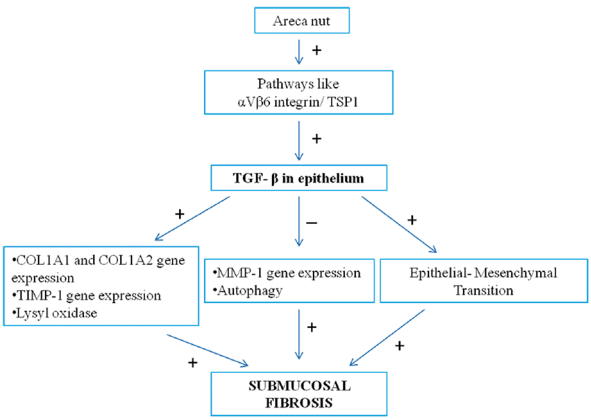
EDITORIAL

Transforming growth factor-β - The master switch in oral submucous fibrosis

Oral submucous fibrosis (OSMF) is a chronic progressive, debilitating disorder of oral cavity, oropharynx and upper third of the esophagus. Scientific data confirms the etiological role of areca nut. Submucosal fibrosis due to excessive abnormal collagen being the hallmark, OSMF is accepted beyond doubt as a potentially malignant disorder.[1,2]

The progressive irreversible nature and morbidities associated with OSMF have made combating the disease challenging. Current research is heading toward unveiling the pathogenic mechanisms contributing to fibrosis and thus formulating a definitive treatment strategies. Different mechanisms and molecules are proposed in the pathogenesis of OSMF, to name a few, growth factors and inflammatory cytokines, reactive oxygen species, matrix metalloproteinases - tissue inhibitor of metalloproteinases, copper - lysyl oxidase enzyme and genetic polymorphism.[3]

Most studied among the growth factors is the role of transforming growth factor (TGF) - β isoforms in OSMF. TGF-β is a potent cytokine influencing extracellular matrix deposition and remodeling, secreted in inactive procytokine form demanding activation through different pathways. Of the three isoforms, TGF-β1 seems to be significantly associated with fibrosis in various organs.[4] Tissue fibrosis is the result of increased collagen synthesis and reduced breakdown. TGF-β modulates both of these pathways causing excessive pathological fibrosis.[5] Data from several studies including oligonucleotide assays reveal a significant increase in TGF-β in OSMF tissues.[6] TGF-β1, induced by areca nut in epithelial cells is suggested to be the potent stimulator of fibrogenesis in the connective tissue of OSMF.[7,8] Another attractive role of TGF-β is its potential to induce epithelial-mesenchymal transition (EMT) in chronic inflammatory background resulting in fibrosis of kidney, lung, liver, etc. Although the importance of TGF-β in fibrogenesis via EMT is least studied in OSMF, we may hypothesize it to be the same in OSMF. This concept is strengthened by the ability of TGF-β to induce EMT in cultured epithelial cells *in vitro*. Furthermore, TGF-β1 is expressed at sites of epithelial degeneration and adjacent fibrosis *in vivo*.[4] However, the ability of TGF-β1 to induce the EMT leading to carcinogenesis in OSMF is yet to be explored. Thus, TGF-β is considered the master switch in fibrogenesis. A brief summary of the TGF-β synthesis, activation and its possible impact on tissue fibrosis in OSMF is depicted in Flowchart 1.[5,7,9,10] Thus, a therapeutic intervention targeting TGF-β1 or its activators form a ray of hope for OSMF management.



Flowchart 1: A brief summary of the transforming growth factor-β synthesis, activation and its possible impact on tissue fibrosis in oral submucous fibrosis, TGF-β=Transforming growth factor-β, TSP1=Thrombospondin 1, TIMP-1=Tissue inhibitors of metalloproteinases, MMP-1=Matrix metalloproteinase-1

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