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Statins: much more than cholesterol reduction

Lovastatin was the first statin to be approved in 1987 by the US Food and Drug Administration (FDA). Its approval marked a giant leap forward not only in the treatment of hypercholestolemia, but especially in the primary and secondary prevention of atherosclerosis. However, the approval of lovastatin and the fact that the statin market is growing literally by the minute have also initiated a race among pharmaceutical companies to develop the next blockbuster drug. Whilst the first statins were still natural substances, the latest additions to the class were in fact synthetic products. Indeed, lovastatin is a natural product derived from the mold *Aspergillus terreus*, and simvastatin and pravastatin are likewise products of fungal fermentation. Fluvastatin and atorvastatin are synthetic statins, and the latter has been viewed as the most potent in its class for almost 7 years. The approval of rosuvastatin in August 2003 marked the next rung in climbing the ladder towards the strongest statin. However, its approval also triggered a heated debate about the marketing strategy of the drug and the fact that the FDA denied approval of the 80 mg dose [1].

Since 1987, statins have become something like lifestyle drugs, and in May 2004, British authorities even decided to make the 10 mg dose of simvastatin available on an over-the-counter (OTC) basis, *i.e.* without a prescription being necessary [2]. At that time, the UK authorities said that the balance of benefit to risk was "overwhelmingly positive" and that the move should reduce heart disease. This step prompted the *Lancet* to point out that the British public was now being made "guinea pigs in this large-scale OTC experiment" [3], because data on OTC statins for the primary prevention of heart disease are missing, as are data on compliance. Truly, caution in the use of statins is still warranted. Although statins are generally considered safe, rhabdomyolysis may occur as a very rare side effect. Indeed, cerivastatin was withdrawn from the market in 2001 as it was implicated in a total of 52 deaths worldwide [4].

The primary effect of statin use is the lowering of serum cholsterol levels, and each doubling of the dose of a statin is said to decrease serum cholesterol levels by another 7% [5]. However, statins also possess a large number of effects beyond mere cholesterol reduction. These effects are called "pleiotropic effects", and we have only just started to open our eyes in this respect. It is far from clear if all statins share the same pleiotropic effects and which doses are needed to achieve – or to avoid – such effects. Thus, statins have been shown to confer beneficial effects on endothelial function, to stimulate endothelial progenitor cell release, and to possess anti-inflammatory and anti-tumor effects [6]. Moreover, it is becoming increasingly apparent that cholesterol reduction may not be beneficial in some situations. This appears to be particularly true in the setting of chronic heart failure, chronic obstructive pulmonary disease, AIDS, or advanced age [7]. However, statins might still be indicated in these conditions simply for their pleiotropic actions. The reason for this illogical situation may be the cholesterol paradox.

This issue of *Archives of Medical Science* highlights the current knowledge of lipids, dyslipidemia, and statins in a diversity of situations. Whilst Sandek et al. discuss the cholesterol paradox [8], Höfer and Niebauer describe the management of obesity and dyslipidemia in general [9]. Kovesdy and Kalantar-Zadeh make an important point in discussing the roles of lipids in aging and chronic illnesses [10]. Other articles discuss the roles of statins in the metabolic syndrome [11], in the acute coronary syndrome [12], in patients with arterial hypertension [13], in patients with chronic heart failure [14, 15], and in patients subjected to surgical revascularization [16]. We hope that this special issue will help to pave the way for more clinical awareness of the usefulness of statins in daily practice but also for more research into the pleiotropic effects of this auspicious class of drugs.

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