

Oxidative Stress, Nuclear Factor- κ B Pathway and Current Smoking in Graves' Ophthalmopathy

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Dear Sir,

Increased generation of reactive oxygen species (ROS) is thought to play a role in the pathogenesis of Graves' ophthalmopathy (GO) [1, 2]. Selenium (Se) is an antioxidant agent that has been recently shown to improve significantly the course of mild GO [2]. There is good evidence that oxidative stress plays a role in GO: orbital fibroblasts of GO patients have higher contents of malondialdehyde, superoxide anions and hydrogen peroxide than control orbital fibroblasts [3]. Orbital fibroblasts are recognized as the prime target cells of the autoimmune attack in GO [3].

We suggest a possible interplay between nuclear factor- κ B (NF- κ B), pro-inflammatory cytokines (which activate and are activated by NF- κ B, by amplifying and perpetuating orbital inflammation), ROS, Se and glucocorticoids (GC) (fig. 1) in GO [4, 5]. Many of the GC effects are mediated through an inhibition of NF- κ B [6] (fig. 1). GC binding to its receptor may have a dual effect on gene activation such as activation of transcription (transactivation) or a suppression of transcription (transrepression) by interacting with NF- κ B; consequently, the production of anti-inflammatory proteins is increased (transactivation), whereas the inflammatory ones are diminished (transrepression) [7].

In our view, the decreased efficacy of GC therapy in current smokers [8] might be explained – at least in part – by the antagonism GC – ROS revealed at the NF- κ B level [4] (fig. 1). Cigarette smoking is a major source of ROS which are able to stimulate the NF- κ B pathway (fig. 1), a cornerstone of immune and inflammatory response [5].

Future studies (immunosuppressive therapy plus Se) in patients with more severe GO are, at least in part, justified by the following data: (a) GC [6, 7] and Se [9] seem to have a similar inhib-

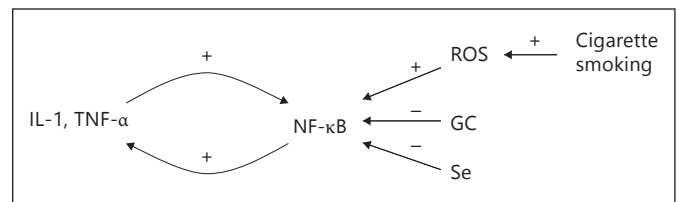


Fig. 1. Positive regulatory loop of pro-inflammatory cytokines (IL-1 = interleukin-1, TNF- α = tumor necrosis factor- α) and NF- κ B regulated by GC, Se and ROS in GO. Cigarette smoking is a major source of ROS.

itory (possibly synergistic) effect on NF- κ B activity (fig. 1), and (b) opposite effects on the NF- κ B pathway of current smoking (stimulatory effect via a prooxidant effect) [5] and Se (inhibitory effect via an antioxidant action) [9] (fig. 1). Therefore, a detailed analysis of the influence of smoking upon any antioxidant therapy in patients with GO would be valuable.

Disclosure Statement

The authors have no conflicts of interest to disclose.

References

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Erratum

In the article 'Side Effects of Anti-Thyroid Drugs and Their Impact on the Choice of Treatment for Thyrotoxicosis in Pregnancy' by Taylor and Vaidya [*Eur Thyroid J* 2012;1:176–185], the sentence in the right column on line 1, p. 179: 'Furthermore, there has been a reported case of aplasia cutis secondary to PTU exposure during pregnancy and choanal atresia [37].' should correctly read: 'Furthermore, there has been a reported case of choanal atresia secondary to PTU exposure during pregnancy [37].'