Thesis Title Lipid Status in Type II Hyperlipoproteinemic Patients on dl-∝-Tocopheryl Nicotinate or 2-[2-(4-Chlorophenoxy)-2-Methylpropionyloxy] Ethyl Nicotinate Treatment

Name Pimporn Watcharangkul

Degree Doctor of Science (Nutrition)

Thesis Supervisory Committee

Vichai Tanphaichitr, M.D.,Ph.D.,F.A.C.P.,F.R.A.C.P.

Ratana Pakpeankitvatana, D.Sc.

Preeya Leelahagul, D.Sc.

Krisana Kraisintu, Ph.D.

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ABSTRACT

The purpose of this study is to evaluate the efficacy and safety of 2 lipid-lowering drugs, dl-∝-tocopheryl nicotinate (dl-∝-TN) and etofibrate (EF) ratard in type II hyperlipoproteinemic patients who attended Nutrition Clinic, Department of Medicine, Ramathibodi Hospital. They had serum total cholesterol (TC) level of ≥5.2 mmol/L and low density lipoprotein-cholesterol(LDL-C) level of ≥3.4 mmol/L. The study consisted of 4 wks of control and 48 wks of drug period. Throughout the study, the patients were instructed to consume diets with 15% protein-, 30% fat-, and 55% carbohydrate-calories and control their daily cholesterol intake to less than 300 mg.

After receiving the treatment for 4 wks, the patients were classified into 2 groups, responders and non-responders; responders were the patients whose serum TC level decreased more than 5% from the level at wk0 whereas non-responders were those who did not show the reduction in serum TC levels.

The study of the efficacy and safety of dl-∝-TN was conducted in 31 patients. After 4 wks of dl-∝-TN treatment, only 11 patients (35.5%) showed a reduction of serum TC levels of >5% from their serum TC levels at wk0. There were significant decreases in their serum TC and LDL-C in dl-∝-TN responders. The mean decreases in their serum TC levels at wks4, 8, 12 and 16 from wk0 were 8.20%, 5.20%, 6.94% and 8.52%, respectively, whereas the corresponding figures for their serum LDL-C levels were 11.21%, 8.24%, 7.78% and 11.67%, respectively. Since there were no significant changes in their cholesterol, energy, saturated fatty acid, monounsaturated fatty acid and polyunsaturated fatty acid intakes throughout the study, dietary intake is not a confounding factor for the interpretation of the cholesterol-lowering effect of dl-∝-TN. The biological role of dl-∝-TN in protecting the cellular membranes from peroxidation was illustrated in this study by the significant increases in serum vitamin E

levels as well as erythrocyte 20:5 n-3, 22:5 n-3 and 22:6 n-3 FA levels with concomitant significant decreases in serum malondialdehyde (MDA) in both responders and non-responders. There were no significant changes in their erythrocyte superoxide dismutase (SOD) and lipoprotein(a), [Lp(a)], but there were significant decreases in platelet aggregation induced by 5 uM of ADP and 3 uM of epinephrine during receiving dl-∝-TN. The consumption of dl-∝-TN is safe, evidenced by no clinical adverse effect and normal hematological parameters, renal and liver function tests.

The study of the efficacy and safety of EF retard was conducted in 34 patients. After 4 wks of EF retard treatment, 20 patients (58.8%) showed a reduction of serum TC levels of >5% from those at wk0. EF retard is effective in lowering serum TC, LDL-C and TG but raising serum HDL-C levels in responders. The mean decreases in their serum TC levels at wks 4, 8 and 12 from those at wk0 were 9.97%, 7.28%, and 5.85%, whereas the corresponding figures for their serum LDL-C levels were 14.52%, 10.60%, and 9.91% and those for their serum TG levels were 21.13%, 23.94%, and 19.72%, respectively. The mean increases in their serum HDL-C at the aforesaid period were 9.77%, 12.03% and 13.53%, respectively. This was supported by their significant decreases in their

plasma S-particle and apo B levels during receiving the EF retard treatment. The significant decreases in plasma fibrinogen levels in both responders and non-responders were observed only for long-term treatment. There were no significant changes in their platelet aggregation induced by 5 uM of ADP or 3 uM of epinephrine, serum vitamin E and MDA levels whereas there were significant increases in erythrocyte SOD activity. The comsumption of EF retard is safe which evidenced by no clinical adverse effect and normal hematological parameters, liver and renal function tests.