Double-blind comparative clinical trial of Abana and Simvastatin in Hyperlipidaemia

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INTRODUCTION

Nikolai Anichkov first proposed a link between cholesterol and atherosclerosis in 1912[1]. Decades later observational studies have established hyperlipidaemia as an independent risk factor for coronary artery disease. It is now proved that hyperlipidaemia is an independent risk factor for ischemic stroke. Additional evidences from the prospective studies have shown the relationship between plasma cholesterol levels and risk of stroke. Reduction in the plasma cholesterol is accompanied by significant decrease in the incidence of coronary artery disease and stroke.

Data from individual randomised trials and meta-analyses of randomised trials consistently show a reduction in risk for both fatal and nonfatal coronary heart disease following primary and secondary prevention[2-6]. A recent comprehensive overview by Law and colleagues incorporated data from 28 trials of cholesterol reduction, including 6 multiple intervention trials that each had a cholesterol-reducing arm. This overview indicated that a 10% reduction in serum cholesterol level resulted in highly significant reductions mortality from coronary heart disease. These data from randomised trials are consistent with observational data when treatment lasts 5 years or more. A 10% reduction in cholesterol levels was associated with a 25% reduction in coronary events among persons treated for more than 5 years. These findings from meta-analyses are also supported by recent reports from the Scandinavian study[7] and the West of Scotland Coronary Prevention Study[8].

Herbs have been used since ancient times for reducing body lipids. Reports on all garlic studies performed, found cholesterol was lowered by an average of 9-12% over a one-to-four month period[9]. Guggul, a mixture of substances taken from the plant *Commiphora mukul*, is an approved treatment for elevated cholesterol in India and has been a mainstay of the Ayurvedic approach in preventing atherosclerosis. One trial studying the effects of guggul reported that serum cholesterol dropped by 17.5%[10]. In another report comparing guggul to the drug clofibrate, average fall in serum cholesterol was slightly greater in the guggul group while HDL cholesterol rose in 60% of people responding to guggul, while clofibrate treatment did not elevate HDL[11]. Wild yam another herb commonly used has also been reported to raise HDL cholesterol in preliminary research[12]. With the above leads we planned a double-blind comparative clinical study using Abana and Simvastatin.

MATERIALS AND METHODS

Seventy patients were evaluated for general health and lipid profile through a medical history and a thorough physical examination. Patients with secondary hyperlipidaemia, alcoholism, or body weight more than 15% above the ideal for their height were excluded from the study. Baseline

cholesterol and triglycerides of estimation were carried out. The patients showing serum total cholesterol levels more than 200 mg/dL or serum triglyceride levels more than 200 mg/dL were included in the study.

After screening fifty patients qualified for the study, their ages ranged from 29 to 64 years, with a median of 46. There were 37 male and 13 female patients. Each patient underwent routine hematological and biochemical laboratory investigations. Patients were asked not to eat any food, except for water, for 12 to 14 hours before taking blood samples. Routine urine analysis and electrocardiography was also carried out. The study planned was double blind, randomized comparative study for 8 weeks. The written and informed consent was obtained from all the patients. Patients took 2 capsules of the drug before breakfast and at bedtime. The patients had to visit every 2 weeks for 8 weeks. A registered dietician interviewed the patients and instructed them to have diet with low cholesterol and saturated fats.

The clinical side effects if any were recorded at each visit and discussed with the patient to know the nature, severity and frequency. Patients were seen by the same dietician at every clinic visit throughout the study and were instructed to follow the same diets and to maintain weight, physical activity levels and smoking frequency for the duration of the study. To evaluate diet compliance, patients made written records of the quantity and type of food consumed in 4 consecutive days, including a weekend, between visits. These food diaries were kept on special forms that were then translated into computer language and analyzed by a program designed for that purpose. Patients reported their usual physical activity and smoking habits on a special card at every visit. All but three patients did not smoke cigarettes. Repeat laboratory investigations and electrocardiography were done after completion of the study.

Concomitant medications were monitored throughout the study. Twenty-three patients took no other drugs, 11 took asprin, acetaminophen, or both, 8 took antihistamines / antiallergic preparations, vitamins, or mineral supplements, 7 took minor tranquilizers, sedatives, or laxatives, 4 took nonsteroidal anti-inflammatory drugs, 4 took antacids or anticholinergic drugs, and 2 took antibiotics. The results were analyzed using paired 't' test.

RESULTS
Of the 50 patients who entered the active-treatment phase of the study, 3 were excluded because of non-compliance. The patients followed fairly uniform dietary patterns during the trial and their compliance was assured by routine interviews with the dietician and review of the computer's analysis of dietary records at every clinic visit. Routine follow-up by the dietician resulted in good overall dietary compliance and accounted for the attainment, in many patients of normal cholesterol levels in both the drug treatment. Results of those patients taking Abana showed a reduction of cholesterol from 215.3 ± 7.42 mg/dl to 192.3 ± 9.08 mg/dl. Reduction in cholesterol from 204.2 ± 8.43 to 157.0 ± 7.54 mg/dl occurred with Simvastatin. Triglycerides levels were also reduced from 216.0 ± 26.37 mg/dl to 187.7 ± 21.28 mg/dl and 214.7 ± 34.09 to 173.5 ± 23.23 mg/dl with Abana and Simvastatin respectively. In HDL, levels were increased in a similar fashion with Abana and Simvastatin treatment. Although, the rise in HDL cholesterol was similar in both the drugs, Simvastatin produced increase of HDL-cholesterol marginally higher than the Abana.

Similarly, LDL levels were reduced from 133.0 ± 7.07 mg/dl to 115.4 ± 8.45 mg/dl and 115.1 ± 7.90 mg/dl to 81.55 ± 6.00 mg/dl with Abana and Simvastatin respectively. The VLDL levels were reduced from 41.57 ± 4.33 mg/dl to 39.53 ± 4.16 mg/dl and 45.93 ± 6.77 mg/dl to 34.15 ± 4.68 mg/dl with Abana and Simvastatin respectively (Table). Thus, both Abana and Simvastatin reduced the cholesterol, triglycerides, LDL and VLDL levels and increase of HDL cholesterol levels. The analysis of both drugs shows the reduction of cholesterol, triglycerides,

Level of lipids before and after treatment				
Parameters	Abana		Simvastatin	
	Before treatment	After treatment	Before treatment	After treatment
Total cholesterol (mg/dl)	215.30 ± 7.42	192.30 ± 9.08*	204.20 ± 8.43	157.0 ± 7.54*
Triglycerides (mg/dl)	216.00 ± 26.37	187.70 ± 21.28*	214.70 ± 34.09	173.5 ± 23.23*
HDL (mg/dl)	39.00 ± 2.84	40.25 ± 2.83	39.38 ± 2.12	41.05 ± 1.45
LDL (mg/dl)	133.00 ± 7.07	115.40 ± 8.45*	115.10 ± 7.90	81.55 ± 6.00*
VLDL (mg/dl)	41.57 ± 4.33	39.53 ± 4.16*	45.93 ± 6.77	34.15 ± 4.68*
*$p<0.001$ as compared to the before treatment value				

LDL and VLDL in comparative manner. However, it is noticed that Simvastatin group presented with more number of side-effects, especially the liver function tests.

DISCUSSION

High serum cholesterol is regarded by many as the main cause of coronary arherosclerosis[13]. Several cholesterol lowering interventions have reduced coronary heart disease (CHD) events in primary and secondary prevention clinical trials[14,15]. Even expert panels in Europe and the USA have therefore recommended dietary changes and, if necessary, addition of drugs to reduce high cholesterol concentrations especially low-density-lipoprotein (LDL) cholesterol[16,17] especially in patients with CHD. No statistically or clinically significant changes were seen in weight, blood pressure, serum blood glucose levels, uric acid levels, or findings of other routine biochemical tests. Until the mid-1990s, the importance of dyslipidaemia as a risk factor for coronary heart disease was controversial, as was the use of lipid lowering treatment. However, after publication of the 4S trial in 1994, four other trials confirmed significant reductions in fatal and non-fatal cardiovascular events when statins were used in both primary and secondary prevention.

Many guidelines have been recommended for reducing levels of total cholesterol, triglycerides and low-density lipoproteins to decrease risk for coronary heart disease. Most cardiologists agree that adherence to these guidelines would reduce rates of morbidity and mortality from heart disease. There is little doubt that elevated cholesterol levels increases the risk for coronary heart disease. Observational research indicates that a linear relation exists: A 20% increase in risk for coronary heart disease is associated with a 10% increase in serum cholesterol levels. This dose-response effect occurs at any cholesterol level and is apparent in both men and women and in both black and white persons.

Since many guidelines for the use of statins recommend in primary prevention in those with the highest absolute risk of coronary heart disease, we decided to compare statins with the herbal preparation Abana. Statins even though have proven to be highly effective in treating hypercholesteremia; it has also shown to have adverse effects such as impotence. Abana however, have shown that it is safe and effective in treatment of hypercholesteremia. In a study Abana reduced total cholesterol, triglycerides and LDLc levels in patients with essential hypertension and

angina[18,19]. In other study conducted on lean and obese postmenopausal women showed reduction in all the lipid levels after 12 weeks of therapy with increase in HDL levels[20]. In another study, Abana increased the TC/HDLc ratio and increased HDLc levels thereby indicating that Abana prevents atherosclerosis and reduces the risk of CHD.

Our findings show Abana to have the unique ability to lower serum low density cholesterol levels with lowering of serum triglyceride levels without causing any side effects and the biochemical tests showed that all the parameters were within normal limits before and after treatment. The reduction of all the lipids was more aggressive in patients who were taking Simvastatin. However there was marginal increase in the liver function tests.

CONCLUSION
According to our results, Abana and Simvastatin both produce significant reduction of cholesterol and triglycerides. The fact that Simvastatin group had marginally increased incidence of side-effects, Abana would be a safer alternative.

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