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Effect of Pravastatin on Development of Diabetes Mellitus - A Statement of Review

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Abstract

According to the ADA, diabetes mellitus is defined as having fasting blood glucose levels >= 7.0mmol/l. Statins are the lipid-lowering agents used to treat dyslipidemia and act by inhibiting the HMG Co-A reductase enzyme. Very few studies have reported the results of drugs concerning the profile of blood lipids or which have anti-inflammatory activity behaviour on diabetes. Pravastatin is such a drug that shows inherent beneficial pleiotropic effects on plasma lipids and inflammatory actions. Pravastatin remarkably reduced the increased levels of plasma glucose when compared with the control group, subjecting to no change in body weight or food intake in mice. By performing certain insulin tolerance tests using tracers like 2- [3 H]-deoxy glucose (2DG), they concluded that insulin-induced glucose uptake is increased in adipose tissue. Pravastatin is shown to reduce the circulating concentration of the interleukin-6, cytokines, and TNF-alpha. Pravastatin's anti-inflammatory properties interrupt the natural progression from central obesity to insulin resistance mediated by cytokines from the adipose tissue. Pravastatin can significantly impact selective tissue perfusion through restoring the endothelial function and thus benefit the transportation of glucose and insulin.

Keywords: Pravastatin; Diabetes Mellitus; Adiponectin; 2-[3H]-deoxyglucose (2DG)

Introduction

According to the ADA, diabetes mellitus is defined as having fasting blood glucose levels >= 7.0mmol/l. Statins are the lipid-lowering agents used to treat dyslipidemia and act by inhibiting the HMG Co-A reductase enzyme [1]. Factors that impact diabetes mellitus induction was the focus of extensive research. Pathology predictors such as blood lipids and lipoproteins levels and markers that detect low-level inflammation made their role exist in detecting the occurrence of diabetes mellitus [2-5]. Very few studies have reported the results of drugs concerning the profile of blood lipids or which have anti-inflammatory activity behavior on diabetes. Pravastatin is such a drug that shows inherent beneficial pleiotropic effects on plasma lipids and inflammatory actions. First reported in 2001 in the West Scotland coronary prevention study (WOSCOPS), the relationship between statins and diabetes development. This randomized 40mg pravastatin placebo-controlled trial showed a 30% reduction in new diabetes incidence [6].

Pravastatin has a spectrum of anti-athero-thrombotic effects, including the recovery of endothelial and anti-inflammatory aspects [7].

Pravastatin and its Mechanism of Action

Pravastatin and other statins are the competitive inhibitors of the HMG Co-A reductase enzyme, they

inhibit the de novo synthesis of cholesterol thus depleting the intracellular levels of cholesterol. The lowering of cholesterol causes an increase in LDL receptors on the cell surface that can bind and attribute the circulating LDLs. This results in a decrease in plasma cholesterol.

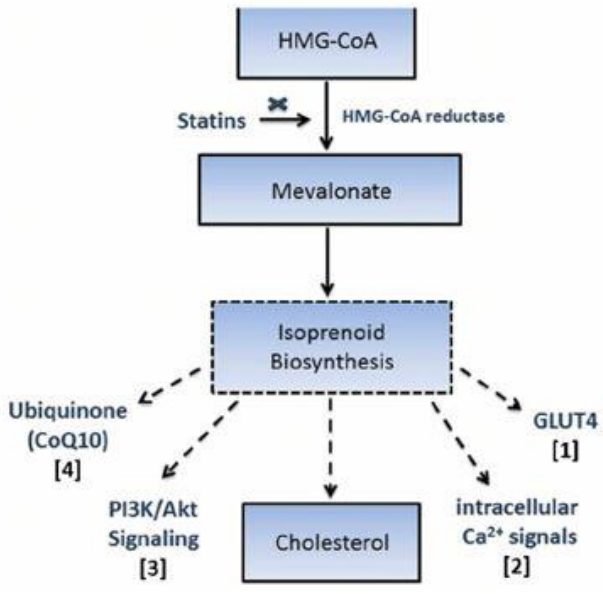

Figure 1: Mechanism of action for statins.

Pravastatin and its Association with the Development of Diabetes

Several explanations account to explain the association between pravastatin and the occurrence of diabetes mellitus. In a study performed by Takagi et Al. on mice in 2006, pravastatin remarkably reduced the increased levels of plasma glucose when compared with the control group, subjecting to no change in body weight or food intake [8]. By performing certain insulin tolerance tests using tracers like 2- [^{3} H]-deoxy glucose (2DG), they concluded that insulin-induced glucose uptake is increased in adipose tissue [9]. The current study reports that pravastatin increases plasma adiponectin levels which were associated with a reduction in the risk of type 2 diabetes mellitus [10].

In reducing the risk of insulin resistance development, the triglyceride-lowering effect of pravastatin therapy may be significant over the longer term. For several years, high triglyceride levels have been known to have been associated with diabetes development [11].

Pravastatin is shown to reduce the circulating concentration of the interleukin-6, cytokines, and TNF-alpha [12]. These inflammatory mediators inhibit lipoprotein lipase and stimulate lipolysis in adipose tissue [13,14]. These tissue-derived cytokines are responsible for insulin resistance metabolic syndrome. Pravastatin's anti-inflammatory properties interrupt the natural progression from central obesity to insulin resistance mediated by cytokines from the adipose tissue [6].

The influence on endothelial function is another effect of pravastatin consistently demonstrated [14-16]. The endothelial function has recently been decreased and correlations with the degree of insulin resistance have also been shown [17]. Pravastatin can significantly impact selective tissue perfusion through restoring the endothelial function and thus benefit the transportation of glucose and insulin [6].

The risk of developing diabetes and macrovascular complications was lower in patients receiving pravastatin. Therefore, it may be recommended to prescribe statins which are neutral in glucose homeostasis [18]. The connection between statin therapy duration and the risk of newly diagnosed diabetes is uncertain [19]. However, a recent study has found that compliance with statin therapy causes an increase in the risk of statin-induced diabetes mellitus [20]. **Figure 1** provides the systematic representation of mechanism of action of statins [21]. **Table 1** Summarizes the mechanism of pravastatin associated with diabetes mellitus.

Table 1: Summary of mechanisms od pravastatin associated with the Diabetes mellitus.

Drug	***Possible mechanism's associated with reducing diabetes mellitus***
Pravastatin	Increasing plasma adiponectin levels, thereby reducing the risk of diabetes mellitus
	Long term reduction triglycerides levels, reduces the risk of insulin resistance development
	Reducing the levels of inflammatory mediators
	Restore the endothelial function enhancing

Conclusion

Patients who were taking pravastatin had a decreased risk of diabetes compared to patients who were taking other diabetes statins. Thus, it may be advisable to prescribe statins that neutrally or positively affect glucose homeostasis.

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Conflict of Interest

The authors declare no conflict of interest.

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