Survivin level in keloids before and after treatment with FK506 (tacrolimus) versus intralesional steroid injection, correlating its level with clinical and histopathological treatment outcome.

Thesis

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Summary

Keloid is one of the most frustrating problems of the wound healingand no treatment is completely effective against these lesions. Keloids are considered as benign overgrowth of dense fibrous tissue resulting from excessive deposition of ECM.Keloid fibroblasts (KFs) persistently proliferate and fail to undergo apoptosis.

One of the first-line options to treat keloid scars is IL steroid injection. The most effective IL steroid used is triamcinolone acetonide (TAC). The effects of corticosteroids are primarily due to their suppressive effects on the inflammatory process in the wound and secondarily due to reduced collagen and glycosaminoglycan synthesis, inhibition of fibroblast growth, and enhancement of collagen and fibroblast degeneration.

Survivin is a unique member of the inhibitor of apoptosis proteins (IAP).Survivin inhibits the activity of caspase-3, thereby exerting an anti-apoptotic effect. Previous studies showed that survivin expression was significantly higher in keloids than in normal skin.

Tacrolimus (FK506) is a kind of natural macrolide immune- suppressant isolated from Streptomyces whose immunosuppressive activity is 10- 100 times that of cyclosporin A.It binds to FK506 binding protein (FKBP) to form a complex that inhibits calcineurin phosphatase and suppresses production of T lymphocytes cytokines, mainly IL-2.Tacrolimus also induces fibroblastsapoptosis through increase expression ofcaspase-3 andinhibiting survivin expression. Patients with keloids did experience

decreased induration, tenderness, erythema, and pruritus in keloids after topical tacrolimus treatment.

The aim of our study was to estimate the role of survivin in keloid formation and to evaluate the therapeutic effect of topical tacrolimus (FK506) on keloids immunohistochemically and clinically compared to intralesional steroid as a documented keloid treatment.

The study included 40 patients with keloid, 20 of them received tacrolimus topically under occlusion for three months and the other 20 patients received IL triamcinolone for three months with four weeks interval between sessions, and 20 healthy individuals as controls. Biopsies were taken from keloids before and after treatment, from both treatment groups, andfrom normal controls' skin. Survivin was measured in all biopsies and both treatment groups were evaluated clinically by VSS and immunohistochemically. Finally patient and physician satisfaction were assessed.

Our study showed that there was a statistically significant higher dermal and epidermal survivin level (p-value <0.05) inkeloid tissue compared to normal skin tissue. Also there wasstatistically significant decrease (p-value <0.05) in epidermal and dermal survivin level after treatment by both IL steroid and topical tacrolimus. In steroid group, there was statistically significant improvement (p-value <0.05) in itching, tenderness, pliability, vascularity and height levels. On the other hand there was no statistically significant difference (p-value >0.05) in pigmentation.In tacrolimus

group, there was statistically significant improvement (p-value <0.05) in itching, tenderness, pliability, vascularity, and pigmentation level before and after treatment with no statistically significant difference(p-value >0.05)in the height levels of keloids. There was a closely similarstatistically significant (p-value <0.05) decrease in VSS after treatment among both steroid and tacrolimus groups and both treatment modalities improved keloid lesions clinically. However, improvement of VSS washigher in steroid group (45%) than in tacrolimus group (25%).There was negative correlation between survivin level and age of the patients. However, there was no significant relation between survivin and other clinical data of patients, clinical findings or VSS. Both patient and physician satisfaction were statistically higher (p-value <0.05) among steroid group compared to tacrolimus group.

In conclusion, survivin may play a role in pathogenesis of keloid evidenced on its higher level in keloid than in normal skin.Topical tacrolimus showed a promising therapeutic effect clinically and pathologically,however, more satisfying results were achieved by IL steroid.