CLINICAL PRACTICE

Phytosterols — a new dietary aid for the treatment of hypercholesterolaemia

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It is estimated that ischaemic heart disease (IHD) will be the leading contributor to the global burden of disease in the future, moving from fifth place in 1990 to first in 2020.[1] Changes in lifestyle such as increased smoking, sedentary occupations, adoption of high-fat, high animal protein diets and increased exposure to stressful urban situations will increase the risk of IHD and stroke.[2-4] It can be accepted that cardiovascular disease, already high among whites, coloureds and Indians, will become a major public health problem among all South Africans in the future.

Hypercholesterolaemia is the main risk factor for both IHD and stroke. It is not surprising that all recent guidelines for prevention and treatment of cardiovascular disease[5-7] emphasise prevention of hypercholesterolaemia through lifestyle modification and treatment with appropriate lipid-modifying drugs in high-risk patients. There is no doubt that the modern statins and fibrates are effective hypocholesterolaemic agents and that they reduce cardiovascular morbidity and mortality. However, the introduction of these drugs should be approached with care, considering the expense, possible side-effects and the necessity for lifetime compliance.[5] Behavioural changes are never easy. The low-fat, high-fibre diet prescribed for prevention and treatment of hypercholesterolaemia is less palatable than the typical Western diet. Consequently, worldwide compliance with this diet has been disappointing.[8]

It seems, therefore, that there is a need for palatable and affordable food products that can effectively and safely lower blood cholesterol levels, reducing risk of IHD and stroke. Such a food, a spread (margarine) with added plant sterols, has been developed in Europe and is now available on the South African market (Pro.active). Plant sterols, β-sitosterol, campesterol and stigmasterol, are structurally related to cholesterol and usual dietary intakes vary from 200 mg to 450 mg / day. In larger quantities, they lower low-density lipoprotein (LDL) cholesterol by inhibiting exogenous (dietary) and endogenous (biliary) cholesterol absorption in the intestine.[9] The questions medical professionals need answered before recommending this margarine, centre around efficacy, safety, target groups and affordability.

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Efficacy

Extensive clinical testing[9-11] involving hundreds of hypercholesterolaemic subjects has shown that in a dose-response manner up to 2 g per day of plant sterols incorporated into food vehicles significantly lowers LDL cholesterol by approximately 10 - 15% without influencing high-density lipoprotein (HDL) cholesterol or triglyceride concentrations. The few studies[12] that showed no effect offered plausible explanations such as giving the sterol in capsules which prevented mixing of the sterol with gut contents and consequent absorption of cholesterol, as well as the type of experimental subjects.[12] There is convincing evidence from randomised clinical trials that plant sterols, when added to a spread or salad dressing, effectively lower total and LDL cholesterol in adult hypercholesterolaemic men and women, independent of their baseline cholesterol levels or background diet.[9-11]

Safety issues and target market

The recommended daily portion of the margarine with added plant sterols provides approximately 10 times more plant

sterols than normally present in the average Western diet. Because of possible detrimental effects, the safety of this spread has been extensively examined in doses of up to 3 g/day for periods of up to 3 years.[13,14] None of these studies found any evidence that sterol hormone functions, reproductive characteristics, gut microflora, short-chain fatty acid production or formation of secondary sterol metabolites were influenced. There is some concern about a reduced absorption of lipid-soluble vitamins and pro-vitamins (α- and β-carotenes and serum lycopenes). Eating more fruit and vegetables should counter this effect.[9] However, there may be some individuals with a genetic defect resulting in abnormally high absorption of these plant sterols — sitosterolaemia should be suspected in a patient who has Achilles tendon as well as cutaneous xanthomata with normal to severe hypercholesterolaemia in an autosomal recessive pattern. It is not known if individuals heterozygous for this condition also absorb higher amounts of phytosterols. It is advised that homozygous individuals should not use products with added phytosterols.[15] It is also advised[15] that the target market for these products should be adult, non-pregnant, non-lactating individuals with raised cholesterol levels or an increased risk of IHD. If the spread is considered for use in hypercholesterolaemic children, lipid-soluble vitamin status should be monitored. Before long-term safety studies have been completed, routine ingestion by the general population to lower IHD risk is not advised.[15] It is recommended that post-marketing surveillance should be established to determine the long-term safety of phytosterol spreads.

Affordability and practical issues

Spreads are used to provide lubrication and taste for the consumption of bread. Butter contains about 4 g of fat per 5 g portion, chiefly as saturated fat. Margarines simulate this fat content but contain plant oils. These may be hydrogenated and converted to trans-isomers when processed to hard margarines and are undesirable. The soft margarines have not undergone these processes and consist mainly of mono- or polyunsaturated fatty acids. The new spread on the South African market contains polyunsaturated fatty acids as well as the plant sterols.

Because of cost and its high water content, the spread should not be used for baking or frying of foods. It can be expected that compliance with such a small change in diet, namely replacing one spread with another, will be better than compliance with more dramatic dietary interventions. It can be concluded from the available evidence that this product can be used to lower total and LDL-cholesterol in hypercholesterolaemic individuals.

The addition of plant sterols to a spread does not change taste, consistency or acceptability of the spread. These products are, however, expensive compared with other spreads, because 2 500 parts of raw material are needed to extract one part of sterol. But compared with hypolipidaemic drug treatment the spread with plant sterols may be cost-effective when at-risk subjects need to lower plasma cholesterol concentration. Together with a strict lipid-lowering diet, the plant sterol spread may achieve target concentrations in a significant number of subjects with moderate hypercholesterolaemia. In severe hypercholesterolaemia, the LDLcholesterol-lowering power of the statin drugs is superior, but the combination of a statin and the spread with added plant sterols displays an additive effect.[9] Where a statin dose has to be doubled to achieve a LDLcholesterol target concentration, it may therefore be cost-effective to use the combination of the statin and the plant sterol-containing spread.

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