CHANGES IN BLOOD LIPIDS DURING ANTI-HYPERTENSIVE TREATMENT*

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Abstract

Serum lipids were monitored before and after anti-hypertensive therapy in 51 patients suffering from essential hypertension. After 1-1/2 years of treatment with methyldopa, a rise was noted in total lipids and triglycerides. There were no significant changes in the levels of phospholipids, free fatty acids and esterified free fatty acids while serum cholesterol values fell significantly. The implication of these findings is discussed.

Introduction

Most commonly used anti-hypertensive drugs exert their therapeutic effect by interfering with the sympathetic nervous system. This component of the nervous system is known to be involved in mobilization of lipids and thus may have a significant influence on the lipid metabolism and their blood levels.

The treatment of hypertension has resulted in a fall in the incidence of deaths caused by cerebrovascular accidents, renal impairment and congestive heart failure. However, it has been shown that there is an apparent increase in the number of deaths due to coronary heart disease following treatment of hypertension. In view of the well known association of serum lipids in the genesis of atherosclerosis, the possible changes in serum lipids following antihypertensive therapy may be of some importance. There is a relative paucity of reports on the behaviour of serum lipids during anti-hypertensive therapy and in this study we have attempted to monitor different fractions of blood lipids in 51 hypertensive patients before and after drug therapy.

Material and Methods

51 patients (26 males and 25 females), between the ages of 27 and 64 years were studied. All these subjects had a diastolic blood pressure of 110 mm of Hg or more, checked on three separate occasions. They had not received any anti-hypertensive therapy previously and none was obese or had clinical evidence of atherosclerosis. Clinical and laboratory evidence confirmed that these patients had essential hypertension with normal renal function. Also, there was no evidence of myxoedema, nephrotic syndrome or gout Study of blood lipids was done before and 1-1/2 years after anti-hypertensive therapy. Methyldopa was the main drug used, while diuretics were added in a few patients according to clinical situation. No special dietary instructions were given.

Blood was drawn in the fasting state for estimation of serum lipids which included total lipids, triglycerides, cholesterol, phospholipids, free fatty acids and esterified fatty acids. The following methods were used for the estimation of various lipid fractions:—

(*a*) Total lipids were estimated by sulpho-phosphovaniline method described by Chabrol and Charonet and modified by Zollner and Kirsch (1962).
(*b*) Triglyceride estimation was done by Royer and Ko's procedure (1969).
(*c*) Serum cholesterol was estimated by Leffler and McDougald's method (1963).
(*d*) Fiske and Subbarow's method (1925) was used for estimation of phospholipids.
(*e*) The free fatty acid levels were measured by the method of Duncombe (1964) while levels of esterified free fatty acids were determined by the method of Stern and Shapiro (1953).

Results

1. *Total Lipids* (*Table I*):-In the group as a whole, the total serum lipids increased from 967±163 mg% to 1093±187 mg%. This rise was significant ($P < 0.001$). When serum total lipids were assessed separately for males and females, the rise was again found to be significant ($P < 0.05$) in both the sexes.

Table I: Changes in Serum Total Lipids in Hypertensive Patients before and after Anti-Hypertensive Treatment.

2. *Serum Triglycerides* (*Table II*):-There was an overall increase in the mean triglycerides from the pre-treatment values of 224±57 mg% to 250±57 mg% ($P < 0.05$). A similar significant rise ($P < 0.05$) was observed when the mean triglyceride values were compared separately in either sex.

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Table IV: Changes in Serum Phospholipids before and after Treatment in Hypertensive Patients.

Patients		*Total Lipids*		*Significance*	*Patients*		*Phospholipids*		*Significance*
		Before treatment (mg%) Mean±SD	*After treatment (mg%) Mean±SD*				*Before treatment (mg%) Mean±SD*	*After treatment (mg%) Mean±SD*	
Female	(25)	1035 ±154	1133 ±183	$P < 0.05$	Female	(25)	272 ± 46	281 ± 48	Not significant
Male	(26)	899 ±141	1051 ±180	$P < 0.05$	Male	(26)	249 ± 34	260 ± 32	Not significant
Total Patients	(51)	967 ±163	1093 ±187	$P < 0.001$	Total Patients	(51)	261 ± 42	272 ± 42	Not significant

Table II: Changes in Serum Triglycerides in Hypertensive Patients before and after Treatment

Patients		*Serum Triglycerides*		*Significance*
		Before treatment (mg%) Mean ± SD	*After treatment (mg%) Mean ± SD*	
Female	(25)	241 ± 53	265 ± 51	P ≤ 0.05
Male	(26)	205 ± 55	232 ± 58	P ≤ 0.05
Total Patients	(51)	224 ± 57	250 ± 57	P ≤ 0.05

3. *Serum Cholesterol* (*Table III*):- The mean serum cholesterol values in the total group fell from the pre-treatment values of 263±42 mg% to 245±30 mg% (P <0.05). A similar significant fall was noted in the group of female patients. In the males, although the mean values decreased from 248±39 mg% to 236±30 mg%, the difference was not significant.

Table III: Changes in Serum Cholesterol in Hypertensive Patients before and after Treatment.

Patients		*Serum Cholesterol*		*Significance*
		Before treatment (mg%) Mean ± SD	*After treatment (mg%) Mean ± SD*	
Female	(25)	278 ± 39	250 ± 30	P <0.05
Male	(26)	248 ± 39	236 ± 30	Not significant
Total Patients	(51)	263 ± 42	245 ± 30	P <0.05

4. *Serum Phospholipids* (*Table IV*):-In the total group, there was a small rise in the mean serum phospholipids from the pre-treatment values of 261±42 mg% to 272±42 mg% but the difference was not significant. A similar small but non-significant rise in the mean serum phospholipid values was seen when comparisons were made separately in two sexes.

5. *Free Fatty Acids and Esterified Free Fatty Acids*:-There was small but non-significant decrease in the mean free fatty acids level from 26±4 mg% to 24±4 mg% in the whole group. A similar non-significant fall was noted in the two sexes assessed separately. The esterified free fatty acids showed a non-significant rise in the mean values from 331±120 mg% to 355±123 mg%. A similar trend was noted in the males and females assessed separately.

6. *Lipoprotein Electrophoresis*:-Lipoprotein electrophoresis was done in only 5 patients but no changes were observed in the lipoprotein pattern during treatment with anti-hypertensive drugs.

Table V: Changes in Free Fatty Acid in Hypertension before and after Treatment

Patients		*Free fatty acids*		*Significance*
		Before treatment (mg%) Mean ± SD	*After treatment (mg%) Mean ± SD*	
Female	(25)	27 ± 4	25 ± 4	Not significant
Male	(26)	25 ± 4	22 ± 4	Not significant
Total Patients	(51)	26 ± 4	24 ± 4	Not significant

Table VI: Changes in Esterified Free Fatty Acids in Hypertensive Patients before and after Treatment

Patients		*Esterified free fatty acids*		*Significance*
		Before treatment (mg%) Mean ± SD	*After treatment (mg%) Mean ± SD*	
Female	(25)	368 ±112	392 ±110	Not significant
Male	(26)	300 ±118	310 ±104	Not significant
Total Patients	(51)	331 ±120	355 ±123	Not significant

Discussion

There are few studies in which behaviour of lipids during anti-hypertensive therapy has been studied. Libman et al. (1974) studied blood lipids in 8 previously untreated hypertensives, before and after treatment with methyldopa and bendrofluazide. These workers did not find any significant changes in lipid profile after over 5 months of therapy. On the other hand Ames and Hill (1976a&b) in a study comprising of 63 patients with uncomplicated hypertension found a significant rise of serum cholesterol and triglycerides in 32 patients receiving chlorthalidone as compared to 31 patients who did not receive drug therapy. These workers also observed that overall increase in serum lipids was accounted for by a notable increase in lipids in a subgroup of 15 patients which was aptly called a 'dicotomous response'.

In our study methyldopa was the main stay in the treatment and diuretics were used episodically in a few patients. In this study we were able to document a significant rise in total lipids and triglycerides. On the other hand no significant change was noticed in free fatty acids, esterified free fatty acids and phospholipids while serum cholesterol values fell generally.

The precise mechanism of these findings remains unclear and obviously more studies are needed to confirm these observations. The

clinical implications of the alterations in serum lipids are difficult to evaluate at present. Serum lipids have a well recognised role in the pathogenesis of atherosclerosis. In hypertension, life long therapy is required and small increase in various lipid fractions if sustained over a long period could possibly have a cumulative effect.

There is some evidence that raised serum lipids may be more common in patients with hypertension (Thomas et al., 1977). Viewed in this context it may be important to be aware of the possible changes in lipids that may be brought about by anti-hypertensive drugs.

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References

Ames, R.P. and Hill, P. (1976a) Increase in serum lipids during the treatment of hypertension with chlorthalidone. Lancet, 1:721.

Ames, R.P. and Hill, P. (1976b) Elevation of serum lipid levels during diuretic therapy of hypertension. Am. J. Med., 61:748.

Duncombe, W.G. (1964) The colorimetric microdetermination of non-esterified fatty acid in plasma. Clin. Chim. Acta, 9:122.

Fiske, C.H. and Subbarow, Y. (1925) The colorimetric determination of phosphorus. J. Biol. Chem., 66:375.

Leffler, H.H. and Mc Dougald, C.H. (1963) Estimation of cholesterol in serum; by means of improved technics. Am. J. Clin. Path., 39:311.

Libman, L.J., Arrowsmith, D.E., Dormandy, T.L., Heal, J. and Hoffbrand, B.I. (1974) Blood lipids and treatment of essential hypertension with methyldopa and bendrofluazide. Postgrad. Med. J., 50:671.

Royer, M.E. and Ko, H. (1969) A simplified semiautomated assay for plasma triglycerides. Anal. Biochem., 29:405.

Stern, I. and Shapiro, B. (1953) A rapid and simple method for the determination of esterified fatty acids and for total fatty acids in blood. J. Clin. Path., 6:158.

Thomas, G.W., Mann, J.I., Beilin, L.T. and Ledingham, T.G. (1977) Hypertension and raised serum lipids. Br. Med. J., 2:781.

Zollner, N. and Kirsch, K. (1962) Colorimetric determination of total serum lipids. Medizin, 135:545.