LETTER

Effect of statins on cancer in chronic obstructive pulmonary disease

We read with interest the article by van Gestel et al reporting a protective effect of statins on cancer mortality in chronic obstructive pulmonary disease (COPD) patients and suggest here a plausible explanation.

Consistent with the literature, the study shows that COPD is associated with an elevated risk of lung cancer. Recently, we reported that COPD is pre-existing in 70% of lung cancer cases compared with 15% in unselected matched smokers. We agree with van Gestel et al that this link is likely to be secondary to a pro-inflammatory disposition resulting from both smoking and genetic susceptibility. In this regard serum interleukin (IL)-6, which is elevated by genetic and smoking effects, has been shown to be inversely correlated with the forced expiratory volume in 1 s in prospective studies. In a murine model, overexpression of IL-6 resulted secondary to a pro-inflammatory disposition. It has been proposed that elevated IL-6 is also associated with epithelial cancers through its growth-promoting effects and the promotion of epithelial–mesenchymal transition (EMT), a well recognised feature of chronic inflammation and a precursor to malignant transformation in the lung. Other cytokines involved in pulmonary inflammation are tumour necrosis factor alpha, IL-1β and IL-8, which, together with growth factors like transforming growth factor beta 1 are implicated in EMT. All of these pathways are mediated via guanosine triphosphatase (GTPase) signalling molecules (Rho, Rac and Ras). There is also growing interest in the role of systemic inflammation, which not only characterises COPD, but may also be relevant in extrapulmonary epithelial cancers (e.g., prostate, breast and colon). These findings might partly explain the increased susceptibility of COPD patients to both lung cancer and extrapulmonary cancers (figure 1).

In a recently published review of statins in COPD, we suggest that the anti-inflammatory effects of statins, through inhibition of GTPases, may explain the protective effect of statin use on lung cancer incidence as reported in three large observational studies (OR 0.45–0.70) and also by van Gestel et al (OR 0.46–0.74). Studies show that statins can directly inhibit EMT through GTPase inhibition and inhibit the effects of IL-6, an effect that has been shown to block tumour progression. We suggest that the anti-inflammatory actions of statins (eg, anti-IL-6 activity) could underlie the protective effects for both lung cancer and extrapulmonary malignancies (figure 1). These observations add considerable weight to existing data that suggest that statins may be very beneficial to patients with COPD.

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Figure 1  Relationship linking chronic obstructive pulmonary disease (COPD), lung cancer, extrapulmonary cancer and inflammation.

Competing interests None to declare.
Provenance and peer review Not commissioned; not externally peer reviewed.
Accepted 11 December 2009

Thorax 2010;65:1. doi:10.1136/thx.2009.131250

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Thorax published online October 26, 2010

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