ECLIPSE\textsuperscript{11} and the NIH funded COPDGene Project. It is not essential to solve the dilemma of whether the term COPD expresses correctly the protean clinical presentations of the same disease or that it combines different clinical entities, but it is necessary to realize that there are needs and research opportunities in an area that is largely unknown. The words “expiratory airflow limitation” expresses our present inaccuracy in differentiating increased airway resistance from increased lung compliance.\textsuperscript{27} HRCT studies have shown that at least two radiological patterns exist in which either airway obstruction or emphysematous destruction predominate. Ogawa and colleagues\textsuperscript{2} have convincingly demonstrated that, regardless of expiratory airflow limitation, the different pathological changes seen in vivo by HRCT are brought by people with different body habits. Let us jump over the hindering barrier of airflow limitation and explore the COPD world beyond!

Competing interests: None.


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Statins for the treatment of asthma: a discovery well, dry hole or just snake oil

Bruce K Rubin

Until the 1906 Food and Drug Act in the USA, it was common for travelling salesman to move from town to town selling miraculous cures in the form of patent medicines. With the widespread promotion of Clark Stanley’s Snake Oil Liniment, the term “snake oil” became a widely accepted derogatory phrase for ineffective patent medications sold with claims for curing an extraordinarily variety of illnesses.\textsuperscript{1} Statins are inhibitors of the 3-hydroxy-3-methylglutaryl coenzymes A (HMG-CoA) reductase. These are among the most widely prescribed medications in the world today. Statins are dramatically effective, treating hyperlipidaemia and preventing cardiovascular disease, particularly in high risk populations.\textsuperscript{2} Statins have also been shown in the laboratory to have impressive immunomodulatory effects.\textsuperscript{3} These drugs suppress T helper (Th)\textsubscript{1} cell development and promote Th2 polarisation from CD4 cells in vitro.\textsuperscript{4} Statins act as direct inhibitors of major histocompatibility antigen (MHC) class 2 expression and interferon \(\gamma\) (IFN\(\gamma\)) and thus inhibit T cell activation.\textsuperscript{5}

In animal models, statins can ameliorate Th1 inflammatory disorders such as collagen induced arthritis and are being considered as a promising therapy for rheumatoid arthritis.\textsuperscript{6} They have also been shown to be effective in models of autoimmune encephalomyelitis,\textsuperscript{7} inflammatory colitis\textsuperscript{8} and even psoriasis.\textsuperscript{9}

There have also been experimental and clinical observations related to the use of statins for the treatment of lung disease. McKay \textit{et al} showed that high dose simvastatin (40 mg/kg) attenuated eosinophil driven inflammation in a murine model of ovalbumin induced asthma. This was mediated, at least in part, by suppressing T lymphocyte secretion of interleukin (IL)\textsubscript{4} and IL\textsubscript{5}.\textsuperscript{10} Samson \textit{et al} showed that fluvastatin decreased peripheral blood mononuclear cell proliferation

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production of IL5 and IFNγ after both allergen specific and non-specific stimulation. However, in contrast with earlier studies, fluvastatin did not decrease MHC2 expression on dendritic cells or lymphocytes.11 More recently, it was reported that in a large matched cohort study, the use of statins was associated with a significantly decreased risk of death from influenza, pneumonia and chronic obstructive pulmonary disease.12

In 2136 pulmonary function measurements performed prospectively in 803 elderly men in the Normative Aging Study, statin use attenuated the normal decline in lung function but the size of the beneficial effect was modified by smoking status.13

In this issue of Thorax, Imamura and colleagues14 report that pravastatin inhibits antigen sensitisation presentation in the lungs of ovalbumin sensitised mice, both when administered simultaneously with ovalbumin sensitisation and after the sensitisation protocol has been completed (see page 44). This appears to be mediated, at least in part, by suppressing IL17 production. Pravastatin also attenuated ovalbumin induced cell proliferation, IL5 production and eosinophilic airway inflammation. On the basis of this, the authors suggest that pravastatin may be a useful therapy for the treatment of asthma. There are a number of caveats that make this interpretation a bit troublesome. The authors acknowledge that experimental ovalbumin induced asthma is very different from human asthma, making it difficult to predict the effects of therapeutic interventions in humans. They acknowledge that the mice were given a large dose of pravastatin (10 mg/kg/day) because 2 mg/kg did not attenuate allergic airway inflammation. Thus the dose administered was more than 30 times that used in humans for the treatment of hyperlipidaemia. In addition, this was a short term study and it is not obvious that the long term use of statins would continue to demonstrate immunomodulation or a non-linear effect on the immune system.

In fact, there have now been two published clinical trials evaluating the use of statins for the therapy of asthma. In a 1 month randomised placebo controlled trial of simvastatin in 16 subjects with asthma who had all anti-inflammatory medication withdrawn, there was no improvement in asthma symptoms, pulmonary function or measures of asthma inflammation, including exhaled nitric oxide, sputum or serum eosinophils, serum C reactive protein and salivary eosinophilic cationic protein, although subjects on the statin did have a significant decrease in serum cholesterol.15 There were similar findings in an 8 week duration randomised clinical trial of 40 mg/day atorvastatin added to inhaled corticosteroids (ICS) compared with ICS alone in 54 adults with allergic asthma.16 The authors of these studies concluded that statins were ineffective for the short term therapy of asthmaic inflammation.

Considering what is practical, we already have extremely effective medications for the treatment of allergic asthma in the form of ICS. For most patients the problem does not appear to be that ICS do not work, but rather that they are often not taken as prescribed.17 It does not appear that adding a statin to an appropriate dose of ICS would provide any additional benefit for patients with asthma.

Thus we are left with exciting data but a nagging dilemma. In the oil exploration industry, a discovery well is drilled as the first oil well in a new field to reveal the potential for an integrated treatment approach. Br J Dermatol. 2008;159(Suppl 2);10–17.

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