Thesis Title Effect of HMG-CoA Reductase Inhibitors on Lipid Metabolism in Type II Hyperlipoprotienemic Patients

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ABSTRACT

The purpose of this study is to evaluate the efficacy and safety of 2 lipid-lowering drugs, pravastatin and simvastatin which are HMG-CoA reductase inhibitors in type II hyperlipoproteinemic patients attending the Nutrition Clinic, Department of Medicine, Ramathibodi Hospital.

Twenty-four type II hyperlipoproteinemic patients having serum total cholesterol (TC) levels $\geq$5.2 mmol/L and low density lipoprotein-cholesterol (LDL-C) levels $\geq$3.4 mmol/L were recruited for the pravastatin study. The patients were instructed to consume diets with

energy distribution of 15% protein, 30% fat, 55% carbohydrate; and restrict their cholesterol intake to less than 300 mg/day. After 4 wks of dietary advice only, if the patients still had serum TC levels of $\geq$5.2 mmol/L they were treated with 10 mg pravastatin once daily for 48 wks. After 4 wks of the pravastatin treatment, there were significant decreases in their serum TC, LDL-C, apo B and plasma S-partiele levels. The reduction in these serum lipoprotein levels remained throughout the study. The mean decrease in their serum TC levels during receiving the pravastatin treatment from that at wk0 ranged from 13.8 to 20.0% whereas the corresponding figures for serum LDL-C levels ranged from 18.2 to 28.1%. However, their mean serum TC and LDL-C levels during the pravastatin treatment did not reach the desirable TC and LDL-C levels of 5.2 and 3.4 mmol/L, respectively. Though there were significant decreases in their serum TC and LDL-C levels during the first 4 wks of dietary advice only (wk0 vs wk-4) but the decreases were much lower than those during receiving the pravastatin treatment. The mean decrease in their serum LDL-C level at wk0 from that at wk-4 was only 9.4% of that at wk4 from wk0. Since there was no significant difference in their body composition during receiving the pravastatin treatment, body composition should not be a confounding factor for the interpretation

of the cholesterol-lowering effect of pravastatin. However, their hematological status influenced their serum lipid levels evidenced by the significantly positive correlations between Hb or MCV and serum TC levels and significantly negative correlations between Hb, MCV or McH and serum HDL-C levels. There were no significant decreases in their platelet aggregation during receiving the pravastatin treatment. The study also revealed the safety in taking 10 mg pravastatin daily for 48 wks in type II hyperlipoproteinemic patients evidenced by no clinical adverse effects, normal hematologic parameters, liver and renal function tests.

Twenty-nine type II hyperlipoproteinemic patients having serum TC levels $\geq$6.2 mmol/L and LDL-C levels $\geq$3.4 mmol/L were recruited for the simvastatin study. The patients were instructed to consume cholesterol-lowering diets as in the pravastatin study. After 4 wks of dietary advice only, if the patients still had serum TC levels $\geq$6.2 mmol/L and LDL-C levels $\geq$3.4 mmol/L they were treated with 10 mg simvastatin once daily for 8 wks. After 8 wks of 10 mg simvastatin treatment (wk8) if their serum TC levels became <5.2 mmol/L they continued to take 10 mg simvastatin daily for another 40 wks. For those having serum TC levels $\geq$5.2 mmol/L, they were treated with 20 mg simvastatin daily for another 8 wks; for those having

serum TC levels $\leq$5.2 mmol/L at wk 16, they continued to take 20 mg simvastatin daily for another 32 wks. At week 16; for those having serum TC levels $\geq$5.2 mmol/L, they were treated with 40 mg simvastatin daily for another 32 wks.

After 4 wks of the simvastatin treatment, there were significant decreases in their serum TC, LDL-C, apo B and plasma S-particle levels. The mean decreases in serum TC levels during receiving simvastatin treatment from that at wk0 ranged from 18.5 to 27.8% whereas the corresponding figures for serum LDL-C ranged from 21.6 to 38.9%. Dose-dependent response to simvastatin treatment was observed. Genetic traits are most likely to be the cause of the different response to the simvastatin treatment. The prevalences of corneal arcus in patients responding to 10, 20, and 40 mg simvastatin were 20.0, 62.5, 72.7%, respectively. Since there was no significant difference in their body composition during receiving the simvastatin treatment, their body composition should not be a confounding factor for the intepretation of the cholesterol-lowering effect of simvastatin. However, their hematological status influenced their serum lipid levels evidenced by significantly positive correlations between MCV and serum TC levels as well as between Hb or MCHC and serum TG levels whereas significant negative

correlations were observed between Hb or MCHC and serum HDL-C levels There were significant decreases in their platelet aggregation induced by 0.4 mg/mL of collagen at wks 32 and 48. The safety of long-term treatment of 10, 20, and 40 mg simvastatin in type II hyperlipoproteinemic patients was evident by no clinical adverse effects, normal hematological parameters, liver and renal function tests.