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# IMPACT OF ROSUVASTATIN IN HYPERTENSIVE PATIENTS – A REVIEW

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ABSTRACT – Atherosclerosis (high levels of lipophilic substance) causes degenerative changes in the intima of medium and large arteries. The deposits or plaque decreases the lumen of artery, reduce its elasticity and may create foci for thrombi and subsequent occlusion in their arteries.

Statin drugs class is effective as lipid-lowering agents, particularly in patients with hypertension.However,the evidence as lipid-lowering agents, particularly in patients with hypertension.However,the evidence for role of statins in blood pressure lowering is controversial. Statin drug has been reported endothelium-dependent vasodilation which is reduced in dyslipidemia subjects. Rosuvastatin is a new generation HMG-CoA reductase inhibitor. Rosuvastatin reduces inflammation and oxidative stress. It also reduces blood pressure in patients with hypercholesterolemia. Coronary flow reserve(CFR) significantly improve after rosuvastatin therapy in hypertensive patients. The blood pressure response to statin was unrelated to age, changes in serum, cholesterol or length of trial. Cardiovasular (CV)diseases are a major cause of premature death and disability. Non-communicable diseases(NCD) are responsible for 52% of mortality amongst Indian, of these CV diseases are responsible for 66% of NCD mortality in India. C-reactive protein(CRP) has been shown to function as an inflammatory factor. Statin lowered C-reactive protein as well as cholesterol. Rosuvastatin attenuated the increase in blood pressure in(AAV-hCRP) adeno associated virus to induce overexpression of human CRP treated rats through endothelial protection and antioxidant effects. Benefit of statin in such patient who are undergoing hemodialysis has been proved recently. Patients with high blood pressure level at baseline as well as those treated with ACE inhibitor and calcium channel blocker are expected to benefit more in this regard.

INTRODUCTION-Cardiovascular disease(CVD) leading cause to death globally. Many risk factor hyperlipidemia, with elevated lipoprotein level, arterial hypertension, with elevated systolic blood pressure(SBP) and diastolic blood pressure(DBP) are among the major risk factor that are associated with development of CVD,inducing myocardial infraction, stroke and congestive heart failure. The underlying mechanism of BP-lowering effect of statin should be related to the modulation of endothelial function and vascular oxidative stress. Rosuvastatin is one of the most potent and commonly prescribed statin for treatment of hyperlipidemia, hypertension. The beneficial cardiovascular mechanism of statins include anti-inflammatory actions and anti-oxidant properties.Recently,the university of California, an Diego,statin study demonstrated that statins moderately but significantly reduced systolic B.P. by 2.2mmHg and diastolic B.P. by 2.4mmHg relative to placebo.Several clinical trials, including the JUPITER study have shown that statin therapy could significantly reduce CRP levels and improve outcomes. In Mexico, the prevalence of non-transmissible chronic disease such as high blood pressure (HBP) and diabetes mellitus, has grown exponentially over the last 2 decades. The prevalence of HBP has reached 30.1% & is one of main risk factor associated with cerebrovascular & coronary heart disease.

Rosuvastatin is a HMG-CoA reductase inhibitor. It has an additional polar methane sulphonide group. This makes rosuvastatin less lipophilic & improves its ionic interaction with HMG-CoA reductase. The inhibition is selective & reversible. This inhibition leads to decreased sterol synthesis & hence decreased hepatocellular cholesterol, resulting in enhanced synthesis of LDL receptor & hence more LDL is being taken from circulation from liver. This leads to decrease in LDL-C & total cholesterol (TC) concentration in circulation. It has shown anti-inflammatory effects which is due to reduction in high sensitivity C-reactive protein.The anti-thrombotic effects of rosuvastatin are due to its ability to reduce platelet aggregation. The only large scale trial involving greatly increased risk of CVD patients population, Die Deutsche Diabetes Dialyse Studie(the 4D study),showed on significant benefit of statin therapy with regard to a composite cardiovascular end point.

Clinical Pharmacokinetics-1)Absorption- Rosuvastatin has oral bioavailability of 20% with peak plasma levels achieved in 5 hours.2)Distribution- Rosuvastatin is 88% plasma protein bound with volume of distribution being 134 litres.3)Metabolism- It is mainly metabolized by CYP 2C9 to a less potent metabolite N-desmethyl rosuvastatin.It shows minimal drug-drug interactions & plasma half-life of rosuvastatin is 19 hours.4)Elimination- Approximately 90% of rosuvastatin is eliminated in faeces with 10% being eliminated in urine.

MATERIALS & METHODS

The patients included RCTs that investigated the effect of rosuvastatin on B.P.Studies were eligible to meet following criteria-

1) Patients with hypertension.

2) Rosuvastatin treatment.

3) Standard care or placebo.

4) Outcome: changes in DBP or SBP.

Patients of 18 to 25 years of age were eligible if they had at least one vessel with 20% stenosis on clinically indicated coronary angiography & a target vessel for imaging which less than 50% obstruction. Patients who had not been treated with statin in there preceding 4 weeks were required to have an LDL cholesterol level at entry that was higher 100mg per deciliter(2.6mmol per lit);those who have not received such treatment were required to have a level higher than 80mg per decilit.(2.1mmol per lit).

During treatment, levels of HDL & LDL cholesterol & triglycerides were measured at 6, 12,18 & 24 months. Levels of CRP were measured at 12 & 24 months. Men 50 years of age or older & women 60 years of age or older were eligible for the trial if they did not have a history of cardiovascular disease & if at initial screening visit, they had an LDL cholesterol levels of less than 130 mg per decilit.(3.4 mmol per lit.) & high sensitivity CRP level of 2.0mg per lit or more

**DISCUSSION**

We found that addition of rosuvastatin to lifestyle modification & antihypertensive medications was associated with improvement of CFR in hypertensive patients with cardiovascular risk factor. By taking into account this assertion together with the quality of evidence found in the study aforementioned; rosuvastatin could be considered as the first choice for cardiovascular high-risk patients.

**Duk-Hyun Kang,et al** –Found that statin therapy decrease cardiac morbidity & mortality in patients with CAD & hypercholesterolemia including regression of atheroma & stabilization of atherosclerotic plaques.

2)**Sungjae Lee, et al** –Suggested that rosuvastatin exert a modest DBP-lowering effect in patient with hypertension & dyslipidemia when combined with antihypertensive agent.BP-lowering effect of statin,with are currently the best selling prescription drug worldwide.

3)**D.Sriram and P.Yogeeswari,et al**-Suggested that statins are most effective cholesterol- lowering drugs. Thay are competitive inhibitor.

4**)Pena Seijo,et al**-Rosuvastatin reduces ambulatory BP & increases nocturnal BP declined when administered at bedtime apart from lipid lowering effect.This BP lowering effect may be related to improved endothelium dysfunction that use to be common at dyslipidemia subjects.

5)**Anel Gomez-Garcia,et al**-The results show that patients with HBP & dyslipidemia who are treated with rosuvastatin 10mg/day experience a significant reduction in their LDL-C plus a moderate increase in their HDL-C concentration. Rosuvastatin reduce inflammation & oxidative stress & may therefore offer a protective effect against CVD.

6**)Xuguang Li,etal**-effect of rosuvastatin on CRP-induce increase in SBP. Therefore, rosuvastatin modestly, but significantly, lowered SBP induce by CRP overexpression.

7)**Ahai Luvai,et al**- Rosuvastatin is synthetic with a relatively low lipophilicity when compared with other statin & has minimal entry into peripheral cells. JUPITER showed that reduction in CV events & all-cause mortality of rosuvastatin in primary prevention in patients with lower CV risk.

8**)Sung-A Chang,et al**-The 3-hydroxy-3-methylgutaryl-CoA reductase inhibitor ,commonly referred to as statin, are well-known potent lipid lowering agent. In addition to their primary effect, the statin have been shown to have cleiotropic effect on cardiovascular system, including anti-inflammatory, ant oxidative & endothelial protective effect & thus have been tested as a therapeutic agent.

9)**Shingo Seki,et al-** suggested that BP lowering effect may be related to improved endothelium dysfunction that use to be common at dyslipidemic subjects.

10)**Tasquale Strazzullo,et al**-The meta-analysis provided evidence of a favorable effect of statin on BP, particularly SBP & indicated that the effect was larger in individuals with elevated BP.

11)**Gurpreet S Wander,et al**-Found that rosuvastatin is one of most commonly used statin.It is a potent, effective & safe HMG-CoA reductase inhibitor. It is more effective LDL reduction.

. 12)**Francesca Cortese,et al**-Rosuvastatin is fully synthetic statin.Interfer with the endogenous synthesis of cholesterol through competitively inhibiting the 3-hydroxy-3-methyl glut aryl CoA reductase,a liver enzyme responsible of the rate-limiting step in cholesterol synthesis.

13**)Mariusz Stepien,et al**-Statins may exert a mild, but clinically relevant, antihypertensive effect which is probably mediated by mechanisms that are independent of their lipid-lowering effect.

14**)Stethen J,et al**-Maximal doses of rosuvastatin & atorvastatin resulted in significant regression of coronary atherosclerosis. Be spite the lower level of LDL-cholesterol & the higher level of HDL-cholesterol achieved with rosuvastatin.

15**)Bengt C,et al**-In patient undergoing hemodialysis, the initiation of treatment with rosuvastatin lowered the LDL-cholesterol level.

16)**Paul M Ribker,et al**-apparently healthy person without hyperlipidemia but with elevated high-sensitivity CRP level, rosuvastatin significantly reduced the incidence of measure CV event.

17)**Hyoeum Kin,et al**-In the field of CV preventive medicine, statin have become an indispensible component.

18)**Toshiyuki Nishikido,et al**-High-dose statin therapy significantly reduced the sd-LDL & MBA-LDL component of atherosclerotic lipoprotein without adverse event in comparison with low-dose statin therapy.

19)**Jaakko Tuomilehto,et al**-Rosuvastatin offer several advantages in the treatment of dyslipidemia. Rosuvastatin is particularly suitable for patient with metabolic syndrome since it also raises HDL-C & lower serum triglyceride significantly. It produces beneficial effects on all key lipid parameter at low doses.

20)**John E.Feliciano-Alfonso,et al**-It is possible to assert that rosuvastatin is more advantageous & cost-effective than other statins with regard to its LDL-C reduction & percentage of patients reaching a goal, with a similar safety profile.

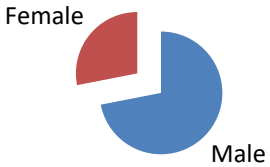


Fig:1 :Shows gender incidence of Hypertension associated with hyperlipidaemia

RESULT-Rosuvastatin reduces BP in hypertensive & dyslipidemic patients. It also reduces ambulatory BP & increases nocturnal BP. Rosuvastatin lower SBP induced by CRP overexpression. Maximal dose of rosuvastatin & atorvastatin resulted in significant regression of coronary atherosclerosis. The overwhelming benefit of statin in the reduction of CV event outweighs the small risk of developing diabetes therefore; statin therapy should therapy should be used in patients with high CV risk.

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