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Role of Topical Enalapril in Treatment of Hypertrophic Scars

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Abstract

Hypertrophic scars are a result of exuberant wound healing following skin injury and deposition of excess collagen. Despite the introduction of a wide variety of management protocols for hypertrophic scars, no definitive treatment has been established with optimal clinical results so far. Angiotensin II activation by angiotensin-converting enzyme (ACE) is a significant mediator in wound healing and collagen production. In this study we aim to evaluate the role of topical enalapril in hypertrophic scar treatment.

Keywords: Enalapril; Hypertrophic scar; Vancouver scar scale.

Introduction

Hypertrophic scars are a result of exuberant wound healing following skin injury and deposition of excess collagen.[1] Hypertrophic scars occur as a result of prolonged inflammatory response to injury and persistent fibrosis which results in a red elevated hard scar with cutaneous and joint contractures. Hypertrophic scars involve deep dermis but there is no expansion onto surrounding tissues and beyond the margins of the wound. They occur usually in second or third decade and have equal sex distribution. Despite the introduction of a wide variety of management protocols for hypertrophic scars, no definitive treatment has been established with optimal clinical results so far. Hence, patients may need combination therapeutic modalities based on size, depth and location of the lesion and response to therapy.[2] Treatment options include excision with or without grafting, interferon therapy, bleomycin, silicone gel sheeting, laser therapy, compression therapy. Although among these methods intralesional steroid therapy is regarded as the benchmark treatment, complications with steroid injections such as repetitive painful injections and unpredictable efficacy are widely reported.[3] In this case the effect of topical application of ACE inhibitor enalapril on hypertrophic scar formation has been studied.

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Materials and Methods

In this study of a 23 year old female with hypertrophic scar post trauma we had applied topical enalapril over the hypertrophic scars (fig. 1) and observed over 6 weeks follow up. Topical enalapril was applied twice daily on the scar site

(fig. 2). The scars were observed after the period of 6 weeks (fig. 3). Improvement in the scars were noted with picture comparison and clinical examination over the period of time. To avoid observer bias comments were taken from other authors of the case report.

Result

In our study topical enalapril was successful in treatment of hypertrophic scars over the short period of 6 weeks follow up. Prior to application of enalapril the Vancouver scar score was 9 and following treatment the score was.[7]

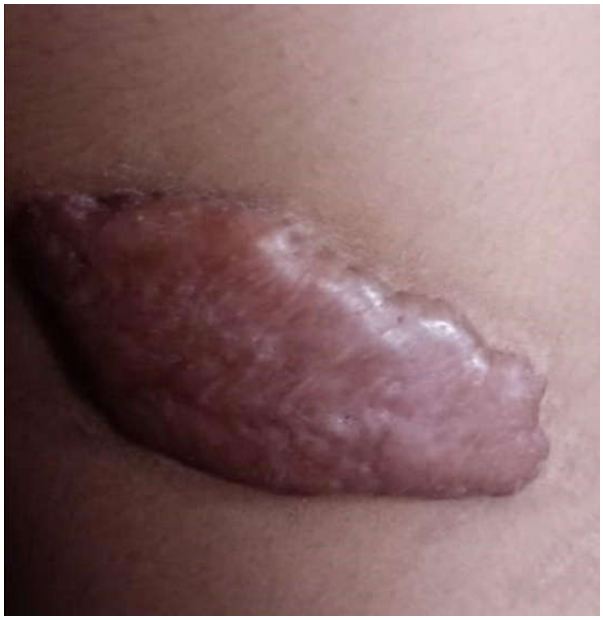

Fig. 1: Case of hypertrohic scar of right thigh

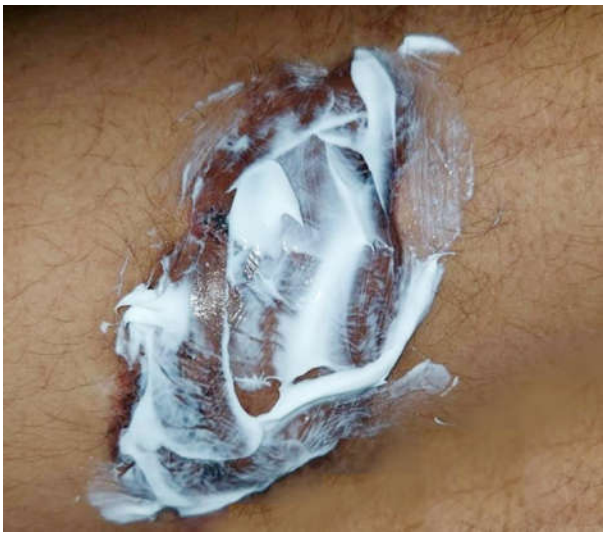

Fig. 2: Application of topical enalapril on hypertrophic scar.

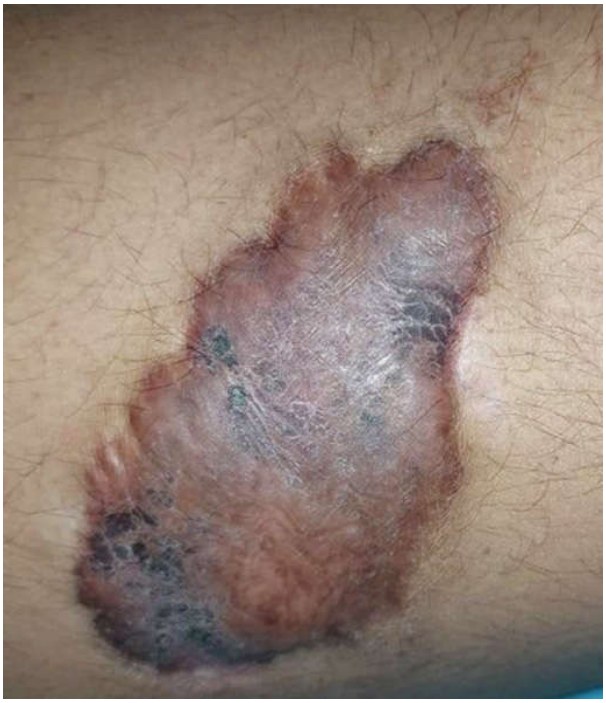

Fig. 3: hypertrophic scar after treatment with topical enalapril

Vancourver Scar Scale

Scar Characteristic	Score
Vascularity	
Normal	0
Pink	1
Red	2
Purple	3
Pigmentation	
Normal	0
Hupopigmentation	1
Hyperpigmentation	2
Pliability	
Normal	0
Supply	1
Yielding	2
Firm	3
Ropes	4
Contracture	5
Height (mm)	
Flat	0
<2	1
2~5	2
>5	3
Total Score	**13**

Discussion

Several pharmacological and non pharmacological management options have been proposed for hypertrophic scars however high cost and risk of recurrence are still a major impediment to their adoption. The pathogenesis of hypertrophic scars includes excessive and abnormal composition and metabolism of collagen and other extracellular matrix components in the wound site. The main processes that are regulated by TGF-β in wound healing are angiogenesis, inflammation, fibroblast proliferation, collagen production and deposition and remodeling of the ECM.[5] PDGF and TGF-β1 are 2 main role players in the production of key ECM components, such as collagens and fibronectin. On the other hand, macrophages and neutrophils cause collagen breakdown by releasing matrix metalloproteinases (MMPs). However, TGF-β1 inhibits MMP synthesis and cause greater accumulation of collagen fibers.[6] ACE, angiotensin II and angiotensin type 1 receptors all have increased expressions in human hypertrophic scar fibroblasts.[7] Tang et al. showed that angiotensin II induces mRNA and protein expression of type I collagen gene in human dermal fibroblasts through an TGF-β1-dependent pathway which were abolished by the angiotensin type 1 (AT1) receptor antagonist.[8] Angiotensin II can cause upregulation and activation of TGFβ via 2 distinct signaling pathways. In the first pathway, TGF-β after binding to receptor activin receptor like kinase 5 (ALK5) which phosphorylates Smad2/3 induce recruitment of Smad4 and subsequently cause nuclear translocation of the Smad2/4 or Smad3/4. The second pathway involves regulation of mitogen activated protein kinase (MAPK) signaling including extracellular signal regulated kinase (ERK), and p38.

In an investigation of formation of hypertrophic scars in a rabbit ear wound model by Uzun et al, authors indicated that as decrease in angiotensin II level leads to nonselective reduction of TGF-β isomers, which is only desirable for TGF-β1 and TGF-β2 in the prevention of hypertrophic scars, addition of TGF-β3 to an ACE–inhibitor may be synergistic for scar improvement in the wound area.[9] It was demonstrated that after bleomycin induced lung injury, concentration of lung angiotensin II increases and precedes the increment in lung collagen. Administration of ramipril (an ACE inhibitor) and losartan (an angiotensin II type 1 receptor antagonist) attenuated TGF-beta expression, and collagen deposition. These observations not only suggest the important role of ANG II in the fibrotic response to acute injury, at least mediated in part via TGF-beta, but also manifest the potential of ACE inhibitors, as widely used clinical drugs, for therapy of fibrotic diseases.[10] The Vancouver scar scale is used to characterize hypertrophic scars.[11]

Conclusion

In our study we have observed that topical enalapril has a role in treatment of hypertrophic scar. But since it is a study involving a single patient and for a short period of time, a definitive conclusion cannot be made. Large randomized control trials are required to confirm the efficacy of this method.

Conflicts of interest: None

Authors' contributions: All authors made contri butions to the article

Availability of data and materials: Not applicable

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Consent for publication: Not applicable

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