Serum Cholesterol Binding Reserve in Hypertension: Its Role in Atherogenesis *

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SUMMARY:

Serum cholesterol binding reserve (SCBR) depicts an intrinsic capacity of human plasma to solubilize the additional cholesterol and hence to act as a possible carrier of cholesterol in 'reverse cholesterol transport' in atherosclerosis regression. To study its correlation with hypertension. 56 hypertensives, with and without atherosclerotic vascular complications (old myocardial infarction and atherothrombotic cerebral stroke) were compared with 46 nonhypertensives with their serum cholesterol binding reserve percentage values. Mean serum cholesterol values were not different in various groups. Mean SCBR% of hypertensives (34.8±8.0), was significantly different from that of nonhypertensives (49.9±9.1), but was not different from SCBR% of nonhypertensives complicated by atherosclerotic complications, (37.9±7.4). This indicates that despite similar serum cholesterol levels, lower levels of serum cholesterol binding reserve percentage may be underlying pathophysiological mechanism for enhanced atherogenesis in hypertension, besides the raised level of blood pressure.

INTRODUCTION

Hypertension is one of the major risk factors for atherogenesis(1). Raised level of serum cholesterol is another risk factor(2). The interrelationship of hypertension and serum lipid profile is not well established, but combined together, they lead to accelerated atherosclerosis and its various lethal complications(3).

Serum cholesterol binding reserve (SCBR) is postulated to be an inherent capacity of human plasma to solubilize additional cholesterol, and thus to act as a carrier for cholesterol in reverse cholesterol transport(4,5). Reduced SCBR levels have been shown to be associated with premature atherosclerosis leading to myocardial infarction in younger age group(4). It has also been shown to be reduced in diabetics who are at a higher risk of developing early atherosclerosis and its complications(6).

In present study serum cholesterol and SCBR% was estimated in hypertensives to study the probable underlying pathophysiology for atherogenesis in these individuals.

MATERIAL AND METHODS

One hundred and two patients were taken for the study from amongst those admitted to this centre. They were divided into two groups. Group I consisted of 56 patients of mild and moderate essential hypertension diagnosed on the criteria laid by WHO(7). None of these patients were having any detectable underlying etiology for hypertension on routine preliminary screening. They were further subgrouped

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into two, group IA consisting 26 uncomplicated hypertensives and group IB consisting 30 patients with atherosclerotic complications: 15 with established old myocardial infarction and 15 others with atherothrombotic cerebral infarction. Group II comprised of the 46 non-hypertensive patients with minor ailments admitted to this hospital. They also consisted of 13 patients with old myocardial infarction in group IIB to serve as control for group IB. Remaining 18 uncomplicated nonhypertensives comprised group IIA. None of them were having renal disease, liver disease, diabetes mellitus, thyrotoxicosis, nephrotic syndrome, pregnancy or obesity. No patient was on potential lipid altering drugs.

All patients were subjected to detailed clinical examination and routine investigations to rule out secondary hypertension. All the hypertensives were then shifted randomly to alphamethyl dopa (500-2000 mg/day) or and clonidine (150-400 mg/day) for 4 weeks for controlling blood pressure. Samples for serum cholesterol estimation were drawn after the end of that period. Samples from control group were also collected.

In all of them, serum cholesterol was measured within 24 hours by Zlatkis method(8). SCBR was then measured by incubating patients, serum with exogenously added pulverized cholesterol for 24 hours at 37°C and then serum cholesterol content was measured after the filtration of undissolved cholesterol from the incubated serum. The difference of the cholesterol contents of serum before and after the incubation was termed as SCBR. SCBR, when expressed as percentage of serum cholesterol was termed as SCBR percentage (SCBR%).

Values for analysis and comparison were expressed as mean±standard deviation and the significance was assessed by student's 'p' test.

OBSERVATIONS

Characteristics of study group A, are given in Table 1. It comprised of 30 males and 26 females, with a mean age of 56.4±12.3 years. Table 2 demonstrates that there was no significant difference in the values of serum cholesterol and SCBR% when males and females were compared in the same group.

TABLE – 1

Total number	56
Males	30
Females	26
Mean Age (years)	56.4 ± 12.3
Mild Hypertensives (diastolic BP 95-104 mm Hg)	24
Moderate Hypertensives (Diastolic BP 105-114 mm Hg)	32
Uncomplicated Hypertensives	26
Complicated Hypertensives	30
Myocardial infarction	15
Atherothrombotic stroke	15

Table 1 : Characteristics of Study Group I.

There was statistically no significant difference in serum cholesterol levels in group I and group II, though group II patients were having apparently higher mean serum cholesterol level (Table 3).

Further analysis of Table 3 shows that mean

TABLE – 2

Group	Subgroup	S. Cholesterol (mg%)	SCBR%
I	Males (n=30)	182.8 ± 18.7	34.6 ± 8.5
	Females (n=26)	194.6 ± 22.6	35.1 ± 6.8
II	Males (n=25)	179.5 ± 19.3	58.3 ± 9.3
	Females (n=21)	176.8 ± 17.3	63.1 ± 8.6

Table 2 : Serum Cholesterol and SCBR% in different sex in study groups.

TABLE – 3

Group	Subgroup	S. Cholesterol (mg%)	SCBR%
I	A (n = 26)	179.6 ± 21.6	35.4 ± 8.2
	B (n = 30)	193.8 ± 19.9	33.7 ± 8.1
	Total (n = 56)	188.5 ± 22.4	34.8 ± 8.0
II	A (n = 18)	172.4 ± 18.7	65.9 ± 10.2
	B (n = 28)	185.8 ± 23.4	37.9 ± 7.4
	Total (n = 46)	178.5 ± 26.3	49.9 ± 9.1

Table 3 : Serum Cholesterol and SCBR% in study subgroups.

SCBR% of group I was significantly lower than that of group II, ($p < 0.05$). SCBR% of subgroup IA and subgroup IB were not different from each other, and from group IIB, but they were significantly lower from group IIA ($p < 0.001$). This indicates that hypertensive patients, whether uncomplicated or complicated were having similar serum cholesterol level and SCBR% as compared to complicated non-hypertensive patients.

DISCUSSION

Atherosclerotic cardiovascular disease is major vascular sequalae of hypertension and coronary heart disease is the most common such outcome(1). Increased blood pressure as a mechanical factor is evidently a critical factor in atherogenesis(9). On the other hand, a number of studies indicate the role of catecholamines, renin and angiotensin, mineralocorticoids, dietary sodium, serotonin, histamin and bradykinin in alterning the cellular metabolism of arterial wall and producing the vascular damage causing atherosclerosis. But atherosclerotic lesions seldom develop in low pressure segments of circulation such as veins or the pulmonary artery despite being faced to the same internal metabolic malieu as the systemic arterial circuit(12). Blood pressure predisposes to two major complications: an atherothrombotic cerebral infarction and myocardial infarction. Mere presence of these two complications establishes atherosclerosis as the only primary underlying cause.

The lipoproteins are fundamental to the atherosclerotic process and they greatly influence the impact of hypertension on the pace of atherosclerosis. An association of serum total cholesterol and enhanced rate of occurrence of atherosclerotic coronary artery disease is well recognized in hypertensives(2,13). But serum cholesterol has not shown any constant liner relation with levels of blood pressure. Normal as well as raised levels of cholesterol has been reported in hypertensives(9,14), but it is established beyond doubt, that when combined together, they lead to rapidly progressing atherosclerosis(3).

Attention has also been paid to the possibility of efflux of cholesterol from arterial wall regulating the process of atherosclerosis regression(15). Possible significance of HDL in transporting the cholesterol out of arterial wall has been suggested(15). In search of other serum factors that might take up the mobilized cholesterol from arterial wall, Hsia et al found that human sera is capable of dissolving exogenously added cholesterol(4). This capacity of sera was termed as 'serum cholesterol binding reserve'. The chemical nature of SCBR, when investigated revealed that two sub-fractions of lipoprotein — SFV (subfraction of very low density lipoprotein) and SFH (subfraction of high density lipoprotein) collectively are responsible for solubilizing and carrying extra cholesterol(4). The combined amount of SFV and SFH constituted about 80% of SCBR. Since SFV and SFH are normal constituents of human sera, they are the most likely candidates to function as vehicle in reverse cholesterol transport(16). This leads to conclusion that persons with low SCBR will have reduced cholesterol clearance from the arterial wall — since the cholesterol carrier will be comparably less in quantity in their sera, and thus they will be at a higher risk of developing atherosclerotic complications.

SCBR has been shown to be significantly diminished in myocardial infarction and diabetes mellitus (4,6). This has also been shown to be diminished in obesity and smokers(17).

Our study did not show any significant difference in serum cholesterol values in different

groups. But SCBR% in hypertensives was found to be significantly lower than non-hypertensives. Non-hypertensive controls with atherosclerotic complications have similar SCBR% values as those of hypertensives — whether complicated or uncomplicated, but predictably their SCBR% values are significantly lower than those of uncomplicated non-hypertensives. This indicates that same underlying pathophysiology is involved in genesis of atherosclerotic complication which is not dependent on the level of blood pressure. Lower SCBR% level in them is a common denominator. This shows that low SCBR% which has been proved to be an indicator of risk of atherogenesis in myocardial infarction and diabetes mellitus may be taken as a indicator of ongoing enhanced atherosclerosis in hypertensive patients. It should be considered a better parameter than serum cholesterol levels while assessing the risk of development of atherosclerotic complications in them.

REFERENCES:

1. Kannel WB. Hypertension and other risk factors in coronary heart disease. Am Heart J. 1987; 114: 989.
2. Kannel WB & Castelli WP. Cholesterol in prediction of cardiovascular disease, new perspectives based on Framingham study. Ann Int Med. 1979; 90 : 85.
3. Kannel WB. Hypertension — a component of cardiovascular risk profile. Proceedings II International Congress on Hypertension. 1977, Hoechst Pharma. Bombay.
4. Hsia SL, Chao, Yu-Shen, Heenekens, Charles H, Reader WB. Decreased serum cholesterol binding reserve in premature myocardial infarction. Lancet 1975, ii: 1000.
5. Hsia SL, Briese F, Hoffman J. Serum cholesterol binding reserve and myocardial infarction. Lancet 1976; i: 799.
6. Hsia SL, Fishman LM, Briese F, Christakis G, Burr J, Bricker LA. Decreased serum cholesterol binding reserve in Diabetes mellitus. Diabetes Care 1978; 1: 2: 89.
7. WHO Expert Committee on arterial hypertension, WHO Technical Series Report No. 628, 1978.
8. Zlatkis A, Zak B, Boyle AJ. A new method for direct estimation of serum cholesterol. J Lab Clin Med. 1953; 41: 486.
9. Hollander W. Hypertension, antihypertensives and atherosclerosis. Circulation 1973; 48: 112.
10. Lorenzen NL, Garbarsch C, Mathiessen ME. Arteriosclerosis in rabbit aorta induced by norepinephrine, Atherosclerosis 1979; 12: 125.
11. Hollander W, Kramsch DM, Yagi S. In-vitro effects of vasopressor agents on metabolism of the vascular wall. Circulation 1964; 30 (Suppl. II): 1.
12. Glagov S & Ozoa A. Significance of relatively low incidence of atherosclerosis in pulmonary mesentric & renal arteries. Ann N Y Acad Sci. 1968; 149: 940.
13. Kannel WB. Nutritional contributors to cardiovascular disease in the elderly. J Am Geriatr Soc 1986; 34: 27.
14. Weisner RL, Fuchs RJ, Kay TD, Treibwasee R, Lancaster MC, Body fat : its relationship to coronary heart disease, blood pressure, lipids and other risk factors measured in large male population. Am J Med 1976; 61: 815.
15. Miller GJ, Miller NE. Plasma high density lipoprotein concentration and development of ischemic heart disease. Lancet 1975, i: 16.
16. Iverius PH. The interaction between human plasma lipoproteins and connective tissue glycosaminoglycons. J Biol Chem 1972; 247: 2607.
17. Chandra R, Singh R, Alam SM, Agarwal BD, Srivastava DK, Gupta SK. A study of SCBR in cases of diabetes mellitus, hypertension, obesity and smokers. J Asso Phys Ind. 1979; 27: 884.