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Original article:

Effect of beta blocker – atenolol on lipid profile in hypertensive patients

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Abstract:

Hypertension is emerging as a serious public health problem in developing countries. It is estimated that more than 40 million people suffer from high blood pressure in India. The adverse lipid profile could decrease the coronary heart disease risk reduction from lowering blood pressure with these drugs. The cardio selective beta blocker Atenolol is commonly used as first line drug in the treatment of hypertension in out hospital Government General Hospital, Kakinada. The study was undertaken to examine the effects of Atenolol on blood lipids. Thirty patients of essential hypertension were treated with atenolol and thiety were propronolol. Lipoprotein alternations were measured in all patients at 0,4 and 8 weeks of therapy in each group. It was concluded from the study that there was no alternation in lipid profile pattern in atenolol treated group. The total cholesterol and LDL were significantly increased at 8 weeks of therapy with propronolol. There was no alternation in TGL, VLDL and HDL cholesterol in the propronolol treated group. There was no significant difference in atherogenic index in both the groups during the treatment period.

Introduction:

Hypertension is emerging as a serious public health problem in developing countries. It is estimated that more than 40 million people suffer from high blood pressure in India. World Health Organization reported that in adults aged 40-55 years blood pressure levels were the highest among Indian men as compared to those of 20 other developing countries. In India urban population who are being exposed to stress of acculturation and modernization the hypertension prevalence rates have more than doubled in the last 30 years. In South India the prevalence has been reported as high as 17% compared to North India shows 10% prevalence. Hypertension carried increased risk of cerebrovacular disease and coronary heart disease and is 2nd only to diabetes as the most important cause of renal failure. Treatment of hypertension with the first line agents diuretics and beta blockers has been shown to r educe morbidity and mortality from cardiovascular disease. The treatment of mild hypertension study showed that while reduction in stroke was consistent with expectation based on epidemiologic data. The reduction in coronary heart disease was less than expected. One hypothesis to explain this discrepancy was adverse effects on blood lipids associated with diuretics and beta blockers especially when no concurrent nutritional hygienic intervention is undertaken to limit or prevent these effects on lipids. The adverse lipid profile could decrease the coronary heart disease risk reduction from lowering blood

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pressure with these drugs. The cardio selective beta blocker Atenolol is commonly used as first line drug in the treatment of hypertension in out hospital Government General Hospital, Kakinada. The study was undertaken to examine the effects of Atenolol on blood lipids.

Materials and methods:

The study was conducted on patients suffering from essential hypertension attending medical OP of Government General Hospital, Kakinada. The laboratory investigations were carried out at biochemistry department. 60 patients established essential hypertension were recruited ito two groups each group consisting of 30 patients. One group assigned to propronolol and the other to attenelol. These 30 patients included 21 males And 9 females. The lipid profile was estimated at the time of entry, 4 weeks and the end of 8 weeks in both the groups. All patients were examined clinically and blood pressure was recorded at each visit. The other laboratory parameters including chest X-ray and ECG were taken at the time of entry. At 4 weeks and the end of 8 weeks in both the groups.

From the patients attending medical OP at Government General Hospital, Kakinada 30 patients for each group were selected for the present study. They all satisfied the JNC-VII criteria. They were untreated earlier and had an established high BP (SBP+DBP) readings for 3 readings prior of diastolic blood pressure in excess of 90 mm/hg prior to the enry into the present study. Urine,Albumin, and Sugar, microscopic examination, blood urea, serum creatinine were estimated. Chest X-ray, ECG were taken at the time of entry. Physical examination including height in inches and weight in Kgs were taken.

Blood Pressure readings were taken with random zero sphygmomanometer after resting the patient for 30 minutes on a couch in lying down position at 'O' 4 weeks and 8 weeks of treatment. The patient were allocated with ropronolol (40-80mg) sustained release preparation or atenelol (50-100mg) randomly.

Lipid profile estimation:

Lipid profile was done in all patients at the time of entry, 4 weeks And 8 weeks of therapy. Total cholesterol. TGL and HDL – C were estimated by enzymatic method using autopack kits. These reagents were manufactured by the standard company Bayer Diagnostics India Limied. Before the procedure. Patients were asked to come on 12 hour over night fasting between 8-9 a.m. Patients were made comfortable for approximately 30 minutes. About 10ml of whole blood was collected and processed with the testing.

1. Cholesterol Estimation**:** Allain CC, et al, 1974; Richmond W, 1973; Tarbuttor PN, et al, 1974

2.Triglycerides estimation: Rossati P. et al,1982,Eggstein M,et al,1974

3.HDL estimation: Lopes,1977, Allain CA,1974,Richmond W,1973, Castelli WP et al,1977,Miller NE,et al,1977 ,Friedewald WT et al,1972

4.The VLDL and LDL fractions are calculated as below Friedwald WT et al ,1972

VLDL = TGL/5

LDL = Total cholesterol – (HDL + VLDL)

Statistical analysis:

The data was analysed by using student –t test for paired values.Prabability value was read from the available tables

Results and observations:

The study sample included 30 in each group and there are two such groups who were suffering from essential hypertension patients of which 21 males and 9 females in the above two groups. For the convenience and

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analysis purpose subjects studied have been divided into two groups.

Gropu-A: This group includes total number of patients suffering from essential hypertension (i.e. 30) to whom atenelol was allocated. Of 30 patients 11 patients received 100mg/day, 19received 50mg/day.

Group-B: This groups includes 30 patients with essential hypertension and were randomized to propronolol. Of them, 12 received 80 mg/day and 18 patients received 40mg/day.

In both the groups the lipid profile was estimated at 3 different intervals. The study period was 8 weeks. The baseline lipid profile would serve as initial as well as the control reading for comparison purpose. Apart from lipid profile the blood pressure readings were recorded at regular intervals.

Group-A: This group represents total number of patients (30) who were randomized to atenolol. Of which 21 were males and 9 females. The mean age of male patients was 50.7,13.3(range 38-65 years) and for females 46±5 years (40-50 years). Tables I,II & III

Table – 1:

Sex	Group A	Group B
Male	21	21
Female	9	9

Table-II: Demographic chart and distribution of patients according to age group.

Age Distribution	Group A	Group B
35-40	3	7
41-45	8	7
46-50	10	8
51-55	3	5
56-60	2	2
>60	4	1
Total	30	30

Table – III: Showing mean age of both groups:

Sex	Mean Age		't'
	Group A	Group B	
Male	F50.7±13.3	45.14±10.98	1.79
Female	46±5	47.2±15	0.41

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Group-B : This group represents the total number of patients (30) who were given propronolol. Of which 21 males and 9 females. Tables I,II and III. The mean age of male patients was 45.14±10.98 years and that of female was 47.2± 15 years. The different between the age group was satistically not significant. of illness of both groups is depicted in Table IV.

Table – IV: Showing the distributuion of duration of illness in month

Group A	14.2±5
Group B	14.8±12

Weight and Height of the Patients:

The weight and height of both groups are depicted in Table V. The mean weight of group A was 62.16±17.98Kg. (range 46 – 82 kgs) and that of group B was 63.8±17.5 kgs (range 45-80 kg). The height of the group A was 5'3.6"±0.47" (range 4' 8"-5' 11") and that of group B was 5' 3.6" ± 0.63" cm (range 4'6"-5'9").

The difference in the twp groups for 2 parametres was statistically not significant

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Table – V: Showing the height and weight differences in two groups.

	Group A	**Group B**	**'t'**	**P**
Height	5'36"±0.47	5'36"±0.63	'p' 'o'	NSD
Weight (kg)	62.16±17.98	63.8±17.5	0.362	NSD

Table – VI: Showing the BP mm/hg. Recordings of Group A and B

Group	**Duration of weeks**		
	0	**4**	**8**
A	170/105 ±40/10	143.5/91.8 ±25/30	125/85 ±30/10
B	160/105 ±20/15	140.8/105.8 ±22.5/13.3	126/84 ±15/12.5

The hypertensive efficacy of both atenelol and propronolol was comparable. Both groups achieved good control of blood pressure by the end of 8 weeks (Table VII). The mean blood pressure at '0' week in group A was 170± 40/105±10 mm/hg. At 4 weeks the mean was 143.5±91.8±30 mm/hg and at 8 weeks it was 125±30/85±10 mm/hg.

In the group B mean blood pressure reading at'0' week 160±20/105±15 mm/hg. At 4 weeks the mean was 140.8±22.5/105.8±13.3mm/hg and at 8 weeks it was 126±15/84±12.5 mm/hg.

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Table – VII: Blood Pressure Control in Group A

	0-4	4-8	0-8
SBP	3.02(SD)	2.55(SD)	4.8(SD)
DBP	2.22(SD)	1.17(NSD)	7.6(SD)

SBP = Systolic Blood Pressure , DBP = Diastolic Blood Pressure , SD = Significant Difference , NSD = No Significant Difference

Table – VIII: Blood Pressure Control in Group B:

	0-4	**4-8**	**0-8**
SBP	3.43(SD)	2.94(SD)	7.32(SD)
DBP	0.21(SD)	0.54(NSD)	5.79(SD)

Changes in the lipid profile:

Alteration in the lipid profile pattern in both the groups with beta blocker therapy is depicted in Table IX.

Table – IX: Showing the alternation in lipid profile in group 'A' and group 'B'

Type	**Group A**			**Group A**		
	0 weeks	**4 weeks**	**8 weeks**	**0 weeks**	**4 weeks**	**8 weeks**
TC	202±48	210±65	203±51	200.7±32	209.9± 31.45	216.2±25
TGL	156±84	145±105	143±75	155.6±72	164.3± 61.95	176.16± 73.99
HDL	42±11	43±9	41.8±8.9	42.43±8.9	41.43± 8.98	38.7±9
VLDL	30±16	30±21	29±21	32.3±15	33.26± 12.48	33.8±14.5
LDL	132.13± 49.9	132.2±40	129.2± 47.5	125.4±32	135.33± 27.49	142.16± 20.49

The mean total cholesterol in group A at 0,4 and 8 weeks was 202.7±48 mg/dl, 210

The mean TGL of group A at 0.4 and 8 weeks of therapy was 156±84. 145±105 and 143±75 mg/dl respectively.

The mean HDL of group A at 0,4 and 8 weeks of therapy was 42±11, 43±9 and 41.8±8.9 mg/dl respectively.

Discussion:

Hypertension and hyperlipidemia are two major cardiovascular risk factors Favoring the development of atherosclerosis (Kannel et al, 1971. Me Mohan et al, 1990). Although the importance of reducing the high blood pressure has been emphasized, several studies have shown that some antihypertensive drugs adversely affect plasma lipid levels, which my therefore counteract the beneficial blood pressure

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lowering effect (MRC working party on mild to moderate hypertension, 1981; Weidmann et al 1988). Several studies show that many cardio selective and non-cardio selective beta adrenoceptor blocking drugs increase serum total cholesterol and triglyceride levels and decrease HDL concentration. The high concentration of serum cholesterol and the ratio of HDL-C to total cholesterol are thought to reflect the atherogenicity of serum lipids. The little doubt exists that some beta blockers may affect serum lipids in a possibly adverse manner, although acebotolol (Lehtonen A 1984) and pindolol (Lehtonen A et al, 1982; Lehtonen A 1984) which possess ISA, have no untoward effects on serum lipids.

The stimulatory effect of catecholamine's on lipolysis is mediated by beta receptor stimulating property. The importance of catecholamine's in regulating lipolysis is evident in the fact that administration of beta blocking drugs will reduce the free fattty acid levels during different lipolysis conditions such as during fasting and exercise following hyperglycemia (Later T et al, 1979). Pindolol, with strong ISA, does not reduce the concentration of serum free fatty acids (Lehtonen A 1984; Lehtonen A et al 1982) indicating that pindolol is not antilypolytic. In the adipoeyte, the observed biologic response could reflect the balance between two opposing actions, beta blockade and ISA. During treatment with alpha – beta blocker (Lehtonen A, 1981) the unchanged concentration of free fatty acids could, in theory, reflect the existing balance between two opposing actions, alpha and beta blockade in the adipose cell.

The 'general' trend of cholesterol was seen in a large number pf Japanese people over a period of 20 years (Yuchirogoto 1984). In 1961 the average serum cholesterol level in a total of 677 normal subjects was approximately 176mg/dl. The second survey was made in 1970 on 3,555 normal subjects. The mean was 185 mg/dl for men and 187 mg/dl for women. The clearly shows that there is a general trend towards increased total cholesterol level over a period of time, an increase of approximately 15 mg/dl has taken place in 20 years of observation.

Alternation in lipid and lipoprotein was observed as a result ofantihypertensive therapy with adrenoceptor blocking agensts. Extensive study has been carried out as mono therapy with beta blockers. Majority of studies have shown that now relative beta blockers (propronolol, oxprenolol) increase plasma. The concentration from app. 10-65% (Apo Lehtonen, 1985; Day JL et al, 1982; Leren et al 1982; Lithell et al 1986; Weidman et al, 1985) and a decrease in HDL-C level by approximately 16% (Drugs 35, 1988; Leren P et al, 1985; Day JL et al, 1982; Miller NE et al, 1987; Sasaki J et al, 1994; Weidman et al, 1985; Shaw J et al, 1978. VLDL concentration was significantly increased (Miller et al. 1987; Drugs 35, 1988; Day JL et al, 1982) total cholesterol was increased significantly (Shaw J et al, 1978). In the country to the above finding no change in tltal cholesterol was noted by several other authors (Tyagi S etal, 1990); Flamenbaum 1985; Bergland and Anderson Lown Stein J et al, 1984). Treatment with the non selective 'B' Adrenoceptor blocking agents was associated with increased propensity for atherogenesity of serum lipis (Tyagi S, et al, 1980; Miller NE et al, 1987). Treatment with cardio selective 'B' blockers like atenolol causes a lesser degree of raise in plasma TGL and cholesterol levels. However the increase was satistically significant at 6 months (Lehtonin A et al, 1984). TGL was increased by 20 to 34% (Day et al, 1982. Laren et al 1982;

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Lithell et al, 1986; Rouffy and Gillard, 1984). Among the fractions of HDL. The HDL-2 cholesterol decresed significantly during the first month of therapy and remained constant during rest of the treatment. HDL-3 fraction decreased slightly but not significantly. The total cholesterol to HDL was increased (Rouffi and Jail lard 1984). The LDL Triglyceride was increased by 11% in the study of Ellison et al, 1984; Rouffi and Jail lard, 1984) free fatty acids were estimated in one study; Day et al (1979). Both selective and non-selective 'B' Blockers (atenelol and propronolol respectively) reduced basal plasma free fatty acid concentrations after treatment. However, they returned to pre-treatment level after 6 months of therapy. Tyagi S et al (1990) drew conclusion in his study, among Indian population, that treatment with propronolol monotherapy increasd serum TGL, VLDL-C and decreased serum HDL-C and worsened atherogenic index (A1 = TC – HDL-C/HDL-C). On the other hand, acebutalol (cardio selective) showed no significant changes im plasma lipids. The blood levels of ghlucose and insulin apart from PPAs, represent the most important components for hepatic lipoprotein production. The serum insulin levels have been reported to remain unaltered during beta blocker therapy (Lehtonen A, 1984; Lehtonen A et al, 1982; Holm G et al, 1973), but there are reports of impaired glucose tolerance (Lehtonen A 1984, 1982). In the present study, the atenolol group showed no lipid abnormalities during the treatment period. However, the propronal group showed a significant adverse raeaction in total cholesterol and LDL level 8 weeks of propronolol monotherapy.

However, the catabolism of TG rich lipoproteins in plasma may be slightly disturbed (Tanaka N, et al, 1976; Day JL et al, 1982; Barboriak et al, 1973). The concentration of plasma total HDL and its subfraction HDL-2 known to be regulated by two lipolytic enzymes located in the vascular endothelium.

Conclusion:

Thirty patients of essential hypertension were treated with atenolol and thiety were propronolol. Lipoprotein alternations were measured in all patients at 0,4 and 8 weeks of therapy in each group. It was concluded from the study that there was no alternation in lipid profile pattern in atenolol treated group. The total cholesterol and LDL were significantly increased at 8 weeks of therapy with propronolol. There was no alternation in TGL, VLDL and HDL cholesterol in the propronolol treated group. There was no significant difference in atherogenic index in both the groups during the treatment period.

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