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Effectiveness of basic fibroblast growth factor for pediatric hand burns

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ABSTRACT

Aim of the study: Pediatric hand deep dermal and deep burns may lead to serious hand deformity with functional impairment and result in an esthetically unfavorable outcome. Since there is no guideline regarding the use of growth factors for pediatric hand burns, we sought to investigate the effectiveness of an angiogenic and regenerative growth factor, basic fibroblast growth factor (bFGF).
Methods: Consecutive series of second degree or third degree palmer burns at less than 3 years of age seen from January 2010 to June 2014 were included for evaluation at 6 months post-wound healing. The bFGF treatment started from just after injury and continued up to 21 days. Each patient had their scars scored using the Vancouver Scar Scale (VSS) at 6 months after wound healing.
Results: There were 34 children with 49 acute palmar burns. The mean healing period was 13.5 ± 4.3 days (7–44 days) and 43 wounds healed within 21 days. There was no need of additional surgery in the 43 wounds, healed within 21 days. In comparison to the wounds for which healing took more than 21 days, the wounds that healed within 21 days demonstrated significantly better pigmentation, pliability, and height according to the VSS ($p < 0.05$), as well as no scar contracture or hypertrophic scars.
Conclusion: bFGF treatment was effective in cases that healed within 21 days, avoiding scar contractures and hypertrophic scars. Our methods using bFGF to complete wound healing are less invasive and produce better results in pediatric palmer burns.

1. Introduction

Pediatric palmar hand burns are of common etiology, especially in the preschool age group. Although these burns may not be life-threatening, they have long-term complications in function, necessitate hand rehabilitation, and contain the psychosocial well-being of the pubertal patients [1]. Despite their relatively high incidence, there is controversy about the ideal treatment and management of pediatric palmar burns [2–5]. The main aims of treating a pediatric palmar burn are bringing positive esthetic and functional outcomes while minimizing or avoiding contracture and donor-site morbidity.

Growth factor therapy is effective and safe for deep dermal burns and third-degree burns [6]. Among the cytokines, basic fibroblast growth factor (bFGF) plays an important role in early burn wound healing [7]. The application of bFGF reduced time to second-intention healing and resulted in a more cosmetically acceptable scar in pediatric burn patients, showing less damage to the function of the stratum corneum after healing in clinical assessment and moisture meter analysis [8,9]. Initial treatment with bFGF for pediatric palmar burns may also result in better functional and esthetic outcomes. Since there is no guideline regarding the use of growth factors for pediatric palmar burns, we sought to investigate the effectiveness of an angiogenic and regenerative growth factor, bFGF, in the management of pediatric hand burns.

2. Methods

Consecutive series of second degree or third degree hand burns at less than 3 years of age seen from January 2010 to June 2014 at the department of Plastic and Reconstructive Surgery at National Nagasaki Medical Center were analyzed. Patient data including age, sex, and cause of burn were collected. Time to wound healing was defined as the number of days until the wound was completely epithelialized, as documented in the medical record. All patients underwent initial wound care, which consisted of debridement of loose blisters and the application of ointment-impregnated gauze.

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The bFGF (Trafermin, Fiblast Spray®, Kaken Pharmaceutical, Tokyo, Japan) treatment started from just after injury and continued up to 21 days. Genetically recombinant human bFGF-containing clear solution was sprayed over the wound daily. The concentration of bFGF was 30 μg of bFGF per 6 cm^2 area or at a concentration of 1 μg/cm^2 as 100 μg of freeze-dried bFGF dissolved in 1 mL of solution of benzalkonium chloride, with 300 μL being sprayed once a day over a 6 cm^2 area from a distance of 5 cm. The ointment-impregnated gauze was applied to wounds 30 s after the application of bFGF.

If wound exudate was still present after 21 days, a split-thickness skin graft from the scalp was applied for the residual burn wound. After wound healing, physiotherapy management of palmar burns consisted of a combination of pressure therapy, softening massage therapy, passive stretching, and movement exercises. If there was scar contracture clearly affecting the range of motion of a finger joint, released of the contracture and full-thickness skin grafting harvested from the foot pedal region were performed.

Three different board-certified plastic surgeons reviewed all scars in the subjects approximately 6 months after wound healing. Each patient had their scars scored using the Vancouver Scar Scale (VSS), which involved assessment of pigmentation (0 = normal, 1 = hypopigmented, 2 = mixed, and 3 = hyperpigmented); pliability (0 = normal, 1 = supple, 2 = yielding, 3 = firm, 4 = ropes, and 5 = contracture); height (0 = flat, 1 = <2 mm, 2 = 2 mm–5 mm, and 3 = >5 mm); and vascularity (0 = normal, 1 = pink, 2 = red, and 3 = purple). Scar firmness or pliability was assessed by wrinkling a skin fold. The height of a scar was measured by a simple measurement caliber. Pigmentation and vascularization were determined visually. Points were given for the various degrees of findings. Each parameter with the exception of pliability was obtained by averaging a unique value of three observers. Pliability was confirmed in all cases by one evaluator.

For statistical analysis, Statview (Statview version 5 for Windows; SAS Institute Inc., Cary NC) was used. All variables were compared using Welch's *t*-test, and $p < 0.05$ was considered statistically significant.

3. Results

There were 34 children with 49 acute palmar burns during the 4.5-year period. The causes of the burn injuries were contact (n = 17), scald (n = 10), steam (n = 5), and flame (n = 2). The mean age at the time of injury was 17.1 ± 11.9 months (range, 1–36 months). A total of 31 patients (91.2%) had superficial and deep partial-thickness burns, while 3 patients (8.8%) had full-thickness burns. The mean healing period was 13.5 ± 4.3 days (7–44 days); 43 hands (87.8%) healed within 21 days, while in 6 hands (12.2%), more than 21 days were required before healing. The reason why the 6 hands (in which two hands were third degree burn at the initial assessment) took longer than 21 days to heal was the progression of burn depth. Four hands progressed to third degree burn with widespread areas. These 6 hands underwent excision and split-thickness skin grafting from the scalp. One hand among them suffered partial graft loss due to infection, but did not require regrafting. Of those patients who underwent excision and grafting, 3 patients (4 hands) developed contracture affecting the range of motion and underwent secondary reconstruction at an average of 61 days after the initial surgery (Table 1). They were followed-up for a period lasting at least 6 months up to 4 years.

In cases in which healing lasted less than 21 days, we needed no reconstruction in secondary intention for the burn scars because the functional and esthetic results were quite acceptable, and there was no contracture, hypertrophic scar, or hyperpigmentation (Fig. 1). Two clinically hypertrophic scars and 4 contractures were observed after the split-thickness skin grafting (Fig. 2). Clinical evaluation of the burn scars in terms of pigmentation, pliability, and height demonstrated significant differences between the group with healing lasting less than 21 days and the split-thickness skin grafting group (pigmentation, 0.4 ± 0.57 vs. 2.2 ± 0.41, $p < 0.05$; pliability, 0.3 ± 0.49 vs. 3.7 ± 1.03, $p < 0.05$; height, 0.1 ± 0.30 vs. 2.0 ± 0.58, $p < 0.05$; and vascularity, 0.6 ± 0.69 vs. 1.0 ± 0.63, $p > 0.05$). However, after secondary reconstruction, pigmentation and pliability were improved significantly (pigmentation, 2.2 ± 0.41 vs. 0.25 ± 0.50, $p < 0.05$; pliability, 3.7 ± 1.03 vs. 1.5 ± 0.58, $p < 0.05$; height, 2.0 ± 0.58 vs. 1.5 ± 0.58, $p > 0.05$; vascularity, 1.0 ± 0.63 vs. 0.8 ± 0.50, $p > 0.05$) (Fig. 3). All patients achieved adequate digital lengths, palmar web contours, and full range of motion of finger joints after the treatment. Obvious complications associated with the use of bFGF were not observed.

4. Discussion

There is controversy over the treatment for pediatric palmar burns. It is difficult to determine the depth and range of a burn, and to reach consensus agreement on post-surgery management, especially in pediatric cases. The decision to perform split-thickness skin grafting or full-thickness skin grafting in the acute phase of burn wounds is also undetermined. The take rate of full-thickness skin grafts is lower than that of split-thickness ones because of edema and inflammatory reactions. Therefore, consideration should be given to preserving limited donor skin for further secondary full-thickness skin grafts.

Conservative treatment for pediatric palmar burns produces excellent results, and only wounds that do not heal in 3 weeks should be considered as candidates for excision and grafting [4,10]. We have to preserve the palmar-cutaneous ligaments, which provide stability for the palmar skin. If early excision is performed, the ligament may also be excised.

Early administration of bFGF for conservative treatment resulted in better scar quality and accelerated burn wound healing. In our series, the bFGF treatment was effective to prevent scar contracture when skin grafting was unnecessary. Our findings are consistent with the work of Barret et al., who reported relative success with conservative management of pediatric palm burns [11]. In their series of 120 patients, 4 patients (3.3%) required excision and skin grafting within 3 weeks after injury. However, 16 patients (13.3%) developed palmar contractures and 9 patients (7.5%) required reconstructive procedures. Jeffrey et al. recommended aggressive hand therapy and conservative management of palmar burns in children [4]. In their series of 168 hands that healed within 3 weeks, 4 hands (2.4%) required late reconstruction. In cases in which healing lasts less than 21 days, these conventional therapies necessitate reconstructive surgery, but our bFGF treatment group healed within 21 days needed no skin grafting or secondary reconstruction. Besides, these reports did not mention the discoloration of the epithelialized skin. Clinically, pigmentation or discoloration of the skin may be of concern for patients, especially when it occurs in the exposed extremities. Accelerated wound healing in non-skin grafted wounds, maintenance of a complex system of melanization, and diminishing activity of erythema following bFGF treatment led to a better clinical color match to the surrounding skin. Objective analysis of the burn scars showed that wounds treated using bFGF were significantly closer in color to adjacent skin than wounds in the control group [8,10]. There was no obvious hyperpigmentation in the resurfaced palms that healed in less than 21 days in our bFGF treatment group. In this regard, bFGF treatment was also effective to prevent hyperpigmentation in pediatric palmar burns.

However, wound healing time seems to give the greatest impact

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