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Original Research Article

A Hospital Based Study to Assess the Effect of Radiotherapy on Minimizing Acute Rejection and Enhancing Wound Healing in Children with Deep Burns: An Observational Study

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Abstract:

Aim: The aim of the present study was to assess the effect of radiotherapy on minimizing acute rejection and enhancing wound healing in children with deep burns.

Methods: We conducted this prospective randomized controlled trial on 50 children (age: below 12 years) who were admitted to our burn unit for the period of 12 months. On admission, the total body surface area of the burn was calculated using Lund and Browder's chart, and the patients received resuscitation treatment, including airway securing, fluid replacement, warming, and supportive medication, until their general condition stabilized.

Results: Group 1 consisted of 25 patients (10 females and 15 males) with a mean age of 8.32 years (range: 1–12 years) and a mean percentage of burns of 33.3%. Group 2 included 25 patients (7 females and 18 males) with a mean age of 9.5 years (range: 2–12 years) and a mean percentage of burns of 28%. The mean values of the laboratory parameters (ESR, CRP, IL-6, and TNF) for all burn patients in the study showed a significant difference, with $p < 0.001$. This finding demonstrates a significant decrease in values for graft radiotherapy, indicating minimal inflammatory and immune reactions. We found a difference in hospital stay duration between groups 1 and 2, with a mean of 32.4 and 22.0 days, respectively. Irradiation reduces immune reactions and the possibility of eschar tissue formation, resulting in the acceleration of wound epithelialization which reduces hospital stay duration and morbidity.

Conclusion: The exposure of skin homografts from related living donors to a local low dose of radiotherapy can reduce a graft's ability to initiate inflammatory and immunological reactions, thereby minimizing rejection of a graft and enhancing epithelialization in children with deep second- and third-degree burns.

Keywords: burn, deep, children, homograft, radiotherapy, rejection

Introduction

Advances in burn care have decreased mortality rates and improved quality of life. Improvements in the treatment of shock, fluid resuscitation, and control of infection have been at the cornerstone of these advances. The development of topical and systemic antimicrobial agents, nutritional support for the hypermetabolic response, and the use of surgical techniques to assist early wound closure have helped to decrease bacterial colonization and invasion that lead to sepsis and multiorgan failure. Streptococcal and pseudomonal burn wound infections were once the main causes of sepsis and death. Early wound excision, topical antimicrobials, and improved wound dressings have significantly reduced the incidence of these complications. [1-3] Scald burns account for approximately 85% of thermal injuries in the podiatric population [4,5] and lead to nearly 60% of all admissions to pediatric burn units. [6]

The majority of these injuries are superficial but, at the initial clinical presentation, determination of the actual depth of injury in larger deep partial-thickness and full-thickness scald burns remains difficult. Deep partial-thickness burns exhibit hyperemia followed by damage to collagen and the deep vascular plexus despite the early survival of the superficial dermal layer. Traditionally, partial-thickness burns have been treated with topical antimicrobial agents during twice daily dressing changes until the eschar separated. The traditional approach leaves the burn wound open for long periods, increasing the potential for wound infection and exposes patients to the pain of daily cleaning and dressing changes.

More recently, severe large partial-thickness burns were treated with early excision of the burn wound to the level of vital tissue and subsequent grafting with cadaveric skin. The gold standard of operative wound coverage is autologous split-thickness skin graft. However, in patients with viable skin elements remaining autograft is not necessary for wound healing. The wounds do remain open requiring the utilization of other methods of wound coverage which includes cadaver allograft/homograft. Homograft serves as a biologic dressing as it “takes” like a skin graft and is then rejected via cell-mediated immunity 10–14 days later. [2]

The aim of the present study was to assess the effect of radiotherapy on minimizing acute rejection and enhancing wound healing in children with deep burns.

Materials and Methods

We conducted this prospective randomized controlled trial on 50 children (age: below 12 years) who were admitted to our burn unit at RDJM Medical College and Hospital, Muzaffarpur, Bihar, India for the period of 12 months. On admission, the total body surface area of the burn was calculated using Lund and Browder's chart, and the patients received resuscitation treatment, including airway securing, fluid replacement, warming, and supportive medication, until their general condition stabilized. Local burn care was routinely provided while adhering to aseptic precautions.

Inclusion and Exclusion Criteria

The inclusion criteria of this study were as follows: children with intermediate, major, and deep second- and third-degree burns with eschar formation, necessitating escharectomy and wound coverage.

The exclusion criteria of this study were as follows: children with first-degree and superficial burns that appeared to be healing conservatively without requiring surgical intervention.

Study Groups

This study had the following two patient groups:

Group 1 (control, nonexposed) included 25 patients with a skin homograft that was not exposed to radiotherapy.

Group 2 (case, exposed) included 25 patients in which the skin homograft was exposed to local radiotherapy (single, low dose of 500 centigray [cGy]) before application to the burn wound.

Homograft Source and Preparation

Patients in both the groups received skin homografts from living first-degree relatives (i.e., father, mother, brother, or sister). All donors provided written consent to donate their skin after a thorough discussion on all procedural steps and the anticipated time for donor site healing. The thigh was the preferred donor site for homografts, and medium-sized split-thickness grafts were harvested and applied on a sterile glass plate soaked with gentamicin solution.

Local Radiotherapy

Inside the tomotherapy unit for radiation, a calibrated dosimetric system consisting of an electrometer and an ionization chamber (M23332, Safe Work Permit process) was used. Beams were delivered using an automated system that moved the phantom at an 11 cm 2 pencil beam in a homogenous-slice rotating attitude. The skin homograft was exposed to a low dose of radiation, 500 cGy, and the delivery process was replicated only once on the graft. The homograft was immediately used for the coverage of a prepared bed after irradiation was completed.

Operative Procedures for Recipient Patients

Under general anesthesia, the burn area was sterilized and escharectomy was performed, followed by immediate wound coverage with a nonexposed skin homograft for patients in group 1 or an irradiated homograft for patients in group 2. Next, fixation was performed with bulking dressing and tie-over sutures.

Follow-Up

To detect differences in the results between the two groups, the following data were collected before and after surgery and compared:

- Laboratory parameters such as the levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukin 6 (IL-6), and tumor necrosis factor (TNF) were measured.
- Time elapsed between homograft coverage and the onset of rejection.
- Percentage of the area requiring an autograft application.

Statistical Analysis

To evaluate the differences between the two groups, we measured various parameters using one-way analysis of variance and posthoc Tukey's honest significant difference test. For statistical analyses, we used the Prism 5 software (GraphPad Software, San Diego, CA USA). We considered $p < 0.001$ as highly statistically significant and $p < 0.05$ as statistically significant.

Results

Table 1: Demographic data

Gender	Group 1	Group 2
Male	15	18
Female	10	7
Mean age	8.32 years	
Mean percentage of burns	33.3%	28%

Group 1consisted of 25 patients (10 females and 15 males) with a mean age of 8.32 years (range: 1–12 years) and a mean percentage of burns of 33.3%. Group 2 included 25 patients (7 females and 18 males) with a mean age of 9.5 years (range: 2–12 years) and a mean percentage of burns of 28%.

Table 2: Changes in the level of the following laboratory parameters including ESR, CRP, IL-6, and TNF before and after the surgery

		Group 1	**Group 2**	**T test**	**P Value**
		Mean ± SD	**Mean ± SD**		
ESR/mm/hr	Before surgery	48.432 ± 12.678	44.336 ± 10.550	2.848	> 0.05
	After surgery	39.631 ± 4.816	12.548 ± 4.876	10.812	0.001
	p -Value	< 0.05	>0.001		
CRP mg/dl	Before surgery	52.618 ± 6.494	54.636 ± 5.385	3.917	> 0.05
	After surgery	39.144 ± 6.64	12.100 ± 3.637	13.348	>0.001
	p -Value	< 0.05	>0.001		
IL-6	Before surgery	112.48 ± 54.116	122.78 ± 71.15	1.678	> 0.05
	After surgery	66.554 ± 46.44	18.46 ± 32.38	.950	>0.001
	p -Value	< 0.05	>0.001		
TNF	Before surgery	45.85 ± 16.54	38.62 ± 8.52	3.67	> 0.05
	After surgery	34.76 ± 8.52	18.840 ± 8.62	1.84	>0.001
	p -Value	< 0.05	>0.001		

The mean values of the laboratory parameters (ESR, CRP, IL-6, and TNF) for all burn patients in the study showed a significant difference, with p < 0.001. This finding demonstrates a significant decrease in values for graft radiotherapy, indicating minimal inflammatory and immune reactions.

Table 3: The statistical difference between two groups regarding clinical outcomes

		Group 1	**Group 2**	**T test**	**P Value**
		Mean ± SD	**Mean ± SD**		
Hospital stay duration		32.4 ± 4.06	22.0 ± 7.03	T = 8.298	< 0.001
Patients number that needs another autograft:	Yes	22	20	1.094	>0.05
	No	3	5		
The period from homograft coverage to rejection started		9.72 ± 1.48	15.36 ± 2.6	7.880	< 0.001
Percentage of the area need autograft application		87.3 ± 12.38	63.7 ± 13.57	10.892	< 0.001

We found a difference in hospital stay duration between groups 1 and 2, with a mean of 32.4 and 22.0 days, respectively. Irradiation reduces immune reactions and the possibility of eschar tissue formation, resulting in the acceleration of wound epithelialization which reduces hospital stay duration and morbidity.

Discussion

Extensive burns destroy the skin, [7,8] lead to the release of proinflammatory mediators at the injury site, [9,10] and cause the malfunction of microcirculation. [11,12] These systemic changes can affect multiple organs in the body [10] in a reciprocating manner. [11] Approximately 45.3% of burn patients develop multiple-organ dysfunction, which is the leading cause of death in children. [12]

An ideal skin substitute should mimic normal skin functions while causing fewer reactions. [13] The skin is protected by a large number of tissue-resident memory T-cells, which are recognized by the immune system and initiate antigen-antibody reactions. [14] Circulating T-cells infiltrate inflammatory sites and produce epithelial immunity with local antigen presentation. [15] As a result, to use skin homografts as a long-term substitute, [16] multiple methods for delaying rejection have evolved, either through systemic or local procedures, in order to minimize inflammatory and immune reactions. [17] Group 1 consisted of 25 patients (10 females and 15 males) with a mean age of 8.32 years (range: 1–12 years) and a mean percentage of burns of 33.3%. Group 2 included 25 patients (7 females and 18 males) with a mean age of 9.5 years (range: 2–12 years) and a mean percentage of burns of 28%. Bhatia et al [18] used homografts for neonates with burns with no donor sites and achieved satisfactory results. Although systemic immunosuppressive drugs can reduce rejection of organ transplants, such as kidneys, they have little or no effects on skin transplantation. [13] Better healing and epithelialization occurs when the homograft rejection process is reduced by minimizing the immune system response. [19]

The mean values of the laboratory parameters (ESR, CRP, IL-6, and TNF) for all burn patients in the study showed a significant difference, with $p < 0.001$. This finding demonstrates a significant decrease in values for graft radiotherapy, indicating minimal inflammatory and immune reactions. We found a difference in hospital stay duration between groups 1 and 2, with a mean of 32.4 and 22.0 days, respectively. Irradiation reduces immune reactions and the possibility of eschar tissue formation, resulting in the acceleration of wound epithelialization which reduces hospital stay duration and morbidity. According to Cheuk et al [20], topical suppression of epidermal memory cells can inhibit episodes of inflammation in certain dermatological diseases. According to Naoum et al, homograft application for extensive burns can improve patient outcomes while reducing length of hospital stay. [21] Khoo et al [9] concluded that burn coverage with homografts can promote angiogenesis with enhanced capillary ingrowth, provide growth factors and cytokines that cause chemotaxis and proliferation as a part of the inoculation process, and act similarly to an autologous skin graft. This incorporation occurs at the dermal collagenous matrix level.

Conclusion

The exposure of skin homografts from related living donors to a local low dose of radiotherapy can reduce a graft's ability to initiate inflammatory and immunological reactions, thereby minimizing rejection of a graft and enhancing epithelialization in children with deep second- and third-degree burns. More multicenter studies are needed in the future to recommend this technique as a safe routine procedure.

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