WOUND HEALING

BOTULINUM TOXIN TYPE A SUPPRESSES PRO-FIBROTIC EFFECTS VIA THE JNK SIGNALING PATHWAY IN HYPERTROPHIC SCAR FIBROBLASTS

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Introduction: Hypertrophic scar (HS) is a dermal fibroproliferative disease characterized by the overproduction and deposition of extracellular matrix (ECM), cell over-proliferation, enhanced angiogenesis, and enhanced differentiation of fibroblasts to myofibroblasts. Although there has been extensive research on botulinum toxin type A (BTX) treatment for the prevention of HS formation, its effectiveness for the attenuation of skin fibrosis and the related mechanism are unclear.

Objective: BTX treatment on HS whould shove suppressive effect on scar-realted factors.

Materials and Methods: Human scar fibroblasts (HSFs) were cultured and stimulated with BTX. MTS, scratch, quantitative polymerase chain reaction, enzyme-linked immunosorbent, and western blot assays were performed to detect changes in fibroblast proliferation, migration, and gene/protein expression of pro-fibrotic factors.

Results: Our study revealed that the proliferation and migration of BTX-treated HSFs were decreased compared to those in untreated controls ($P < 0.01$). The mRNA and protein expression of pro-fibrotic factors including TGF-β1, IL-6, CTGF, and α-SMA was inhibited by BTX treatment, whereas JNK phosphorylation was activated. Blocking the JNK pathway rescued the inhibitory effects on HSF proliferation and the production of pro-fibrotic factors, suggesting that the suppressive effects of BTX are closely associated with JNK pathway activation.

Conclusions: This study showed that BTX has a suppressive effect on ECM production and scar-related factors in HSFs in vitro. Moreover, regulation of JNK signaling played an important role in this process. Our results provide some theoretical basis, on a cellular level, for HS treatment. Further studies are needed to delineate the molecular network of BTX in HSFs.