# Hypercholesterolaemia: from inauspicious to appropriate to detrimental

**André Marais,** MBChB, BPharm, MScPharm, ACCP(SA); Clinical Pharmacologist and Senior Lecturer
Department of Pharmacology, University of Pretoria, Pretoria

**Correspondence to:** André Marais, e-mail: andre.marais@up.ac.za

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Hypercholesterolaemia is a chronic disease that affects up to 53% of the global population.[1] Lifestyle modification and early diagnosis plays an important role in the management of this condition. Various cholesterol screening tests are available, and it is generally accepted that a fasting finger-prick cholesterol test administered by the local pharmacist or primary healthcare provider should not exceed a value of 4.9 mmol/l. However, these screening tests measure the amount of total cholesterol (TC), and rarely differentiate between the individual lipoprotein components. Target values for the different cholesterol components have been well established.[2] Although current practice guidelines stipulate that the patient should be in a fasting state for at least six hours before any formal laboratory assessment necessitating a lipogram is performed, a recent cross-sectional study involving 9 319 patients from Denmark showed a very small change in fasting versus non-fasting levels.[3] The difference after three hours of fasting was a decrease in TC of –0.2 mmol/l, low-density lipoprotein (LDL) cholesterol of – 0.1mmol/l and –0.1 mmol/l for high-density (HDL) lipoprotein. There was a decreased level of 0.3 mmol/l in the triglycerides after six hours, thereby justifying the six-hour fasting rule.

A six-hour fasting lipogram can be interpreted as being normal if the values are within the following ranges:

- *TC:* 2.8-4.9 mmol/l
- *Triglycerides:* 0.5-1.6 mmol/l
- *HDL cholesterol:* 1.0-1.6 mmol/l
- *LDL cholesterol:* 1.6-2.9 mmol/l.[2]

However, most South African medical insurance schemes do not consider the lipoprotein levels individually, but rather make use of the Framingham classification scale[4] to allocate benefits to members suffering from hypercholesterolaemia. The Framingham risk score is a gender-specific algorithm which takes factors such as age, smoking status and systolic blood pressure, into consideration, in addition to TC and HDL cholesterol values. Patients are then classified as being at low, moderate, high and very high risk. Frequently, benefits are only approved in high-risk cases where the likelihood of a major cardiovascular event exceeds a 15% probability in a 10- year period. Unless concomitant diseases, such as previous myocardial infarction or diabetes mellitus, are present, the presence of a raised LDL value is not taken into account. This raises serious concerns since it is known that a direct link has been documented between elevated LDL and mortality and morbidity, in relation to cardiovascular disease.[5]

Statins, or 3-hydroxy-3-methylglutaryl-coenzyme reductase inhibitors, are the prescribed drugs of choice in achieving target cholesterol levels, and are responsible for reducing major cardiovascular events (coronary, cerebrovascular and peripheral arterial disease and heart failure) by 25-40%.[2] Statins are the most widely prescribed drug group worldwide and are generally well tolerated, with few side-effects. Untoward class side-effects include muscle pain (myopathy and myalgia), the elevation of liver enzymes, and in rare instances, kidney failure, due to rhabdomyolysis, i.e. muscle breakdown, causing proteins to precipitate in the kidney. It is reported that simvastatin is associated with a slightly higher tendency to cause myalgia (3.4%) than atorvastatin (2.7%).[6]

Non-approved alternative medical treatments include herbal supplements, vitamins and traditional remedies lacking adequate safety and efficacy data, but are freely available in our multicultural society.

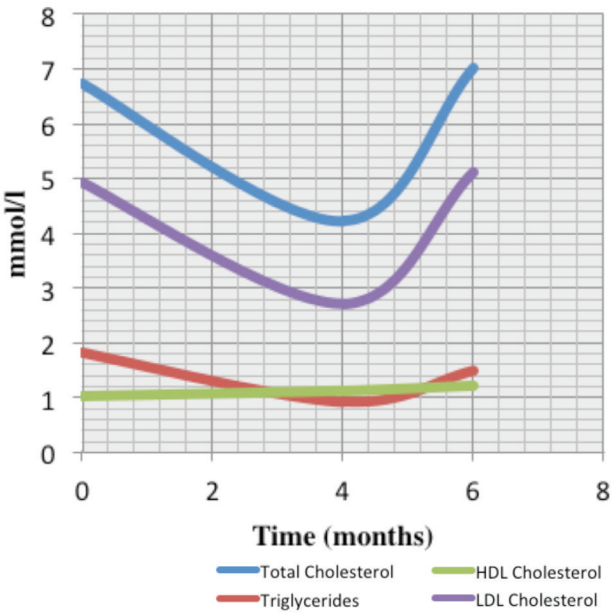
## Case study

A 49-year-old man residing in a middle-class urban area in Pretoria, with a weight of 86 kg and height of 182 cm, presented with an eight-month history of intermittent chest pain (unrelated to stress or physical activity), myalgia, dizziness and general malaise. There was no history of smoking or excessive alcohol use, and he was employed as a manager in the motor industry. He had been on treatment by his general practitioner for hypercholesterolaemia (simvastatin 10 mg) and hypertension (enalapril 20 mg) for the past three years. A positive family history of coronary artery disease and familial hypercholesterolaemia was elicited through the history taking.

**Table I:** Fasting lipogram values on the respective treatments[1]

| Lipopram values | Serum reference ranges (mmol/l) | 16 September 2014 (month 0) | 23 January 2015 (month 4) | 23 March 2015 (month 6) |
|---|---|---|---|---|
| | | Simvastatin | Atorvastatin | "Supplement X" |
| TC | 2.8-4.9 | 6.7 | 4.2 | 7.0 |
| Triglycerides | 0.5-1.6 | 1.8 | 0.9 | 1.5 |
| HDL cholesterol | 1.0-1.6 | 1.0 | 1.1 | 1.2 |
| LDL cholesterol | 1.6-2.9 | 4.9 | 2.7 | 5.1 |
| Framingham risk score | | 15.6% | 11.2% | 15.6% |

TC: total cholesterol, HDL: high-density lipoprotein, LDL: low-density lipoprotein




HDL: high-density lipoprotein, LDL: low-density lipoprotein

**Figure 1:** Change in the patient's cholesterol levels with time

The physical examination revealed severe epigastric tenderness. His blood pressure was within acceptable limits (135/85 mmHg) and a stress electrocardiogram showed no significant changes. The patient was subsequently prescribed a proton-pump inhibitor (lanzoprazole 30 mg). The symptoms, except for the myalgia, soon receded. As part of routine management, he was sent for a lipogram evaluation (Table I). Less-than-favourable cholesterol values were demonstrated on the simvastatin 10 mg management plan. Kidney function and serum creatinine kinase were normal.

It was suggested during the follow-up consultation that the simvastatin 10 mg should be replaced with atorvastatin 20 mg. The patient accepted the change in treatment, and conceded that the treating general practitioner had initially suggested the latter, but according to his medical scheme's core chronic disease list formulary, reimbursement for atorvastatin was not permitted, so it amounted to an out-of-pocket expense. After a four-month period on atorvastatin, a marked improvement was shown in the cholesterol values which were within an acceptable reference range.[2] However, the patient still complained of muscle pain, which was now tolerable. Thus, he was counselled and advised to continue therapy.

During an unscheduled consultation after two months for an unrelated complaint, it was revealed that he had been advised by a pharmacist to discontinue the atorvastatin, and manage the condition with a popular herbal over-the-counter drug ("Supplement X"). The drug claimed to control high cholesterol levels, and to have an excellent safety profile with no side-effects. The treatment team requested a follow-up lipogram (Table I, Figure 1). The patient's TC had increased by 67%, triglycerides by 63%, and LDL cholesterol by 88%. The only benefit seemed to be a slight increase of 8% in the HDL cholesterol. The calculated probability of suffering a major cardiovascular event had increased by 4.4% using the Framingham risk assessment algorithm.

## Discussion

Myalgia is an unavoidable class side-effect experienced by 5-10% of patients on statin therapy,[7] and this should be explained to patients prior to starting therapy. This responsibility should be shared between the prescriber and the pharmacist in order to increase adherence to treatment. Statins show a definite benefit in reducing cardiovascular mortality in patients with hypercholesterolaemia, and should be regarded as a life-saving intervention. Dietary and exercise advice must be discussed at every possible encounter, whether it is with regard to the refill of the prescription or during a full consultation.

Although pharmacies and health shops stock an array of vitamins and herbal products which claim to be beneficial in treating hypercholesterolaemia, there is insufficient evidence to recommend the exclusive use of supplements in patients with dyslipidaemia. It has even been shown that some of these "magic cures" may be harmful to health.[8] Unsubstantiated advertising claims and inadequate enforcement by the regulatory authorities are partly to blame. Prescription medication may not be advertised to the general public in South Africa. However, unscheduled, poorly regulated and mostly unproven supplements feature regularly in the free press.

The General Regulations of the Medicines and Related Substances Act, 101 of 1965 was amended in November 2013, so as to make the regulations applicable to complementary medicine.[9] In addition to the requirement for registration, it is mandatory that the public should be alerted to the fact that unregistered

products have not been evaluated by the Medicines Control Council, and are not intended to diagnose, treat or prevent any disease. Certain warnings, and information on the side-effects and use of a given product during pregnancy, are required. Despite these legal requirements, most complementary medicines remain unregistered and are usually freely available without a prescription.

It must be noted that medical insurance companies often only approve the least expensive drug in a certain class owing to the apparent therapeutic equivalence of the related agent. This does not take into account individual response and the adverse effects of certain drugs. Despite provision being made by the Council for Medical Schemes to motivate for a certain non-formulary drug, the motivational requests hardly ever succeed, resulting in the patient often defaulting on treatment or receiving a substandard intervention.

## Conclusion

Medical ethics dictate and recognise autonomy as a key pillar in patient care, where the patient reserves the right to self-determination and to ultimately choose the treatment, thus justifying this patient's decision to take "Supplement X" in lieu of atorvastatin. However, the issues of beneficence and nonmaleficence on the part of the pharmacist also need to be addressed. Miscommunication and improper advice may have played a role in this serious incident of the patient switching from one treatment to another. Any deviation from the treatment plan should be discussed with the primary physician, and acceptable treatment guidelines adhered to in order to act in the best interests of the patient.

## Conflict of interest

The author declares that there was no conflict of interest, and that financial gain was not received, in the publication of this article.

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