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GENERAL MEDICINE**RESEARCH ARTICLE**

**STATINS IN THE PREVENTION OF DIABETIC MICROVASCULAR DISEASE - A STUDY IN 100
TYPE 2 DIABETIC PATIENTS IN RURAL POPULATION**

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Abstract

Study involving 100 patients of type 2 DM – with microvascular complications (renal, retinal, neuronal, cardiovascular and Erectile Dysfunction) - benefits of statins.

Key words:-

Type 2 Diabetes Mellitus - Benefits of
Statins Therapy

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Introduction:-**Material and Methods:-**

In this prospective study of 100 patients in the years 2018- 2019 in Vizianagaram district of Andhra Pradesh between the ages 48 to 65 yrs (all male patients) with body weights 67 to 74 kgs selected from rural population, primarily screened for elevated serum lipids. Participants prior consents were obtained and approval of ethics committees were taken. 80% had elevated small dense LDL cholesterol (sdLDL) > 260mg/dl, with elevated triglycerides (TGs) > 340mg/dl with decreased HDL cholesterol < 26 mg/dl and with increased procoagulant factors thereby enhancing thrombogenicity. With added atherosclerosis, these combined factors hastened macro and microvascular complications in type 2 diabetes involving carotids, aortic arch branches, renal, retinal, abdominal aorta and myocardial blood vessels. Involved neuronal vessels produced peripheral neuropathy and mononeuritis and also trophic foot ulcers. Involvement of peripheral vessels produced ischemic claudication. 75% patients exhibited proteinuria (320mg excretion in 24 hours), 30% patients had undergone laser photocoagulation for retinopathy, 40% suffered silent myocardial infarctions (mostly in the age groups between 58 to 63 years).

25% patients suffered from TIA's (transient ischemic attacks) and frank cerebrovascular events. 15% suffered from Erectile dysfunction (ED) with other disturbances of autonomic dysfunction like postural hypotension, resting tachycardia, impaired cutaneous sweating. Very few had cutaneous xanthomata, tinnitis, dribbling of urine (due to bladder atony) and diarrhoea (due to impaired motor function of colon). 65% had elevated blood pressure, mostly systolic pressures touched between 180 to 200 mm Hg. Majority had poor glycemic control revealed by raised fasting blood glucose (160mg/ dl) and postprandial blood glucose (290mg / dl) with HbA1c above 9%. Majority (74%) did not adhere to lifestyle modification advices aimed at diet and weight control methods. 14% patients were habituated in smoking and ethanol usage habits. 96% patients were using oral hypoglycemic drugs like metformin, glipizide, gliclazide and glibenclamide., few patients were using human insulin for blood sugar control. Most patients did not adhere to dietary restrictions. All patients were continued on 10 mg of atorvastatin towards life long and were advised to report any muscle aches.

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advanced
of nitric
cytokines

generation by macrophages (see Fig 1). Most significant cardiovascular risk factor in type 2 diabetes patients are elevation of serum VLDL – triglycerides and lowered HDL – Cholesterol.

Nephropathy:

Diabetes is the most common cause of end stage renal disease (ESRD) with an increase in urinary albumin excretion with type 2 DM (hazard ratio HR 0.39), about 20% patients will have progressed to ESRD within 20 years. Renal damage occurs with increased glomerular capillary pressure with added systemic hypertension. Finally macroalbuminuria ensues. Ultrasound reveals larger sized kidneys.

Retinopathy:

Diabetic retinopathy cause blindness in working-age adults and is preventable. The incidence increases with long standing diabetes (hazard ratio HR 0.41). More than 60% of patients with type 2 DM will have retinopathy in the first 20 years of the disease. Endothelial dysfunction result in decreased retinal perfusion and is implicated in the genesis of macular edema and neovascularization. Weakened vessel wall causes microaneurysms and retinal hemorrhages. In advanced stages, a proliferative retinopathy ensues characterized by growth of new vessels in the retina and posterior vitreous.

Neuropathy:

Two Major complications of diabetic neuropathy are foot complications and erectile dysfunction (ED). Neuropathy involves both sensory and autonomic neurones, prevalence of foot ulcers estimated to be 3 to 8% in type 2 DM. ED occurs in men over 44 years in 46% patients, is considered to be due to failure of nitric-oxide mediated smooth muscle relaxation as a result of autonomic neuropathy (hazard ratio HR 0.38).

Role of Lipids and microvascular complications:

UKPDS (United Kingdom Prospective Diabetes Study) showed that hyperglycemia, hypertension and dyslipidemia contribute towards the development of microvascular complications. With intensive treatments of these macrovascular and microvascular complications can be reduced. There is positive association between nephropathy/retinopathy and lipid levels. Apolipoprotein B shown to be an independent risk factor for progression of renal disease. Serum cholesterol of > 250 mg/dl, LDL-C > 170 mg/dl were associated with retinal hard exudates. Raised total cholesterol and low HDL –C were shown to be risk factors for ED.

Discussion:-**Statins and Fibrates for microvascular complications:**

Finofibrate treatment led to statistically relevant reduction in the rate of retinal laser treatment, there was also improvement in albuminuria, with added reductions in the number of foot amputations. Data suggest early usage of finofibrate in a primary prevention setting. Combined use of atorvastatin 10mg, finofibrate 200mg changed HsCRP (high sensitivity C reactive protein) and fibrinogen levels to a greater extent when compared to independent use of atorvastatin and finofibrate.

Statins and Nephropathy:

GREACE study (Atorvastatin and Coronary heart disease Evaluation study) revealed improvement in renal function with atorvastatin. Rosuvastatin may arrest the progression in renal disease. Finofibrate significantly reduced the worsening of albumin excretion. CARDS study (Collaborative Atorvastatin Diabetes Study) showed 42 % reduction in acute coronary heart disease, 62% reduction in stroke with atorvastatin.

Statins and retinopathy:

Atorvastatin have a role in reducing retinal complications and decrease in mean PSVs (peak systolic flow velocities) of the ophthalmic artery and central retinal artery. Atorvastatin therapy reduced the severity of hard exudates. Parvastatin treatment resulted in decrease in microaneurysms and hard exudates and improved acuity of vision. Statins in ED (erectile dysfunction): Clinical benefits of statins in ED not established. Mechanism of statin benefits on vascular complications: Inhibition of HMG- CoA reductase leads to reduced cholesterol synthesis,

statins improve endothelial function by production of Nitric Oxide (NO), nitric oxide promotes vasodilation. Another added benefit is their antioxidant effect thereby decreasing oxidative stress. Recently found that statins have antiplatelet action.

Statins – Niacin combination therapy:

Combination of simvastatin and niacin was effective in reducing cardiovascular disease events. Niacin increases HDL – Cholesterol to a greater extent than any other agent.

Conclusion:-

The lipid triad of raised sdLDL (small dense low density lipoproteins), lowered HDL (high density lipoproteins), and elevated TGs (triglycerides) – the cause of this lipid triad is due to insulin resistance, which is likely to be the consequence of elevations in plasma FFAs (free fatty acids) production seen with visceral obesity and high energy diets. Elevated sdLDL and TG levels and a low HDL-C levels independently increase the risk of Cardiovascular disease. Activation of PPAR alpha occurs with fibrates, lowers FFA levels. PPAR gamma agonism seen with thiazolidinediones, promotes redistribution of FFAs from visceral stores to more inert subcutaneous depots. Activation of PPAR alpha and PPAR gamma improves lipid metabolism.

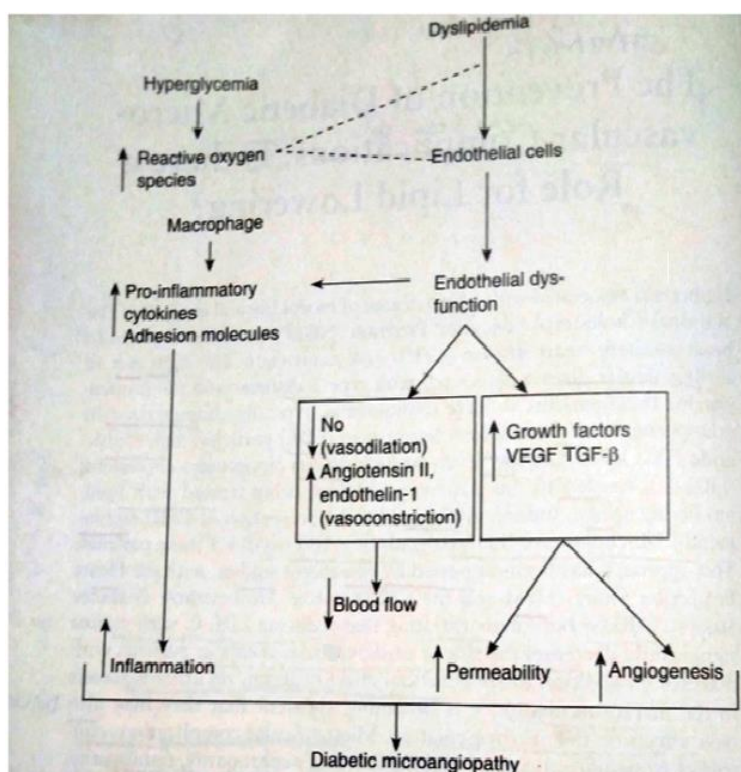


Fig 1:- Mechanism by which hyperglycemia – dyslipidemia producing microvascular damage.

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