

Management of Dyslipidemia in the Elderly

INTRODUCTION

The treatment of hyperlipidemia is a relatively new concept in medical therapeutics. A relationship between serum cholesterol and the risk of cardiovascular disease has been firmly established in the early 1960's, but only in 1984 the LRC-CPPT trial (1) was the first to confirm the "cholesterol hypothesis", that is that lowering of serum cholesterol results in a reduction in cardiovascular morbidity. In the past 25 years multiple clinical trials have documented the cardiovascular benefit of treatment of hyperlipidemia. Drugs used are usually referred to as "lipid lowering "rugs although their mechanism of action might not be limited to a decrease in the number of atherogenic lipoprotein particles. In spite of the successful use of these drugs, treatment of hyperlipidemia in the "elderly", irrespective of the definition of this group, has remained the subject of controversy. In this chapter we present the evidence of the benefit and risk of lipid lowering in the older age group.

Characteristics of the Aging Process Relevant to Lipid Intervention

The US population is aging. In the last 100 years the life expectancy has increased by 30 years. In 2004, 12.4% of US population was in the Medicare age group and this percent is expected to increase progressively in the future (2). In this segment of the population, cardiovascular disease is by far the main cause of mortality in both men and women. This justifies cardiovascular prevention as a subject of academic research and policy debate. Lipid pharmacological intervention is one of the most successful cardiovascular preventative interventions. Concerns about its safety and efficacy in this age group have led different countries to adopt different strategies concerning the use of lipid lowering drugs in the elderly. This is based on physiologic, socio-economic and ethical considerations.

Physiologic characteristics of aging:

Atherosclerosis is a continuous process and its burden increases progressively with age. The pathology includes continuous remodeling of the vascular wall and in final stage, occurrence of calcification. Although lipid lowering is statistically successful, its success might depend on the pathology of the arterial wall. The current belief is that the main mechanism of action of lipid lowering drugs is the stabilization of atherosclerotic plaques. A study using intravascular ultrasound has documented that in young survivors of myocardial infarction the culprit vessel is undergoing constrictive remodeling, usually associated with plaque erosion, while in older subjects expansive remodeling predominates (3). Expansive vascular remodeling results in increased irreversible arterial stiffness, particularly in calcified vessels and in fibrotic plaques (4). This in turn decreases the likelihood for a cardiovascular event to be attributable to a ruptured plaque and increases the likelihood of it being related to increased arterial stiffness. It is conceivable that in presence of advanced atherosclerosis, lipid intervention might be less



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successful. On the other hand, the safety of using lipid lowering drugs is diminished in the older age group. The CYP-450 enzyme system and the esterases responsible for drug metabolism may become dysfunctional in the older age group. The kidney function decreases linearly with age further diminishing the excretion of active drugs and their metabolites. All these factors contribute to a modification of the risk/benefit ratio of preventative interventions. In addition, aging increases the number of co-morbidities requiring pharmacologic intervention and this in turn results in polypharmacy. This further decreases the safety of lipid lowering drugs.

Socio-economic characteristics of aging:

The average household net worth increases progressively with age up to age 64, and then it declines slightly (5). In spite of this, almost 10% of people in this age group live in poverty. Gender and ethnicity are important factors since the percent of women living in poverty is double that of men, Asians and Hispanics are twice as likely to live in poverty as Non-Hispanic Whites and African-American three times more likely. The average household net worth is five times lower in Blacks than in Whites. Social isolation is an additional risk factor characteristic for this age group since a third of the women aged between 65 and 74 and half of the women 75 years or older are living alone. In couples, disability of one of the spouses places the other one in the situation of caregiver. This results in an increase in cardiovascular risk for the healthier of the two. The problems are frequently compounded by the occurrence of cognitive impairment affecting understanding of the concept of preventive health care. All these factors contribute to limitations in access to health care and therapeutic modalities.

Ethical considerations in the very old:

There are ethical problems, which need to be addressed when selecting a preventative management program in the elderly. The main question is addressing the value of life versus that of the quality of life. There is a paucity of data concerning the wishes and fears of subjects in this age group. At what point in time is cardiovascular prevention no longer valuable? What is the worst fear of patients in this group, death or disability? If the fear of physical disability prevails, is it the fear of physical disability or of cognitive impairment? At the society level, this is compounded by the cost to society of prolonging a life of doubtful quality to the bearer. All these considerations affect the decisions to treat patients in the older age group with lipid lowering drugs.

LIPOPROTEINS & AGING

Biochemistry and Metabolism of Lipoproteins

Lipoproteins are large particles with a hydrophilic surface and a hydrophobic core. The structure of the surface consists of protein referred to as apolipoproteins and phospholipids. The core contains free and esterified cholesterol and triglycerides. The apolipoproteins are responsible for the binding of the lipoproteins to receptors and enzymes and therefore direct lipoprotein metabolism. Table 1 shows the lipoprotein classes:



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Table 1: Lipoprotein classesLipoproteinDensity (g/mL)

Major Lipid Component Major Apolipoproteins

Chylomicrons