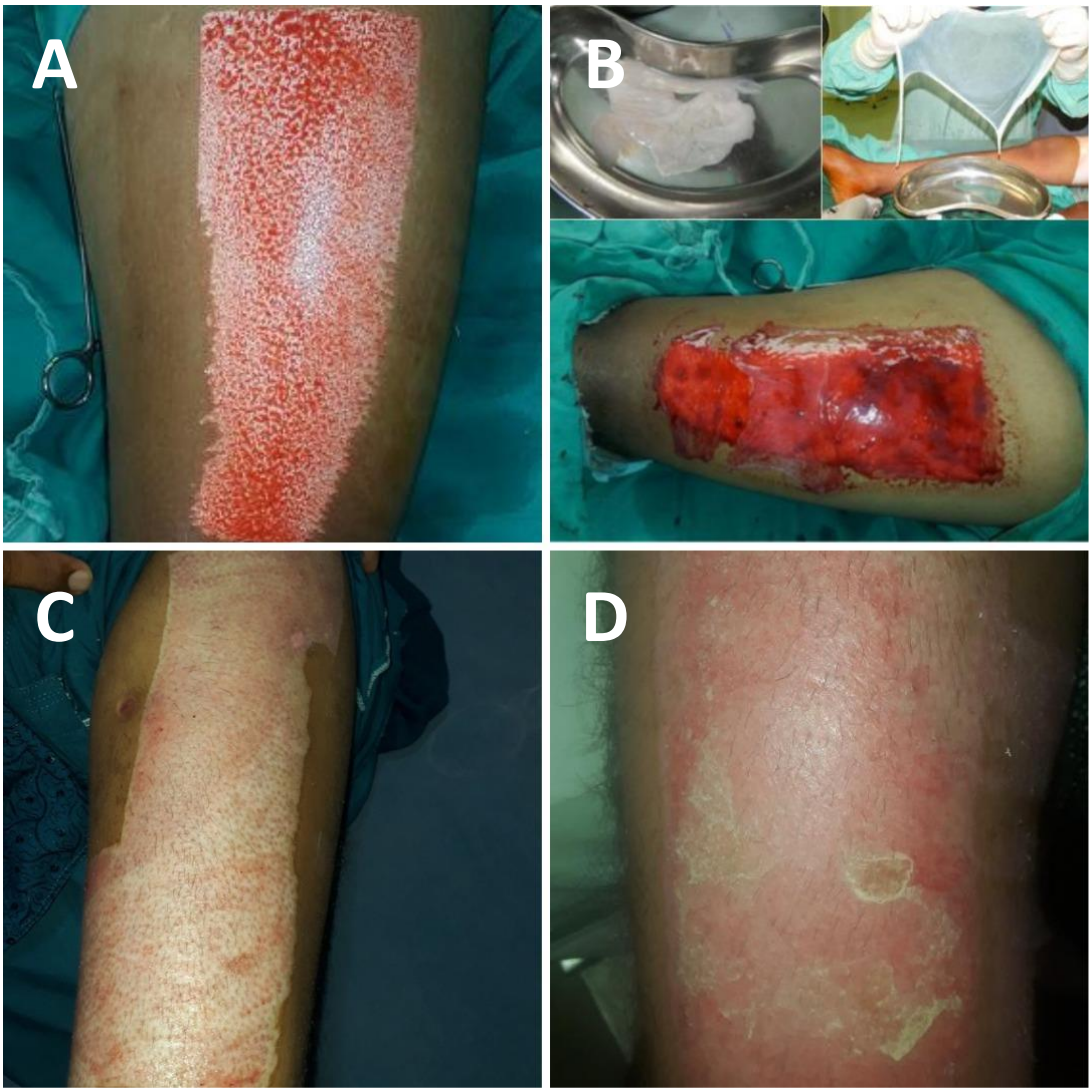

Figure 1: A) Split-thickness skin graft donor site, showing punctate bleeding after harvesting of split-thickness skin graft at 0.01 inch thickness. B) Top right: Amnion placed in normal saline in kidney tray and then applied to donor site. C) Healed donor site on day 10 with Amnion. D) Healed donor site on day 13 with Calcium Alginate dressing.

Table 2: Pain scores, day of healing, wound size, infection

Characteristics	Amnion	Alginate	t-test	p-value
Mean pain score				
Day 1	7.6	8.2	-3.58*	0.001
Day 3	6.6	6.5	0.789*	0.445
Day 7	4.4	4.4	0.000*	1.000
Day of healing	10.7	13.8	12.639*	0.000
Wound size (cm^2)	255.5	262.8	0.952*	0.349
Infection**	2.0	4.0	0.741**	0.389

*Independent t-test was used to determine p-value. A p-value <0.05 was taken as significant.
**The p-value for infection was determined by chi-square test. A p-value <0.05 was taken as significant.

first post-operative day, Group A 7.63 ± 0.56, Group B 8.23 ± 0.73 (p-value 0.001). Day 3 and 7 pain scores were not statistically significant among the two groups (Table 2).

The donor site wound was seen to have healed on day 10.67 ± 0.96 in group A (Figure 1) versus 13.80 ± 0.96 in group B (Figure 1); the difference was statistically significant (p-value <0.001) (Table 2). The average size of the donor site wounds were comparable (Table 2). The frequency of infection was 6.7% (N=2) in group A versus 13.3% (N=4) in group B; the difference was not statistically significant (p-value = 0.389) (Table 2).

DISCUSSION

Many studies have been conducted to determine the ideal skin graft donor site dressing but no consensus has

been reached so far.[11-17] The ideal split-thickness skin graft donor site dressing should be comfortable, not require repeated dressing changes, promote healing and avoid the long-term complication of hypertrophy.[18-22] To the best of our knowledge, this study is unique as there has been no previous study on indexed English literature review comparing the effectiveness of amnion versus calcium alginate on split-thickness skin graft donor sites.

Mentioning researches justifying the efficacy of amnion as a donor site dressing, in a study by Zidan et al[5] amnion is compared with chlorhexidine-impregnated gauze dressing on STSG donor sites. 20 patients are taken in each group. According to the results, the amniotic membrane group showed considerably lower pain scores on second and sixth postoperative days (4 ± 0.8 and 2.7 ± 0.9 vs. 5.6 ± 1 and 4.2 ± 1.2 respectively) (p-value <0.05); was quicker to re-epithelialise, 11.7 ± 2.4 days, compared to the control group 15.4 ± 3.7 days and had 10% infection rates, compared to 15% of the control group.[5] In the study by Singh and associates[1] comparing amnion with paraffin gauze for skin graft donor site dressing, the thickness of the graft harvest was not mentioned, but the average day of healing was noted to be day 10.[1] Salehi and co-workers harvested grafts at 0.016-0.24-inch thickness and noted healing to be complete on an average of day 17.[2] Eskandarlou and friends observed healing to be complete on 8 ± 3 days for a graft thickness of 0.014 inches.[3] Zidan and group documented healing on the 11th postoperative day with amnion, but graft thickness was again not mentioned.[5] Ganatra and co-researchers showed the donor site epithelization in 8.85 days, although the thickness of split skin graft was not mentioned.[23] Our study shows healing with amnion on 10.67 days with a graft thickness of 0.010 inches, thus correlating well with previous studies on amnion.

Lauchli and associates compared Kaltostat (calcium alginate) with polyurethane on skin graft donor site and reported healing on the 18th postoperative day with a graft thickness of 0.008 inches.[6] Our study shows healing on 13.80 days with a graft thickness of 0.010 inches with calcium alginate, which is seen to be quicker as compared to the reference study.

Considering pain at the donor site, all the reference studies[1-3,5,23,24] for amnion scored less pain with amnion as compared to paraffin gauze. Lauchli and co-workers reports pain scores to be higher with calcium alginate than with polyurethane dressing.[6] Our results show pain scores of 7.63 (focus of attention, prevents doing daily activities) with amnion versus 8.62 (awful to unbearable pain) with calcium alginate, showing that amnion does provide better analgesia as compared to the latter.

Reference studies for Amnion[1-3,5,23,24] or Kaltostat[6,7] did not show any significant incidence of infection with either of the two dressings. Our study results are consistent, with 2 cases of infection seen with Amnion and 4 with Alginate; not statistically significant (p- value = 0.389).

Amnion is a suitable dressing for our patients, being readily available and in abundance, requiring only normal saline and glycerol for its preparation.[9] Calcium Alginate provides a moist environment owing to its absorbent and haemostatic properties, allowing and supporting growth of new epithelium, but once dried out it tends to stick to the new epithelium, pulling on it and making dressing change painful due to shear and also affecting the healing duration.

There is still room for further studies to be conducted in order to compare the long-term results of wound healing and nature of scarring seen on donor sites after the application of Amnion and Calcium Alginate.

CONCLUSION

We have found Amnion to be a better skin graft donor site dressing than Calcium Alginate, considering as it provides earlier healing and is more comfortable for the patient.

REFERENCES

1. Singh R, Kumar A, Singh D, Malviya A. use of gamma-irradiated amniotic membrane for the healing of split skin graft donor site. Journal of Tissue Engineering and Regenerative Medicine 2013; 10(3): 110-4.
2. Salehi SH, As'adi K, Mousavi SJ, Shoar S. Evaluation of amniotic membrane effectiveness in skin graft donor site dressing in burn patients. Indian Journal of Surgery. 2015; 77(Suppl 2): 427–31.
3. Eskandarlou M, Azimi M, Rabiee S, Rabiee MA. The healing effect of amniotic membrane in burn patients. World Journal of Plastic Surgery. 2016 Jan; 5(1): 39–44.
4. Slaninka I, Fibir A, Kaska M, Paral J. Use of autologous platelet-rich plasma in healing skin graft donor sites. Journal of Wound Care. 2020 Jan 2;29(1):36-41.
5. Zidan SM, Eleowa SA, Nasef MA, Abd-Almoktader MA, Elbatawy AM, Borhamy AG et al. Maximizing the safety of glycerol preserved human amniotic membrane as biological dressing. Burns. 2015 41(7):1498-503.
6. Läuchli S, Hafner J, Ostheeren S, Mayer D, Barysch MJ, French LE. Management of split-thickness skin graft donor sites: A randomized controlled trial of calcium alginate versus polyurethane film dressing. Dermatology. 2013; 227(4): 361-6.
7. Iliescu Nelea M, Paek L, Dao L, Rouchet N, Efanov JI, Édouard C, Danino MA. In-situ characterization of the bacterial biofilm associated with Xeroform™ and Kaltostat®™ dressings and evaluation of their effectiveness on thin skin

engraftment donor sites in burn patients. Burns. 2019; 45(5): 1122-30.
8. Dhaliwal K, Lopez N. Hydrogel dressings and their application in burn wound care. British Journal of Community Nursing. 2018; 23(Sup9): S24-S27.
9. Raza MS, Asif MU, Abidin ZU, Khalid FA, Ilyas A, Tarar MN. Glycerol preserved amnion: A viable source of biological dressing for superficial partial thickness facial burns. Journal of the College of Physicians and Surgeons Pakistan. 2020 Apr;30(4):394-398.
10. Polomano RC, Galloway KT, Kent ML, Brandon-Edwards H, Kwon KN, Morales C, et al. Psychometric testing of the defense and veterans pain rating scale (DVPRS): A New pain scale for military population. Pain Medicine. 2016;17(8):1505-19.
11. Geoffery C. Gurtner, Peter C. Neligan, Daniel Z. Liu. Plastic Surgery, 4th edition, 2018, pp. 213- 229.
12. Timmons J: Skin function and wound healing physiology. Wound Essentials. 2006, 1: 8–17
13. Serebrakian AT, Pickrell BB, Varon DE, Mohamadi A, Grinstaff MW, Rodriguez EK, et al. Meta-analysis and systematic review of skin graft donor-site dressings with future guidelines. Plastic and Reconstructive Surgery Global Open. 2018; 6: e1928.
14. Poinas A, Perrot P, Lorant J, Nerrière O, Nguyen JM, Saiagh S, et al. CICAFAST: Comparison of a biological dressing composed of fetal fibroblasts and keratinocytes on a split-thickness skin graft donor site versus a traditional dressing: a randomized controlled trial. Trials. 2019; 20(1): 612.
15. Badois N, Bauër P, Cheron M, Hoffmann C, Nicodeme M, Choussy O, et al. Acellular fish skin matrix on thin-skin graft donor sites: a preliminary study. Journal of Wound Care. 2019; 28(9): 624-8.
16. Ki SH, Ma SH, Choi JH, Sim SH, Kim HM. Treating skin graft donor sites: a comparative study between remnant skin use and polyurethane foam. Journal of Wound Care. 2019; 28(7): 469-77.
17. Fang Z, Yang X, Wu G, Liu M, Han J, Tao K, et al. The use of autologous platelet-rich plasma gel increases wound healing and reduces scar development in split-thickness skin graft donor sites. Journal of Plastic Surgery and Hand Surgery. 2019; 53(6): 356-60.
18. White N, Hettiarratchy S, Papini RP. The choice of split-thickness skin graft donor site: patients' and surgeons' preferences. Plastic and Reconstructive Surgery. 2003; 112(3): 933-4.
19. Kung TA, Chung KC. Fundamental Principles of Plastic Surgery. In Kevin C. King (Eds.), Grabb and Smith's Plastic Surgery, 8th Ed. Philadelphia: Wolters Kluwer, 2020. pp. 21.
20. Pak CS, Park DH, Oh TS, Lee WJ, Jun YJ, Lee KA, et al. Comparison of the efficacy and safety of povidone-iodine foam dressing (Betafoam), hydrocellular foam dressing (Allevyn), and petrolatum gauze for split-thickness skin graft donor site dressing. International Wound Journal. 2019; 16(2): 379-86.
21. Serebrakian AT, Pickrell BB, Varon DE, Mohamadi A, Grinstaff MW, Rodriguez EK. Meta-analysis and systematic review of skin graft donor-site dressings with future guidelines. Plastic and Reconstructive Surgery Global Open. 2018; 6(9): e1928.
22. Rotatori RM, Starr B, Peake M, Fowler L, James L, Nelson J, et al. Prevalence and risk factors for hypertrophic scarring of split thickness autograft donor sites in a pediatric burn population. Burns 2019; 45(5):1066-74.
23. Ganatra MA, Bhura S. Management of skin graft donor site by irradiated amniotic membrane. Pakistan Journal of Surgery, 2003; 19(2): 82-5.
24. Abul A, Karam M,Rahman S. Human Amniotic Membrane: A new option for graft donor sites–systematic review and meta-analysis. International Wound Journal. 2020;17:547–554.

