Optimising Wound Healing in Aesthetic Surgery: From the Laboratory to the Clinic

The goal of any surgical or aesthetic procedure is to leave no scarring. For this, it is essential that wound healing should be optimised so that the skin heals without scars and as quickly as possible. A lot of research has been done on wound healing, but how much of this translates into actual clinical results remains to be seen. Two reviews in this issue focus on these aspects of wound healing; the role of topical retinoids in assisting wound healing following resurfacing procedures[1] and various modalities that increase neocollagenesis and neoelastogenesis in the dermis.[2]

Topical retinoids have been traditionally used before skin resurfacing procedures to enhance wound healing and reduce complications. Studies have shown that Vitamin A can enhance various aspects of wound healing by stimulation of angiogenesis, collagen synthesis, fibroplasia and epithelialisation.[3,4] The site of action is mainly in the papillary dermis where topical tretinoin, the most well-studied molecule, has been shown to increase Type I collagen production by 80% and also at the epidermal level causing epidermal hyperplasia with compaction of the stratum corneum and thickening of the granular layer.[5] The mechanism of action of retinoids and their analogues is through the nuclear receptors (RARs [retinoic acid receptors] or RXRs [retinoic X receptors]) on cells. This interaction activates genes that contain RARE (retinoic acid response elements) or RXRE (retinoic X response elements) in their promoters.[6] They can also regulate gene expression by inhibiting the activity of other transcription factors, such as AP-1. It has been hypothesized that AP-1 may play a substantial role in the inflammation and immune response.[6]

There are very few well-designed studies that conclusively report on the optimum duration and strength of tretinoin that can assist wound healing. Most of the studies are on animal skin and a few studies in the clinic have shown conflicting results. In a study by Orringer *et al*.,[7] application of 0.05% tretinoin 3 weeks before CO_2 laser resurfacing on the forearm skin did not show quicker re-epithelialisation as compared to a control cream. In addition, there was no significant difference in levels of matrix metalloproteinases or pro-collagens. On the contrary, a study by Popp *et al*.[8] showed accelerated wound healing in tretinoin pre-treated sites applied at a strength of 0.05% for 8 weeks, followed by 0.1% for another 8 weeks. There was a significant histological change in full-thickness forearm skin biopsies. In addition, there was also a dramatic clinical difference; the mean wound area from the tretinoin-treated sides was markedly smaller than the control sides. Another comparative study of tretinoin, adapalene and collagenase in an experimental model of wound healing concluded that tretinoin and adapalene enhance the wound healing process by enhancement of collagen production, angiogenesis and granulation tissue formation.[9] A review by Abdelmalek and Spencer[10] drew the conclusion that pre-treatment with topical tretinoin for at least 2–4 weeks is beneficial for facial resurfacing procedures and partial- or full-thickness skin wounds. Retinoic acid can also reverse the inhibitory effects of glucocorticoids on wound healing. In addition, wounds with unfavourable conditions at baseline such as chronic wounds, diabetic complications, presence of a foreign body or steroid depression may benefit from enhanced wound healing with topical retinoid use, whereas sutured wounds may not. Clearly, more studies are required in a clinical setting to resolve the issue.

Based on their review and experience, Buchanan and Gilman[1] recommend that tretinoin cream 0.1% should be applied nightly for 3 months before ablative resurfacing and the strength should be reduced to 0.05% for non-ablative laser resurfacing.[1] They should be discontinued 24 h before the planned procedure. For chemical peels, tretinoin concentration depends on the level of depth of the peel.[1]

Wounding the skin alters the collagen and elastin, the two main fibres of the extracellular matrix of the

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skin. Collagen provides tensile strength, and elastin provides elasticity to the skin. Hence, neocollagenesis and neoelastogenesis hold the key to managing optimal wound healing and scarring and also reduce cutaneous ageing. Retinoids that are derivatives of Vitamin A, Vitamin C, proteins, peptides, amino acids and a host of other factors play an important role in collagen and elastin formation. The recent introduction of controlled skin wounding by energy-based devices such as radiofrequency (RF), infra-red and deep ultrasound therapy has changed the way we modulate wound healing as well as cutaneous ageing.

Monopolar RF leads to neocollagenesis in the papillary dermis, as well as upper, middle and deep reticular dermis. Neoelastogenesis occurs in the papillary dermis and upper and middle reticular dermis. High-intensity-focussed ultrasound leads to neocollagenesis in the middle and deep reticular dermis and neoelastogenesis in the deep reticular dermis.[11] Lasers as well as intense pulsed light treatments have been shown to stimulate new collagen production, which is attributed to the release of inflammatory mediators from vascular epithelial cells.[12] The introduction of micro-needling for collagen induction has been well documented. Platelet-rich plasma also impacts wound healing by release of growth factors and is being widely used for enhanced wound healing and skin rejuvenation.

However, the goal of scarless healing is still far from reality. Studies on the mechanisms of foetal wound healing which heals without scarring and the regenerative capacities of mammalian skin still remain in the realm of the laboratory. The wound healing profile of foetal skin which is characterised by a distinct growth factor profile compared to post-natal wound healing, a muted inflammatory response with an anti-inflammatory cytokine profile, an extracellular matrix that is rich in Type III collagen and hyaluronan, reduced biomechanical stress and a potential role for stem cells needs to be replicated in the adult.[13] The need of the hour is to close the gap between the laboratory and the clinic, through cutting edge research in stem cell therapy. Healing and regenerating without scars, the ultimate goal of wound healing is an exciting possibility in the future for aesthetic surgery.

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