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Dietary interventions to control dyslipidemias and cardiovascular risk

Intervenciones dietéticas para controlar las dislipidemias y el riesgo cardiovascular

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INTRODUCTION

Nutritional interventions for the prevention and control of dyslipidemia and in turn of cardiovascular risk have varied greatly over the last decade. Currently, it is suggested to follow an eating pattern of diets containing specific percentages of macronutrients. Guidance focused on specific dietary patterns is more likely to improve meals quality and promote cardiovascular health. Eating patterns can be defined as the combination of foods and beverages that a person consumes, adaptable to subject's characteristics, allowing the incorporation of foods usually consumed, and considering traditions, culture, and economic possibilities. They need to contain macronutrients, as carbohydrates, proteins, and lipids, as well as micronutrients like vitamins, minerals, and polyphenols. These regimes also must consider the water contained in food groups: fruits, vegetables, grains and seeds, meats, dairy products, fats, and oils. A healthy eating pattern must limit the ingestion of saturated fats (less than 10% of total energy), unsaturated fatty acids of the trans subtype, (that are proinflammatory and proatherogenic), as well as added sugars and sodium.[1]

Examples of eating patterns are the Mediterranean, vegetarian, Dash, and cornfield diet, among others.

WHAT TO EAT TO CONTROL HYPERCHOLESTEROLEMIA?

It is known that approximately 80% of circulating cholesterol in plasma is determined by the human genotype, age, gender, and physiological or pathological states. The remaining 20% is determined by the dietary ingestion of cholesterol and saturated fat.

Among the components of the diet that can help to control plasma lipids concentrations are phytosterols, sterols of plant origin whose chemical structure is very similar to that of cholesterol, and phytostanols (fully hydrogenated, saturated phytosterols). They are found in fruits, seeds, leaves and stems of practically all vegetables. Although more than 25 different compounds constitute this group, three of them are found in the highest proportion in foods: α-sistosterol, campesterol and stigmasterol, that together account for 95-98% of all identified phytosterols.

A consumption of 1.5 to 4 grams/day of phytosterols and phytostanols is recommended, which on average will reduce cholesterol by 10%.[2]

Based on their physicochemical characteristics, they are known to act as cholesterol-lowering agents because they lead to:

a) A decrease absorption of cholesterol by competition in two fronts. Firstly, as these

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compounds are more lipophilic, they limit the incorporation of cholesterol in the mixed micelle formed by the action of phospholipids and bile salts in the intestinal lumen. In this way, phytosterols take the place of cholesterol, and the non-emulsified cholesterol (displaced from the micelle) cannot be absorbed and is eliminated in the feces in the form of neutral sterols. Secondly, the only entrance way of all type of sterols through the brush border enterocyte membrane is a protein named Nieman-Pick C1L1. Both cholesterol and phytosterols and phytostanols compete for this single input, so the higher the amount of dietary plant sterols, the less cholesterol absorption.[3,4]

b) A reduction of cholesterol esterification in the enterocytes by inhibiting the activity of the enzyme acyl-Co-A-cholesterol-acyltransferase (ACAT). In this process the cholesterol is not re-esterified and as well, it is not incorporated into the chylomicrons, thus stimulating the flow towards the intestinal lumen of unesterified cholesterol.

c) Stimulating the efflux of cholesterol from the enterocytes into the intestinal lumen by increasing the activity and expression of the ABC-type transporters (ABCG5 and ABCG8, mainly), that are membrane proteins specialized in expelling metabolites from the cell.[4,5]

Dairy fats are generally rich in saturated fatty acids and are also high in monounsaturated fatty acids (MUFAs). The latter contrary to the former, decrease plasma cholesterol levels, stimulating the number of low-density lipoproteins (LDL) liver receptors.[6] Additionally, milk fats contain other biologically active lipids, including conjugated linoleic acid and low levels of long-chain n-3 polyunsaturated fatty acids (PUFAs) that have the potential to mitigate coronary heart disease risk factors. Also, dairy products are rich in calcium. Two meta-analyzes have reported an inverse relationship between higher calcium intake and reduced blood pressure.[7]

The consumption of eggs provides great nutritional value due to its richness in minerals (selenium, phosphorus, iodine, and zinc) and vitamins (A, D, B2, B12, pantothenic acid, and niacin). Eggs are rich in proteins of high biological value, its composition includes ovalbumin, the nutrient choline involved in the formation of cell membranes and highly bioactive carotenoids, such as lutein and its isomer zeaxanthin, important for the structure and function of the retina.[8]

In healthy people, the consumption of one egg per day can be salutary without increasing the risk of coronary heart disease or stroke. In patients with dyslipidemia, diabetes or high-risk of atherosclerotic cardiovascular diseases (ASCVD), it is advisable to be more cautious, limiting but not prohibiting the ingestion of cholesterol-rich foods, such as eggs and shellfish.[9]

On the other hand, there is a positive relationship between the consumption of red and processed meat with the risk of ASCVD, not only related to their content in cholesterol, saturated fat, trans-fatty acids, sodium, nitrites, and nitrates, but also to the possibility of conversion of meat choline or carnitine into trimethylamine (TMA) by intestinal bacteria of the genus Prevotella, which in the liver can be converted into trimethylamine N-oxide (TMAO). This compound blocks the synthesis of bile acids, reduces the reverse transport of cholesterol, facilitates the cellular influx of lipids, increasing its *in situ* synthesis, and suppressing their elimination, thus causing lipid accumulation and in consequence the increase of lipid-laden macrophages, what gives rise to the formation of foam cells; events that initiate the atherosclerosis process.[10]

The importance of eating vegetables is based in several facts, one of them is their richness in inorganic nitrates (spinach, lettuce, arugulas, beets, chard, etc.) that during chewing, thanks to oral bacteria, are converted in nitrites. Although nitrites in contact with acid content of the stomach form a variety of nitrogenous compounds, including nitric oxide (NO), that some authors have related to gastric cancerogenesis, the abundant amount of nitrates/nitrites swallowed with saliva is absorbed int the intestine and transported in the blood, being converted in some tissues in NO, which is, in general is a benefic molecule, with vasorelaxation, anti-inflammatory, antioxidant, antithrombogenic and, in some cells, antiapoptotic effects, among

many others.[11] So, although in the past, nitrate/nitrites were seen as inert by-products of the NO metabolism, now there are considered another source of the production of this gas.

The consumption of whole grains is recommended, while refined ones is not, particularly those subjects to ultra-processing. All type of fruits should be consumed, particularly those containing pectin such as peaches, apricots, hawthorn, apples, grapes, strawberries or oranges, lemons, grapefruits, and tangerines. However, the ingestion of juices is not recommended.

The consumption of legumes at least 3 times a week must be a priority due to their fiber content. A consumption of 20-30 grams of total fiber per day has shown to reduce cardiovascular risk 12 to 20%. On this regard, the consumption of fruit fiber (pectin) is associated with a 30% reduction in the risk of coronary heart disease.[12] The action of fibers in the digestive system determines their benefit for the control of dyslipidemias. In the stomach, soluble fiber (such as inulin, pectin, gums, and fructo-oligosaccharides) causes a reduction in gastric emptying, an increase in abdominal distention, helps to have a normal and balanced microbiota, and causes a greater feeling of satiety, useful in weight control. At the level of the small intestine, the absorption of cholesterol, saturated fats, and glucose decreases. There is also a reduction of bile acids reabsorption what leads in turn to the lessening of cholesterol levels, since the liver express more LDL receptors to keep the production of bile acids, whose basic structure comes from cholesterol. At the colon level, soluble fiber undergoes bacterial fermentation, which produces an increase of beneficial short-chain fatty acids (SCFA) with important effects on glucose and lipid metabolism. On the other hand, the insoluble fiber (cellulose, hemicellulose, lignin, and resistant to digestion starch) in the large intestine, causes a reduction in the contact time of carcinogens with the walls of the intestine. There is a significant increase in bacterial fermentation and production of SCFA, particularly of propionate, which once absorbed into the portal circulation reaches the liver and inhibits the enzyme HMG-Co-A reductase, key enzyme that control the endogenous synthesis of cholesterol.

For cardiovascular health, the consumption of cold-water fishes, such as salmon, mackerel, tuna, and anchovies is highly recommended for its content of omega 3 fatty acids (FFA): eicosapentaenoic acid (EPA) and docosahexaenoic (DHA). It was recommended to reduce cardiovascular risk, provide daily 250 to 500 milligrams of omega 3 FFA.[13] Although anti-inflammatory, antithrombotic, antiarrhythmic effects, and the triglyceride reduction of omega-3 FFA have been proved, clinically, their capacity to reduce cardiovascular risk had been controversial. However, a Japanese study on EPA showed a 19% reduction in cardiovascular death, myocardial infarction, that was associated to an increase in HDL-C levels and a concomitant reduction in TG.[14] Icosapent, a free FFA form of EPA, reduced 25% the relative risk of an endpoint composed by cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina in high-risk hypertriglyceridemic patients.[15] Recently a huge metanalysis comprising 40 clinical studies and 135,267 patients, showed a dose related reduction of coronary heart disease events with EPA and DDH.[16]

The best oils and fat for cardiovascular health are those provided by nature such as avocado, oilseeds, and extra virgin olive oil.

Antioxidants. A dietary antioxidant is a substance that is part of certain foods that can prevent the adverse effects of oxygen and nitrogen reactive species on the normal physiological functions of our body. In recent years it has been shown that a diet rich in polyphenols improves health and reduces the incidence of cardiovascular diseases. Especially, those compounds named flavonoids, that are natural pigments present in vegetables. Many polyphenols, among several beneficial effects protect against the damage caused by oxidizing agents. As the human body cannot synthesize these protective chemicals, they must be obtained through food. In the regard, some of their actions are the synthesis/release of endothelial NO, the regulation of the production of reactive oxygen species substances, the prevention of LDL oxidation and cytotoxicity, and the inhibition

of platelet aggregation, among many others: Among the more than 8,000 polyphenols found in vegetables, the most remarkable are catechins, epicatechins, quercetin, and procyanidins, many of them found in products like green tea, blueberries, red onion, apple, and cacao.[17,18] It is necessary to add that aside from their antioxidant action, some of these polyphenols, such as epicatechin from cacao, have marked actions on glucose and lipid metabolism, endothelial function, blood pressure, myocardial infarction, neuroprotection, fatty liver, and striate muscle function, among many others.[19]

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