Research Article

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Hyperlipidemia as a Predictive Risk Factor for Cardiovascular disease and Stroke

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ABSTRACT

Background: *Cardiovascular diseases and stroke are becoming the main challenge in the healthcare field, and this has required the study of their risk factors.*

Aim: *The aim of this study is to assess the hyperlipidaemia as a risk factor for cardiovascular diseases and stroke.*

Method: *Published clinical trials of hyperlipidemia studies were recognized by a search of EMBASE and MEDLINE databases with keywords hyperlipidemia, stroke or cardiovascular disease, or prospective study, and meta-analysis.*

Results: *Cardiovascular and stroke prevention begin with recognizing their risk factors, many randomized trials of statins have revealed a decrease in the chance of cardiovascular diseases and stroke linked to the decrease in the lipid intensity.*

Conclusion: *after the summarized of all the studies stated in this review, it can be recognized that hyperlipidemia is a significant risk factor for cardiovascular diseases and stroke and correlated in patients with atherosclerosis.*

Keywords

Hyperlipidemia, Stroke, Risk factors, Lifestyle.

Introduction

Three decades ago lipids had obtained more importance in the health care field, reflected by the huge amount of publications in the medical literature. Lipids show an important role in human physiology and increase lipids have been presented to be cardiovascular diseases and stroke risk factor [1,2].

Globally, cardiovascular disease is the leading cause of death [3,4]. Coronary heart disease (CHD) is the most common type of heart disease, killing over 370,000 people annually [5]. Moreover, stroke is the second leading cause of death above the age of 60 years, and the fifth leading cause of death in people aged 15 to 59 years old. Also, every year, 15 million people worldwide suffer a stroke. Nearly six million dies and another five million are left permanently disabled. Stroke is the second leading cause of disability, after dementia. Disability may include loss of vision and/or speech, paralysis and confusion [6].

Atherosclerosis is a key pathomorphological method that narrows the arterial walls across the body and within the brain, leading to cerebrovascular disease. It is believed that atherosclerosis arises from chronic inflammation and damage to the arterial wall within the peripheral or coronary vascular system. As a reaction to endothelial inflammation and damage, oxidised lipids from LDL (low-density lipoproteins) particles gather in the endothelial region of the vessel wall [7]. The oxidation of these particles may be brought about by angiotensin II. Monocyte then infiltrates the arterial wall and differentiates into macrophages, which accumulate oxidised lipids to form foam cells. After their creation, foam cells

encourage spread of macrophage and drawing of T-lymphocytes. These T-lymphocytes consequently bring about smooth muscle propagation within the arterial walls and build-up of collagen. This process results in the creation of a lipid dense atherosclerotic lesion with a fibrous cap.

Cerebrovascular diseases adhere to risk factors that are non-modifiable for sex-based orientation, age, race or ethnic groups, and genotype prior to the myocardial infarction, to the stroke and or TIA, in addition to modifiable risk factors such as diabetes, hypertension and hyperlipidemia [8]. There are also coronary artery diseases along with physical immobility, consumption of alcoholic beverages, cigarette smoking and obesity.

Aim

The purpose of this review article is to assess the hyperlipidaemia as a risk factor that is linked with cardiovascular disease and stroke. Having recognized this risk factor, the study assesses how the hyperlipidaemia has been handled earlier and what can be done in the future.

Moreover, this study purposes to recognize the main problems that have directed to increased cardiovascular and stroke risk. This can assist in recommending how to deal with the illness.

Method

Design and Strategy

Published clinical trials studies of hyperlipidemia risk factor for cardiovascular diseases and stroke were recognized by a search of EMBASE and MEDLINE databases with keywords hyperlipidemia, stroke, cardiovascular disease and meta-analysis.

Included are clinical trials involved patients with stroke risk factors (hyperlipidaemia), Date of birth or age, gender, blood pressure, blood sugar and lipid profile documented at baseline. Randomized controlled trials of stroke risk factors published between 1948 and 2016 were eligible for inclusion. Random studies distribution of participants to a stroke risk factors lowering drug or placebo; random distribution of participants to different stroke risk factors lowering drugs; and random distribution of participants to different blood stroke risk factors lowering targets were eligible. To decrease the risk of small-study effects [9], all studies were needed to have at least 1000 patient-years of follow-up in each study group. Studies were involved if they were published or information were reachable from 1990 to 2016, and if they provided information on inclusion criteria, regions and number of randomization method, trial endpoints, duration of follow-up, trial interventions and methods of analyses. Results were independently extracted and summarized. Nevertheless, no further analyses were directed.

Ethical considerations

The references used in the research are well cited and referenced to avoid plagiarism. The sources are paraphrased to ensure that the research is not just a duplicate of the previous research. There are also no incidences where personal ideas that may be biased are included in the research as for facts.

Hyperlipidaemia

Numerous huge randomized trials of statins have revealed a decrease in the chance of cardiovascular diseases and stroke linked to the decrease in the lipid intensity. The experimental research has failed to discover a reliable connection amongst the cholesterol intensity and chance of stroke and cardiovascular diseases. The valuable impacts of statins on the decrease of chance of stroke may be facilitated by further operations like enhancement in endothelial function (supervision of the performance of the heart, blood pressure, and hyperglycemia), antioxidant properties, and reserve of provocative reactions, immunomodulatory activities, and steadiness of atherosclerotic lesions, while assessing the pathomorphological procedures of atherosclerosis. Even though the medication utilized and the frequency is known to differ with every case, but the outcomes are steady, revealing the chance of stroke to decrease from 10-50%. Most of the research involved individuals suffering from a coronary heart condition, so it was undecided if the advantages of a decrease in the chance of stroke were because of the decrease in myocardial infarction and cardiac death.

The effectiveness of simvastatin in individuals suffering from coronary artery conditions, similar occlusive illness and low-density lipoprotein (LDL) levels of cholesterol more than 3.5mmol/L was examined through the Heart Protection Study to diminish the vascular happenings [10]. In the individuals that were given the medication based on simvastatin, in contrast to the people remedied with placebo were witnessed to have a 24% decrease in the intensity of mortality, severe and non-serious vascular conditions. It was also witnessed that the patients underwent a decrease of 25% in the chance of stroke and a 30% decrease in the chance of ischemic stroke. In the individuals subjected to the medication based on simvastatin, the brief ischemic spells were notably lesser than the individuals subjected to placebo based medication (2% against 2.4%). In this experiment, there was no specific arrangement of previous medical conditions, causing the explanation of the impact of the simvastatin based medication within the individuals to be unreliable, due to the individuals with a record of cerebrovascular disease without coronary heart conditions. In this category of patients, a main vascular condition of 21% relative risk reduction (RRR) was observed, but there was no record of the influence of simvastatin on the reappearance of stroke [10].

A lot of research has been carried out on decreasing of lipid and coronary vascular disease prevention over the last ten years. One of these meta-analyses included all studies carried out on the topic from 1966 to 2001 which varied from testing statins, fibrates, resins, niacin to surgical interventions and diet. An analytical study of ten primary and twenty-eight secondary prevention trials showed relative risk reduction (RRR) of stroke up to 17%. No major diversity was observed in different trials whether they included intervention tested (primary versus secondary prevention) or the ones concerned with chemicals, which lower lipid levels. A substantial 24% RRR of stroke is observed in studies related to statins use. In an analysis based on intervention type, stroke

incidence is only limited to secondary prevention that too with 26% RRR of stroke [11]. No effect on the prevalence of ischemic strokes and hemorrhagic stroke was observed about lipid-lowering therapy. A strong correlation between the pathogenesis of stroke and the degree of cholesterol reduction, baseline cholesterol level and final cholesterol level has been found 6 mmol/L is determined as the marker of the risk factor of stroke risk.

Anglo Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm (ASCOT-LLA): According to a study reduction in cholesterol concentrations reduces the risk of cardiovascular disease even in high-risk patients [12]. The advantages of lowering cholesterol are studied about prevention of coronary heart disease (CHD) in patients suffering from hypertension even if they are not dyslipidemic. An additional atorvastatin 10 mg or placebo therapy is given to 10 305 patients with non-fasting total cholesterol concentrations ≤ 6•5 mmol/L. Over a year, the total serum cholesterol level was reduced by approximately 1.3 mmol/L in patients getting atorvastatin about the placebo group. Three years of follow-up further lowered it by 1.1 mmol/L in the test group. Substantial reductions in major cardiovascular events were observed with use of atorvastatin [12].

4444 patients with coronary heart disease were selected for a randomised trial of cholesterol lowering known as 4S (Scandinavian Simvastatin Survival Study). This study lasted over the span of 5.4 years and 4444 patients with angina pectoris or other cardiac event having serum cholesterol 5.5-8.0 mmol/L with lipid-lowering diet plan assigned. 4S is regarded as a breakthrough in cardiology, and evidence-based medicine as the therapeutic effect of statins effected the incidence of cardiac events in patients with coronary heart disease. During six years of follow-upperiod 24%, RRR of stroke was noticed [13]. The Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID): 9014 patients were randomised in a double-blind trial where analyzed the impacts of pravastatin (40 mg daily) in comparison with those of a placebo over a mean follow-up period of 6 years; Pravastatin shows 19% RRR of stroke [14,15].

The Cholesterol and Recurrent Events (CARE) Study: 4159 participants having average total cholesterol levels 209 mg/dL and LDL serum cholesterol levels 139 mg/dL who have suffered from myocardial infarction at average ten months' earlier entry of the study is randomized for pravastatin 40 mg/d or placebo. A well-defined criterion was used for assessment over a 5-year follow-up period was used mainly focusing on a pre-specified secondary end, and transient ischemic attack (TIA). 32% decrease (95% CI, 4% to 52%, P50.03) was observed in all-cause stroke while up to 27% reduction in stroke (95% CI, 4% to 44%, P50.02) was also observed [16].

Stroke Prevention by Aggressive Reduction in Cholesterol Levels Study (SPARCL): It is first of its kind study in which patients without concomitant coronary disease were assessed. In this study patients with recent TIA or stroke (within six months of enrollment) were given 80 mg of Atorvastatin/day and the results were compared with the placebo group. A 2.2% absolute risk reduction in stroke rates was evaluated (adjusted HR 0.84; 95% CI 0.71 to 0.99), this is consequent to reduction in LDL cholesterol levels up to 53% (P<0.001). However, the incidence of hemorrhagic strokes was greater in the atorvastatin group (55) in comparison to the placebo group (33); the difference in the occurrence of fatal hemorrhagic stroke was somewhat same between both groups. The beneficial effects of the use of statins in an ischemic stroke were highlighted in this study [17,18].

Rendering to Northern Manhattan Study (NOMAS), there was lower of 90 days' death ratio observed in patients who are taking a statin in comparison to those patients who are not taking during stroke such as 1.8 percent versus 10.6 percent p = 0.03. An associated study proposes that stroke severity is trimmed down and the likelihood of better result after thrombolysis application are anticipated if a patient does use of low lipid agents. An underprivileged neurological result at 90 days relates to the withdrawal of statin treatment of an intense ischemic stroke. There was then 21 percent RRR for stroke in patients utilizing statins (OR 0.79 and 95 percent CI: 0.73 up to 0.85), the decreasing ratios of deadly strokes is not generous like 9 percent (OR 0.91; 0.76 up to 1.10) and hemorrhagic stroke remains not in substantial factor. With every 10% reduction in LDL-Cholesterol levels of all stroke, risks are also reduced by 15.6% (95% CI: 6.7–23.6%) in patients taking statins [19,20].

According to Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT), the results of this clinical trial presented that decreasing total cholesterol by dropping LDL-C levels can reduce the occurrence of CHD mortality and morbidity in males at high risk for CHD since of elevated LDL-C levels. This randomized, double-blind study affords solid indication for a fundamental role of these lipids in the CHD pathogenesis [21].

Hence, five randomized trials of avoiding pravastatin 40mg/day and Aspirin (73,900 patient based years of perception) were incorporated in one meta-analysis considering the added substance impact of Aspirin and pravastatin. Henceforth, 39 percent reduction in such risks of ischemic stroke was seen in patients being treated with pravastatin and Aspirin in gaps with fake treatment. Better results were accomplished with the utilization of pravastatin and Aspirin in the mixture than headache medicine and pravastatin alone (RRR 29 percent as well as RRR 31 percent, independently) [22]. Aside, statins are prescribed for Stroke avoidance, <5.0 mm/L is the objective aggregate cholesterol level. The scope of LDL level shifts from patient to tolerant contingent upon the assessed hazard, i.e., <2, 59 mmol/L for patients with symptomatic atherosclerotic illness as well as less than 1, 81 mmol/L for those at higher risks. Patients with set up cardiovascular disease and greater amount of significant risk factors ineffectively controlled the risk variables (smoking), as well as the metabolic disorder ('triglycerides >2, 26 mmol/L with HDL cholesterol <1, 03 mmol/L'), coronary artery disorders are known to be of higher risks.

Indeed, the HDL levels should likewise be practically confirmed. An opposite reverse relationship between 'serum HDL' cholesterol

and stroke has been set up in studies in large cohorts. Thus, the elevated amounts of HDL cholesterol have been perceived to have an 'anti-atherosclerotic' as well as 'anti-inflammatory' effects in the studies of humans and animals before reducing chances of having stroke 'OR 0.8, 95 percent of CI 0.6 up to 1'. Several scholars and researchers did contemplate on the option found on niacin and fibrates within a patient/s with HDL of around <1.03 mmol/L as an added treatment [23].

Conclusion

After the summarized of all the studies stated in this review, it can be recognized that hyperlipidemia is a significant risk factor for cardiovascular diseases and stroke and associated with atherosclerosis patients. Also, the importance of prevention and monitoring this risk factor is emphasized in this study. The hyperlipidaemia can be reduced if individuals follow healthy lifestyles and involve in simple daily exercise. This also can decrease blood pressure level.

Author, year	Name of the Study	Participant	Number of risk factors	Findings
Heart Protection Study Collaborative Group, 2002	Heart Protection Study	20536 Age 40-80 years	Those without diagnosed coronary disease who had cerebrovascular disease, or had peripheral artery disease, or had diabetes; men and, separately, women; those aged either under or over 70 years at entry.	Allocation to 40 mg simvastatin daily reduced the rates of myocardial infarction, of stroke, and of revascularization by about one-quarter.
Sever et al., 2003	Anglo Scandinavian Cardiac Outcomes Trial Lipid Lowering Arm (ASCOT-LLA) Double-blind placebo-controlled trial	19342 hypertensive patients (aged 40-79 years	All coronary events, all cardiovascular events, fatal and non-fatal stroke, development of chronic stable angina, heart failure, and peripheral arterial disease.	The reductions in major cardiovascular events with atorvastatin are large, given the short follow-up time.
Scandinavian Simvastatin Survival Study Group, 1994	Scandinavian Simvastatin Survival Study (4S) Randomised double-blind trial	4444 patients	Effect of cholesterol lowering with simvastatin on mortality and morbidity in patients with coronary heart disease (CHD).	Long-term treatment with simvastatin is safe and improves survival in CHD patients.
Tonkin, Simes, Sharpe, & Thomson, 1998	The Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID) Randomized double-blind trial	9014 patients who were 31 to 75 years of age	The patients had a history of myocardial infarction or hospitalization for unstable angina and initial plasma total cholesterol levels of 155 to 271 mg per deciliter. Compared the effects of pravastatin (40 mg daily) with those of a placebo.	Pravastatin therapy reduced mortality from coronary heart disease and overall mortality, as compared with the rates in the placebo group, as well as the incidence of all pre-specified cardiovascular events in patients with a history of myocardial infarction or unstable angina who had a broad range of initial cholesterol levels.
Sacks et al., 1996	The Cholesterol and Recurrent Events (CARE) trial	4159 men and women aged 21 to 75 enrolled 80 centers in the US and Canada	Secondary prevention of CHD 3 to 20 months post-MI Total-C < 240; LDL-C between 115 and 174; Triglycerides < 350 mg/dL 5 years Treatment with Pravastatin 40 mg vs. placebo	The benefit of cholesterol-lowering therapy extends to most patients with coronary disease who have average cholesterol levels
SPARCL Investigators, 2006.	Stroke Prevention by Aggressive Reduction in Cholesterol Levels Study (SPARCL)	4,731,40% female Mean age 63 years	For subjects randomized to atorvastatin 80 mg/d or placebo stroke or TIA without known coronary heart disease	Atorvastatin 80 mg/d is similarly efficacious in preventing strokes and other cardiovascular events, irrespective of baseline ischemic stroke subtype.
Mitchell Elkind et al., 1990	Northern Manhattan Study (NOMAS)	Over 4,400 people from the community were enrolled	Stroke and stroke risk factors in the Northern Manhattan community in whites, blacks, and Hispanics living in the same community. a population-based incidence and case-control study.	The study has already made great advances in the understanding, prevention, and treatment of stroke. Caribbean Hispanics from the Northern Manhattan community had strokes at a younger age than blacks and whites. There was also a higher rate of stroke-related death in Caribbean Hispanic and black patients than in white patients.
Blackburn, Keys, Simonson, et al. 1984	Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT) a multicenter, randomized, double-blind study	3,806 asymptomatic middle-aged men were enrolled with primary hypercholesterolemia	Tested the efficacy of cholesterol lowering in reducing risk of coronary heart disease (CHD)	Reducing total cholesterol by lowering LDL-C levels can diminish the incidence of CHD morbidity and mortality in men at high risk for CHD because of raised LDL-C levels.

Hennekens, Sacks, Tonkin, et al., 2004	Additive Benefits of Pravastatin and Aspirin to Decrease Risks of Cardiovascular Disease Randomized and Observational Comparisons of Secondary Prevention Trials and Their Meta-analyses	73 900 patient-years of observation	Secondary prevention with pravastatin sodium and aspirin (40 mg/d) decrease cardiovascular disease risks	More widespread and appropriate combined use of statins and aspirin in secondary prevention of cardiovascular disease will avoid large numbers of premature deaths.
Prospective Studies Collaboration, 1995	Cholesterol, diastolic blood pressure, and stroke: 13 000 strokes in 450 000 people in 45 prospective cohorts	Review of 45 prospective observational cohorts involving 450 000 individuals with 5-30 years of follow-up	The relations of blood cholesterol and diastolic blood pressure with subsequent stroke rates were examined.	After standardization for age, there was no association between blood cholesterol and stroke except, perhaps, in those under 45 years of age when screened. However, because the types of the strokes were not centrally available, the lack of any overall relation might conceal a positive association with ischaemic stroke together with a negative association with haemorrhagic stroke.

Table 1: Summary of the included hyperlipidemia studies

Limitations

The research findings are limited to the articles that were selected for evaluation. There are many other researchers that have addressed the topic, and it would have been interesting to compare their findings to gain a greater understanding of the issue. Since there is not the time to study all the relevant resources, only the selected resources shaped the findings of this research.

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