EDITORIAL

Targeted therapy for oral submucous fibrosis - Future strategies

This editorial is with the objective of igniting the research minds of the specialists treating “oral submucous fibrosis (OSMF),” a chronic debilitating and potentially malignant condition of the oral cavity.

Though the etiology of OSMF is multifactorial, the most accepted pathway of pathogenesis is dysregulation of collagen synthesis and degradation pathway(1) similar to many other fibrosing conditions explored in the medical literature. This study sketches some of the successful trials that can possibly help in the successful management of advanced cases.

Possible Therapeutic Interventions for OSMF

Current management of OSMF includes the abstinence of habits, along with some of the possible interventions include:
1. Blocking the chronic inflammatory process by anti-inflammatory or immunomodulatory drugs
2. Blocking transforming growth factor-beta (TGF-β) action by antibodies or peptide mimetics of soluble TGF-β receptors
3. Copper chelators like penicillamine to block lysyl oxidase (LOX) activity and prevent cross-linking and other anti-LOX drugs that prevent its action
4. Collagenase activators like colchicine to promote collagen degradation.

Probably a combination therapy of the above-mentioned drugs intervening at multiple points along the pathway might be successful.

The current research trend to be more focused on antifibrotic or anti-fibrogenic agents such as pirfenidone, interferon (IFN) and certain blood-pressure-lowering medications(2) to suppress the aberrant scarring process seen in other fibrotic diseases such as idiopathic pulmonary fibrosis, radiation-induced scarring, wherein the pathway found to be similar to OSMF.

Pirfenidone (Esbriet, InterMune) is an immunosuppressant that is thought to have anti-inflammatory and antifibrotic effects. It effects by suppressing fibroblast proliferation, reducing the production of fibrosis-associated proteins and cytokines and reducing the response to growth factors such as TGF-β and platelet-derived growth factor. Pirfenidone has a UK marketing authorization for the treatment of mild-to-moderate idiopathic pulmonary fibrosis in adults.(3)

IFN-gamma is an immunoregulatory cytokine that directly prevents fibroblast proliferation and collagen synthesis. The clinical trials using ß-IFN treatment showed improvements in the patients’ mouth opening with a net gain of 8 ± 4 mm (42%) in the interincisal distance and a range of 4-15 mm, need to be confirmed by further studies.(3)

Antihypertensive agents affect the myofibroblasts that produce more angiotensin (ANG) II and active TGF-β which has been described as an ANG/(TGF)-β1 autocrine loop. Antihypertensives like Enalapril, losartan that produce inhibition of ANG II or its receptors have been proved to be promising in lung fibrosis.(2,4)

Biologic agents - Monoclonal antibodies inhibit the cytokines like TGF-β, tumor necrosis factor-alpha (TNF-α), and connective tissue growth factors that activate inflammation. To mention a few, anti-TNF-α antibody infliximab indirectly regulates platelet endothelial adhesion molecule-1 gene expression in two models of in vitro blood cell activation. Infliximab also found to reduce the radiation-induced scarring in the experimental animals.(5)

The researchers have studied expression of Insulin-like growth factor, matrix metalloproteinase, nuclear factor kappa-B, studies of genetic predisposition and chromosome or DNA instability etc., however further studies are needed to confirm these risk factors in OSMF, interventions are yet to be proved.

Now the need of an hour is stepping towards the pathogenesis based treatment strategies as interventional, multiphasic randomized clinical trials that could help in the successful management of well-established cases of OSMF and preventing its malignant transformation.

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