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Regression of coronary artery disease with lipid-lowering therapy

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Abstract
Background: The prevalence of CAD has progressively increased in India during latter half of the last century particularly among the urban population. The present study assessed regression of coronary artery disease as a result of intensive lipid-lowering therapy in men.
Materials and Methods: 60 males with coronary artery disease and elevated apolipoprotein B level were classified according to triglyceride level: 73 with less than 2.3 mmol per liter [200 mg per deciliter], and 59 with more than 2.3 mmol per liter) into 3 groups. Group I was treatment with niacin and colestipol, group II treatment with lovastatin and colestipol, and group III with conventional therapy. Patients in group I received Colestipol 10 g three times a day after 10 days and niacin 500 mg four times a day for one month. In group II, 20 mg Lovastatin twice a day was given and Colestipol as given above and in group III, patients received placebos for colestipol and for lovastatin, given as described above.
Results: Age group 20-40 years had 8 in group I, 9 in group II and 10 in group III and 40-60 years had 12 in group I, 11 in group II and 10 in group III. The mean percentage change in stenosis in group I was 2.0, in group II was -0.8 and in group III was -0.9. The difference was significant ($P< 0.05$).
Conclusion: Patients with coronary artery disease who were at high risk for cardiovascular events, intensive lipid-lowering therapy reduced the frequency of progression of coronary lesions, increased the frequency of regression, and reduced the incidence of cardiovascular events.

Keywords: Coronary artery disease, cardiovascular events, lipids

Introduction
The prevalence of CAD has progressively increased in India during latter half of the last century particularly among the urban population. Premature CAD is defined as cardiac events occurring before the age of 45 in men and 55 in women. In its severe form, it is defined as CAD occurring below the age of 40 years. Cardiovascular disease is the leading cause of death in India accounting for 28% of mortality. Risk of CAD in Indians is 3-4 times higher than White Americans [1].
Recent estimates suggest that 80 per cent of CVD deaths occur in developing countries with substantial contribution from India [2]. This high burden is largely ascribed to the industrial and technological progress and the associated economic and social transformations. In India, the estimated adult prevalence of coronary heart disease (CHD) is around 8-10 per cent in urban settings and 3-4 per cent in rural areas, reflecting a rise of six-fold and two-fold respectively between 1960 and 2000 [3].
Cardiovascular benefits are related to the degree of reduction in the low-density lipoprotein (LDL) cholesterol level and possibly to the degree of increase in the high-density lipoprotein (HDL) cholesterol level. However, changes in lipid levels have usually been small, and the overall clinical benefits have been limited; thus, the interpretation of the study results has been the subject of controversy. A related question is whether the progression of atherosclerosis can be retarded or reversed by such treatment [4]. The appearance in the 1980s of more effective therapies for hyperlipidemia, new arteriographic methods for assessing atherosclerosis, and new insights into atherogenesis helped in searching this question [5]. The present study assessed regression of coronary artery disease as a result of intensive lipid-lowering therapy in men.

Materials and Methods
The present study comprised of 60 males with coronary artery disease and elevated apolipoprotein B level. All gave their written consent for the participation in the study.

Data such as name, age etc. was recorded in case sheet. Patients were classified according to triglyceride level: 73 with less than 2.3 mmol per liter [200 mg per deciliter], and 59 with more than 2.3 mmol per liter) into 3 groups. Group I was treatment with niacin and colestipol, group II treatment with lovastatin and colestipol, and group III with conventional therapy. Patients in group I received Colestipol 10 g three times a day after 10 days and niacin 500 mg four times a day for one month. In group II, 20 mg Lovastatin twice a day was given and Colestipol as given above and in group III, patients received placebos for colestipol and for lovastatin, given as described above.

A dietitian counseled each patient for 20 minutes at each visit. Dietary goals, which were the same for each group, were keyed to the American Heart Association's target levels I and II. Three-day food records, completed before counseling and after 12 months of treatment, were coded and analyzed for calorie, cholesterol, and fat intake. Bruce protocol exercise-tolerance testing [39] was performed at the time of study entry. The duration of exercise, hemodynamic response, symptoms, and ST—T changes were recorded in a standard fashion. Arteriography was also performed. Plasma very-low-density lipoprotein (VLDL), LDL, and HDL cholesterol, triglycerides, and apolipoprotein B were measured at base line, at one and two years during therapy, and six weeks after the end of therapy. Results thus obtianed were subjected to statistical analysis. P value less than 0.05 was considered significant.

Results

Table I: Distribution of patients

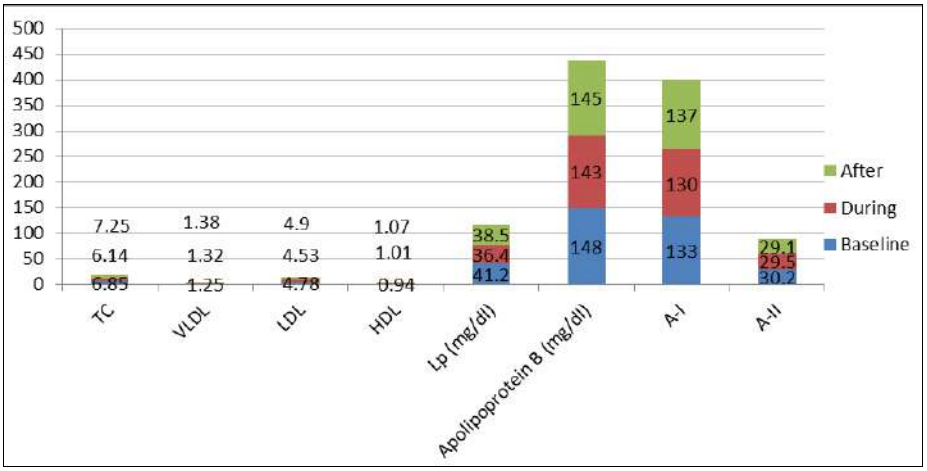
Age group (years)	Group I	Group II	Group III
20-40	8	9	10
40-60	12	11	10

Table I shows that age group 20-40 years had 8 in group I, 9 in group II and 10 in group III and 40-60 years had 12 in group I, 11 in group II and 10 in group III.

Table II: Assessment of lipid and lipoprotein levels in group I

Parameters (mmol/l)	Baseline	During	After	P value
TC	6.85	6.14	7.25	0.05
VLDL	1.25	1.32	1.38	0.12
LDL	4.78	4.53	4.90	0.17
HDL	0.94	1.01	1.07	0.04
Lp (mg/dl)	41.2	36.4	38.5	0.02
Apolipoprotein B (mg/dl)	148	143	145	0.11
A-I	133	130	137	0.82
A-II	30.2	29.5	29.1	0.90

Table II, graph I shows that mean TC (mmol/l) at baseline, during treatment and after treatment was 6.85, 6.14 and 7.25, VLDL was 1.25, 1.32 and 1.38, LDL was 4.78, 4.53 and 4.90, HDL was 0.94, 1.01 and 1.07, Lp (mg/dl) was 41.2, 36.4 and 38.5, Apolipoprotein B was 148.143 and 145, A- I was 133, 130 and 137 and A- II was 30.2, 29.5 and 29.1 respectively. The difference was significant (P< 0.05).



Graph I: Assessment of lipid and lipoprotein levels in group I

Table III: Assessment of lipid and lipoprotein levels in group II

Parameters (mmol/l)	Baseline	During	After	P value
TC	7.12	4.05	7.33	0.04
VLDL	1.20	0.94	1.21	0.01
LDL	5.04	2.65	5.32	0.05
HDL	0.92	1.12	1.14	0.05
Lp (mg/dl)	0.09	0.14	0.12	0.11
Apolipoprotein B (mg/dl)	153	100.4	65.5	0.91
A-I	128	107	132	0.82
A-II	28.9	28.2	28.7	0.94

Table III shows that mean TC (mmol/l) at baseline, during treatment and after treatment was 7.12, 4.05 and 7.33, VLDL was 1.20, 0.94 and 1.21, LDL was 5.04, 2.65 and 5.32, HDL was 0.92, 1.12 and 1.14, Lp (mg/dl) was 0.09, 0.14 and 0.12, Apolipoprotein B was 153, 100.4 and 65.5, A- I was 128, 107 and 132 and A- II was 28.9, 28.2 and 28.7 respectively. The difference was significant (P< 0.05).

Table IV: Assessment of lipid and lipoprotein levels in group III

Parameters (mmol/l)	Baseline	During	After	P value
TC	6.83	5.42	7.12	0.04
VLDL	1.10	0.62	1.14	0.01
LDL	4.52	3.62	5.12	0.05
HDL	1.02	1.25	1.83	0.05
Lp (mg/dl)	32.5	24.9	29.2	0.11
Apolipoprotein B (mg/dl)	156	112	112	0.91
A-I	132	152	180	0.82
A-II	29.4	28.0	31.4	0.94

Table IV shows that mean TC (mmol/l) at baseline, during treatment and after treatment was 6.83, 5.42 and 7.12,

VLDL was 1.10, 0.62 and 1.14, LDL was 4.52, 3.62 and 5.12, HDL was 1.02, 1.25 and 1.83, Lp (mg/dl) was 32.5, 24.9 and 29.2, Apolipoprotein B was 156, 112 and 112, A- I was 132, 152 and 180 and A- II was 29.4, 2802 and 31.4 respectively. The difference was significant ($P< 0.05$).

Table V: Assessment of mean percentage change in stenosis

Groups	Mean	P value
Group I	2.0	0.001
Group II	-0.8	
Group III	-0.9	

Table V shows that mean percentage change in stenosis in group I was 2.0, in group II was -0.8 and in group III was -0.9. The difference was significant ($P< 0.05$).

Discussion

It is widely believed that the association of these risk factors with CAD in other populations needs to be ascertained, and there is speculation that differences might range from the frequency of presence of classical risk factors to their total absence or irrelevance in these populations. Therefore, it is imperative to undertake large population-based, prospective studies in developing countries such as India to identify CAD risk factors, both conventional and novel [6, 7]. However, careful scrutiny of available scientific evidence for modifiable CAD risk factors (elevated serum total and low-density lipoprotein cholesterol [LDL-C], low high-density lipoprotein cholesterol [HDL-C], smoking, diabetes, hypertension, low level of physical activity, and obesity) in this population may be helpful in formulating a more immediate CAD prevention strategy + [8]. The present study assessed regression of coronary artery disease as a result of intensive lipid-lowering therapy in men.

We found that age group 20-40 years had 8 in group I, 9 in group II and 10 in group III and 40-60 years had 12 in group I, 11 in group II and 10 in group III. Brown *et al*. [9] assessed effect of intensive lipid-lowering therapy on coronary atherosclerosis among men at high risk by quantitative arteriography. Of 146 men no more than 62 years of age who had apolipo protein B levels greater than or equal to 125 mg per deciliter, documented coronary artery disease, and a family history of vascular disease, 120 completed the 2 1/2-year double-blind study, which included arteriography at base line and after treatment. Patients were given dietary counseling and were randomly assigned to one of three treatments: lovastatin (20 mg twice a day) and colestipol (10 g three times a day); niacin (1 g four times a day) and colestipol (10 g three times a day); or conventional therapy with placebo (or colestipol if the low-density lipoprotein [LDL] cholesterol level was elevated). The levels of LDL and high-density lipoprotein (HDL) cholesterol changed only slightly in the conventional-therapy group (mean changes, -7 and +5 percent, respectively), but more substantially among patients treated with lovastatin and colestipol (-46 and +15 percent) or niacin and colestipol (-32 and +43 percent). In the conventional-therapy group, 46 percent of the patients had definite lesion progression (and no regression) in at least one of nine proximal coronary segments; regression was the only change in 11 percent.

We observed that mean TC (mmol/l) at baseline, during treatment and after treatment was 6.85, 6.14 and 7.25, VLDL was 1.25, 1.32 and 1.38, LDL was 4.78, 4.53 and 4.90, HDL was 0.94, 1.01 and 1.07, Lp (mg/dl) was 41.2, 36.4 and 38.5, Apolipoprotein B was 148.143 and 145, A- I was 133, 130 and 137 and A- II was 30.2, 29.5 and 29.1 respectively. The mean TC (mmol/l) at baseline, during treatment and after treatment was 7.12, 4.05 and 7.33, VLDL was 1.20, 0.94 and 1.21, LDL was 5.04, 2.65 and 5.32, HDL was 0.92, 1.12 and 1.14, Lp (mg/dl) was 0.09, 0.14 and 0.12, Apolipoprotein B was 153, 100.4 and 65.5, A- I was 128, 107 and 132 and A- II was 28.9, 28.2 and 28.7 respectively. mean TC (mmol/l) at baseline, during treatment and after treatment was 6.83, 5.42 and 7.12, VLDL was 1.10, 0.62 and 1.14, LDL was 4.52, 3.62 and 5.12, HDL was 1.02, 1.25 and 1.83, Lp (mg/dl) was 32.5, 24.9 and 29.2, Apolipoprotein B was 156, 112 and 112, A- I was 132, 152 and 180 and A- II was 29.4, 2802 and 31.4 respectively. We observed that mean percentage change in stenosis in group I was 2.0, in group II was -0.8 and in group III was -0.9. In laboratory studies, the depletion of lipids or connective tissue in plaque or the fibrous transformation of the myointimal cellular response has been shown to diminish the size of plaques [10]. Panwar *et al.* [11] assessed the relationship between atherothrombotic risk factors and premature CHD in young (<55 yr age) Indian population. One of the main findings is that both thrombotic (smoking, low fruit/vegetables intake, fibrinogen, homocysteine) and atherosclerotic (hypertension, high fat diet, dyslipidaemia) risk factors are significant in causing premature CHD in Indian population.

Conclusion

Authors found that patients with coronary artery disease who were at high risk for cardiovascular events, intensive lipid-lowering therapy reduced the frequency of progression of coronary lesions, increased the frequency of regression, and reduced the incidence of cardiovascular events.

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