

## Vitamin E and its clinical challenges in cosmetic and reconstructive medicine with focus on scars; a review

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### Abstract

Hypertrophic scars are abnormal scars that develop after wound-healing, especially in some ethnic backgrounds. The after-effects of these scars result in depression, post-traumatic stress syndrome, anxiety, impaired self-esteem and quality of life. Treatment of these scars still is a subject of different studies and is a challenging issue in reconstructive medicine. We reviewed the current published articles about the effects of vitamin E on scar formation and its clinical effectiveness. The application of vitamin E is popular interest, but it still needs more clinical studies to establish its perceived outcomes.

**Keywords:** Vitamin E, Clinical challenges, Scar.

### Introduction

Keloids are elevated fibrous scars which extend beyond the borders of the primary wound, do not regress, and commonly surface following excision. The term was originated from the Greek word 'cheloïdes,' meaning 'crab's claw.'<sup>1</sup> Hypertrophic scars are identical, but are limited to the wound borders and commonly regress over time.<sup>1,2</sup>

Scar hypertrophy commonly occurs within a month of damage, while keloids might come into being later; from three months to even years.<sup>3</sup> Both are abnormal answers to dermal damages, with exuberant deposition of collagen extending over three basic stages: inflammation (first three to 10 days); proliferation (next 10 to 14 days); and maturation or remodelling (two weeks to years).<sup>1</sup>

The management of keloids and hypertrophic scars is a challenging issue and a subject of both controversy and investigations.<sup>1,4,5</sup>

In North America, one in every 3000 persons experiences a burn injury annually.<sup>6</sup> The most common complication of burning is either hypertrophic or keloid scars.<sup>6</sup>

Studies have reported that the estimated rate of

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abnormal scarring after burn injury might be 70%.<sup>7,8</sup> The tendency to improve abnormal scarring may correlate with age, ethnic background, severity and location of the injury.<sup>8,9</sup>

The after-effects of scars are related to changes that happen in patients' physical appearance.<sup>10</sup> Patients with a scar on their skin are predisposed to depression (13% to 23%); post-traumatic stress syndrome (13% to 45%); and anxiety, decreased self-worth, and, finally, altered pattern of life.<sup>10,11</sup>

Hence, we reviewed one of the popular therapies for scars to clarify its effectiveness and outcomes.

### The Clinical Challenges:

Vitamin E was discovered in 1922 by investigators who explained its effects on the skin, mostly in regenerative medicine.<sup>12</sup> Vitamin E is the major lipid-soluble antioxidant agent in the body.<sup>13</sup> The anti-oxidant features of Vitamin E make the membranes firm, involve inflammatory cells and result in the reduction of chemicals released by these cells.<sup>12</sup>

Vitamin E is an important nutrient (usually supplement) and attracts the attention of many dermatologists and those who work in regenerative medicine due to its anti-oxidant features. Optimum concentrations of vitamin E can be found in fresh vegetables and their oils, and nuts.<sup>14</sup> According to a study, the majority of United States population is using vitamin E.<sup>15</sup>

Two studies which were performed on mouse models showed that localised application of vitamin E increased the rate of wound healing by excluding the oxidative stress mechanisms.<sup>16,17</sup>

A study on the effects of vitamin E in clinical investigation comprised 96 atopic dermatitis subjects who received either placebo or oral vitamin E. The results revealed a development in dermatitis and a 62 per cent reduction in serum Immunoglobulin-E (IgE) concentrations among those who received vitamin E. The association among  $\alpha$ -tocopherol usage, IgE levels, and clinical presentation provided evidence that vitamin E intake could be beneficial in the treatment of atopic dermatitis.<sup>18</sup>

Another study indicated a significant development of melasma and pigmented contact dermatitis damages by combination therapy of vitamins in comparison with mono-therapy groups.<sup>19</sup> Topical and local formulations which were applied for de-pigmentation included vitamins C and E as well as the commonly used hydroquinone and sunscreens. They seemed to be safe and useful.<sup>20</sup>

Some studies showed that oxidative stress plays an important role in pathogenesis of melanoma and non-melanoma cancer, and showed that vitamin E decreased the pace of melanoma growth by inducing tumour cell apoptosis and affecting angiogenesis.<sup>21-23</sup>

Yet another study elucidated that a topical, occlusive pre-treatment with 5% vitamin E for 24 hours would provide protection against ultraviolet-caused up-regulated macrophages metalloelastase in skin.<sup>24</sup> Others showed that vitamin E had the ability to penetrate into the dermal parts with oxidative stress, and have a positive impact.<sup>25,26</sup>

On the other hand, a study showed there was little evidence that vitamin E (alphatocopherol) was efficient, and some patients even showed contact dermatitis which may result in delayed healing.<sup>27</sup>

In one study, researchers added vitamin E to silicone gel sheets to evaluate its effects on 80 subjects between ages 18 and 63 with hypertrophic scars. One group received sheets with vitamin E, while the other received only silicone gel sheets. The former was seen to have additional therapeutic effect.<sup>28</sup>

In contrast, one investigation examined the effects of topical vitamin E on patients who had undergone operation for post-burn contractures, and indicated that there were no appreciable effects.<sup>29</sup>

Another study indicated that topical application of a mixture of an emollient and vitamin E did not cause a better cosmetic impact in comparison with just the emollient.<sup>13</sup>

Recently, researchers performed a prospective randomised double-blinded trial with 5% tocotrienol, a sub-family of vitamin E, on 122 subjects with improved operational scars. They revealed that the prescription of 5% tocotrienol twice daily had no reportable impact on the forms and vessel formation of the scars after 4 months. The most reportable result in the research, they said, was the absence of adverse influences.<sup>30</sup>

Consistent with some of the quoted studies, the usefulness of vitamin E application on surgical scars was

reported in a study of 428 paediatric patients. Localised vitamin E application was prescribed for at least 15 days before and 30 days following inguinal operation. The researchers associated the development in cosmetic outcomes to the pre-surgery application that was believed to have reinforced skin rehydration, developed elasticity and resistance, and resulted in better healing.<sup>30,31</sup>

In another study, 15 subjects with scars in certain parts of the body were examined. The mixture of 0.5% hydrocortisone, silicone and vitamin E lotion was reported to be more effective than onion extract and placebo used in the study.<sup>30,32</sup>

The effectiveness of vitamin E application apparently lies in deep dermal penetration and the ability to decrease oxygen radicals, which encourages collagen and glycosaminoglycan production.<sup>33,34</sup> Early topical application of vitamin E in scar management may cause reduction of the tensile strength of the wound.<sup>35</sup> This might lead to stretched scars and possible dehiscence from diminished wound healing. Side effects from topical vitamin E prescription involve dermatitis and an erythema multiforme-like reaction.<sup>36</sup>

## Conclusion

Despite a lot of investigations and researches performed to identify and clarify the exact effects of vitamin E on hypertrophic scars, there have been no undisputed results about the clinical impact of its usage. Topical application of vitamin E is popular among patients and physicians for cosmetic purposes, but further investigations are needed to confirm the clinical utility of the practice.

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## References

1. Jackson IT, Bhageshpur R, DiNick V, Khan A, Bhaloo S. Investigation of recurrence rates among earlobe keloids utilizing various postoperative therapeutic modalities. *Eur J Plast Surg* 2001; 24: 88-95.
2. Leventhal D, Furr M, Reiter D. Treatment of keloids and hypertrophic scars: a meta-analysis and review of the literature. *Arch Facial Plast Surg* 2006; 8: 362-8.
3. Murray JC. Keloids and hypertrophic scars. *Clin Dermatol* 1994; 12: 27-37.
4. Butler PD, Longaker MT, Yang GP. Current progress in keloid research and treatment. *J Am Coll Surg* 2008; 206: 731-41.
5. Berman B, Perez OA, Konda S, Kohut BE, Viera MH, Delgado S, et al. A review of the biologic effects, clinical efficacy, and safety of silicone elastomer sheeting for hypertrophic and keloid scar treatment and management. *Dermatol Surg* 2007; 33: 1291-303.
6. Herndon DN. *Total Burn Care*. 2nd ed. NewYork: Saunders; 2002.

7. McDonald WS, Deitch EA. Hypertrophic skin grafts in burned patients: a prospective analysis of variables. *J Trauma* 1987; 27: 147-50.
8. Bombaro KM, Engrav LH, Carrougher GJ, Wiechman SA, Faucher L, Costa BA, et al. What is the prevalence of hypertrophic scarring following burns? *Burns* 2003; 29: 299-302.
9. Li-Tsang CW, Lau JC, Chan CC. Prevalence of hypertrophic scar formation and its characteristics among the Chinese population. *Burns* 2005; 31: 610-6.
10. Van Loey NE, Van Son MJ. Psychopathology and psychological problems in patients with burn scars: epidemiology and management. *Am J Clin Dermatol* 2003; 4: 245-72.
11. Robert R, Meyer W, Bishop S, Rosenberg L, Murphy L, Blakeney P. Disfiguring burn scars and adolescent self-esteem. *Burns* 1999; 25: 581-5.
12. MacKay D, Miller AL. Nutritional support for wound healing. *Altern Med Rev* 2003; 8: 359-77.
13. Baumann LS, Spencer J. The effects of topical vitamin E on the cosmetic appearance of scars. *Dermatol Surg* 1999; 25: 311-5.
14. Thiele JJ, Hsieh SN, Ekanayake-Mudiyanselage S. Vitamin E: critical review of its current use in cosmetic and clinical dermatology. *Dermatol Surg* 2005; 31: 805-13.
15. Maras JE, Bermudez OI, Qiao N, Bakun PJ, Boody-Alter EL, Tucker KL. Intake of alpha-tocopherol is limited among US adults. *J Am Diet Assoc* 2004; 104: 567-75.
16. Galeano M, Torre V, Deodato B, Campo GM, Colonna M, Sturiale A, et al. Raxofelast, a hydrophilic vitamin E-like antioxidant, stimulates wound healing in genetically diabetic mice. *Surgery* 2001; 129: 467-77.
17. Altavilla D, Saitta A, Cucinotta D, Galeano M, Deodato B, Colonna M, et al. Inhibition of lipid peroxidation restores impaired vascular endothelial growth factor expression and stimulates wound healing and angiogenesis in the genetically diabetic mouse. *Diabetes* 2001; 50: 667-74.
18. Tsourelis-Nikita E, Hercogova J, Lotti T, Menchini G. Evaluation of dietary intake of vitamin E in the treatment of atopic dermatitis: a study of the clinical course and evaluation of the immunoglobulin E serum levels. *Int J Dermatol* 2002; 41: 146-50.
19. Hayakawa R, Ueda H, Nozaki T, Izawa Y, Yokotake J, Yazaki K, et al. Effects of combination treatment with vitamins E and C on chloasma and pigmented contact dermatitis. A double blind controlled clinical trial. *Acta Vitaminol Enzymol* 1981; 3: 31-8.
20. Guevara IL, Pandya AG. Safety and efficacy of 4% hydroquinone combined with 10% glycolic acid, antioxidants, and sunscreen in the treatment of melasma. *Int J Dermatol* 2003; 42: 966-72.
21. Sander CS, Hamm F, Elsner P, Thiele JJ. Oxidative stress in malignant melanoma and non-melanoma skin cancer. *Br J Dermatol* 2003; 148: 913-22.
22. Malafa MP, Fokum FD, Smith L, Louis A. Inhibition of angiogenesis and promotion of melanoma dormancy by vitamin E succinate. *Ann Surg Oncol* 2002; 9: 1023-32.
23. Malafa MP, Fokum FD, Mowlavi A, Abusief M, King M. Vitamin E inhibits melanoma growth in mice. *Surgery* 2002; 131: 85-91.
24. Chung JH, Seo JY, Lee MK, Eun HC, Lee JH, Kang S, et al. Ultraviolet modulation of human macrophage metalloelastase in human skin in vivo. *J Invest Dermatol* 2002; 119: 507-12.
25. Lopez-Torres M, Thiele JJ, Shindo Y, Han D, Packer L. Topical application of alpha-tocopherol modulates the antioxidant network and diminishes ultraviolet-induced oxidative damage in murine skin. *Br J Dermatol* 1998; 138: 207-15.
26. Sander CS, Chang H, Salzmann S, Müller CS, Ekanayake-Mudiyanselage S, Elsner P, et al. Photoaging is associated with protein oxidation in human skin in vivo. *J Invest Dermatol* 2002; 118: 618-25.
27. Khoosal D, Goldman R. Vitamin E for treating children's scars. Does it help reduce scarring? *Can Fam Physician* 2006; 52: 855-6.
28. Palmieri B, Gozzi G, Palmieri G. Vitamin E added silicone gel sheets for treatment of hypertrophic scars and keloids. *Int J Dermatol* 1995; 34: 506-9.
29. Jenkins M, Alexander JW, MacMillan BG, Waymack JP, Kopcha R. Failure of topical steroids and vitamin E to reduce postoperative scar formation following reconstructive surgery. *J Burn Care Rehabil* 1986; 7: 309-12.
30. Khoo TL, Halim AS, Zakaria Z, Mat Saad AZ, Wu LY, Lau HY. A prospective, randomised, doubleblinded trial to study the efficacy of topical tocotrienol in the prevention of hypertrophic scars. *J Plast Reconstr Aesthet Surg* 2011; 64: e137-45.
31. Zampieri N, Zuin V, Burro R, Ottolenghi A, Camoglio FS. A prospective study in children: Pre- and post-surgery use of vitamin E in surgical incisions. *J Plast Reconstr Aesthet Surg* 2010; 63: 1474-8.
32. Perez OA, Viera MH, Patel JK, Konda S, Amini S, Huo R, et al. A comparative study evaluating the tolerability and efficacy of two topical therapies for the treatment of keloids and hypertrophic scars. *J Drugs Dermatol* 2010; 9: 514-8.
33. Klain GJ. Dermal penetration and systemic distribution of 14C-labeled vitamin E in human skin grafted athymic nude mice. *Int J Vitam Nutr Res* 1989; 59: 333-7.
34. Tanaka H, Okada T, Konishi H, Tsuji T. The effects of reactive oxygen species on the biosynthesis of collagen and glucosaminoglycans in cultured human dermal fibroblasts. *Arch Dermatol Res* 1993; 285: 352-5.
35. Widgerow AW, Chait LA, Stals R, Stals P. New innovations in scar management. *Aesth Plast Surg* 2000; 24: 227-34.
36. Saperstein H, Rapaport M, Rietschel RL. Topical vitamin E as a cause of erythema multiforme-like eruption. *Arch Dermatol* 1984; 120: 906-8.