A basic fibroblast growth factor in scar management

Sadanori Akita, MD, PhD

Division of Plastic and Reconstructive Surgery, Department of Developmental and Reconstructive Medicine, Nagasaki University, Graduate School of Biomedical and Sciences

1-7-1 Sakamoto
Nagasaki, 8528501
Japan

Tel: +81 95 849 7327
Fax: +81 95 849 7330
Email: akitas@hf.rim.or.jp
Hypertrophic scars or keloid scars caused after burns are sometimes problematic when functional regions such as articular joints or conspicuous areas on the face or extremities are involved (1). Massive burn wound scars have a tendency to develop progressive hypertrophic scars, and earlier skin grafting may improve the overall skin quality as well as shorten the hospital stay (2). Also, pediatric burn wounds can be problematic since accurate evaluation is difficult due to anatomically immature vasculature or immobilization failure, especially in second-degree burns. In addition, the burn surface areas and the burn depth tend to worsen over time.

Delayed wound healing results in unsightly scarring, such as hypertrophic scars, which are problematic both aesthetically and functionally. Among cytokines and growth factors, basic fibroblast growth factor (bFGF) is clinically proven, having demonstrated accelerated acute and chronic wound healing. Humoral and cellular mediators have been considered for the pathogenesis of burn wound-induced hypertrophic scars. There is no doubt of the involvement of cytokines such as transforming growth factor-β (TGF-β), which contributes to the high content of extracellular matrices (3), myofibroblasts influenced by interferon-α2b (IFN-α2b) (4) or altered interleukin-6 (IL-6) expression in fibroblasts (5).

A basic fibroblast growth factor (bFGF) may play a pivotal role in cutaneous wound healing by activating local macrophages, with the effects continuing up to the remodeling stage, several weeks after the initial injury. There is another mechanism of bFGF effects in wound healing in which the proliferation of human mesenchymal stem cells (hMSCs) is sustained in vitro (6) and hMSC grafting accelerates wound closure
along with artificial skin substitutes in nude rat model (7). However, burn wound fluids or skin graft wound fluids limited to the dermis contain lower concentrations of bFGF compared with surgical wounds, which is deeper than the dermis with subsequently lower endothelial cell proliferative and chemotactic activities (8). The bFGF is increased by silicone gel application in normal and fetal fibroblast cultures and may result in the prevention of hypertrophic scars (9). We therefore sought to investigate the rate of clinical burn wound healing after split skin grafting, and the quality of the skin, particularly hardness, using a durometer, which is commonly used for industrial materials such rubbers, erasers, and thread-rolls with or without bFGF (Table 1).

Basic fibroblast growth factor (Fiblast spray®)

Genetically recombinant human basic growth factor (bFGF) is used for clinical purpose. The concentration of bFGF was 30 μg of bFGF per 6 cm² area as 100 μg of bFGF dissolved in 1 ml of solution sprayed at 300 μL once per day. The bFGF spray continued until complete wound healing. The bFGF spray was distributed equally to all the burn wounds. The cost of 14-day use is about $100.00. The daily cost per 6 cm² is approximately $7.00.
Case reports

A skin graft case

An 83-year-old female was found in her house. Total burn surface area was 23%; 7% of which was third degree and 16% was second degree burns over her thigh, buttocks, posterior torso and legs. The cause was a flame. The first surgery for debridement and skin grafting was performed on the 7th day after transfer to our hospital. The debridement reached the subcutaneous fat level and 0.01 inch split thickness sheet skin grating over both ischia was performed, in addition to mesh-grafting in the other areas. Scratching habit, lack of immobilization and urine and feces caused the partial loss of skin grafting, therefore, at 4 weeks after the first surgery, the second surgery was attempted to close the residual 5% wound mainly over the bilateral ischia. A 0.009 inch mesh split thickness skin grafting was placed over bilateral buttocks of the anatomically identical areas. bFGF was sprayed over the mesh skin grafting on the left side of the buttock and the same sized area on the right buttock was grafted only with mesh skin. At 1 year after wound healing, clinical hardness score was 3.4 and the durometer reading was 12.7 in the right buttock, while in the left buttock, clinical hardness score (10) and durometer reading were 0.8 and 7.5, respectively (Figures 1–3).
Figure 1: Durometer, which is originally used for industrial measurement of rubber or thread-ball hardness.

![Durometer Image]

Figure 2: An 83-year-old female patient at arrival at our hospital.

![Patient Image]
Figure 3: The patient’s left buttock was treated with bFGF and the right buttock served as a control, undergoing conventional treatment with impregnated gauze alone. Histology demonstrated remarkable rete ridge formation in the bFGF-treated scar and the dermis and epidermis organization were very organized in the bFGF-treated scar at 18 months.
**A pediatric second degree burn**

An 18-month-old boy was involved in an accident in which his upper forearms were covered with boiling water. He was immediately transferred to our hospital and treated either with or without bFGF in conventional impregnated gauze dressings. At first inspection, the appearance of the second degree burn was indistinguishable between superficial- and deep-dermal burns. Use or omission of bFGF on the wounds was decided randomly. At 1 year after grafting, compared with the control, bFGF-treated scar demonstrated less height, better pliability, more normal vascularity and normal pigmentation (0 vs. 2, 1 vs. 3, 0 vs. 1, o vs. 1, Vancouver scar scale, bFGF vs. control, respectively). The effective contact coefficient was significantly greater in conventional wounds than bFGF-treated wounds (12.6 % vs. 7.7 %; conventional, bFGF) and bFGF-treated wounds demonstrated less transepidermal water loss (TEWL) values than conventional treatment (8.5 g/m²/h vs. 3.7 g/m²/h; conventional, bFGF). The bFGF-treated pediatric burns showed less damaging function of the stratum corneum after healing, both in clinical assessment and moisture meter analysis (Figures 4–5).

**Figure 4**

![Figure 4: A moisture meter, the main body of which only weighs 200 grams while the probe weighs 50 grams. The inter-relationship in tape-stripping among surface water content, corneal water and corneal thickness were noted.](image-url)
Figure 5: 18-month-old boy suffered from scalding. bFGF was used to treat the forearm, while the upper arm was treated conventionally. One year after wounding, the scar was remarkably better in the bFGF-treated area.
References


