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COMPARATIVE EFFECTS OF ATENOLOL VERSUS NIFEDIPINE ON SERUM LIPIDS AND OTHER BIOCHEMICAL PARAMETERS IN DIABETIC AND NON-DIABETIC HYPERTENSIVE SUBJECTS

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Abstract: A controlled clinical trial on 65 patients was performed to compare the effects of nifedipine and atenolol in diabetic and non-diabetic hypertensive patients. Patients were from 45 to 70 years in age. The diabetic hypertensive patients and non-diabetic essential hypertensive patients randomly received atenolol (50-100 mg per day) or nifedipine (10-20 mg per day) for 9 months. Both the drugs effectively controlled the blood pressure throughout the therapy. Atenolol treatment significantly increased triglyceride levels and decreased the HDL-cholesterol levels after 9 months in both groups. However, nifedipine therapy did not alter lipid levels to any significant extent. Both drugs did not alter blood glucose, serum creatinine and blood urea levels. It may be concluded from the present study that nifedipine is preferable to atenolol as it does not alter lipid profile to any significant extent in diabetic and non-diabetic hypertensive patients.

Key words: atenolol nifedipine diabetes hypertension lipids

INTRODUCTION

Elevated serum LDL cholesterol, reduced HDL cholesterol levels and hypertension are independent cardiovascular risk factors. The Framingham study showed that hypertensive patients are at greater risk if they also have abnormal serum lipoprotein levels (1). The National Health and Nutrition Examination Survey (2) reported that 40% of hypertensive persons have blood cholesterol levels > 6.23 mmol/liter. Hypertension appears to be critically important when it co-exists with diabetes-mellitus because hypertension accelerates both the microvascular and macrovascular complications of diabetes-mellitus. Diabetes is also associated with hyperlipidemia and ketoacidosis which produce deleterious effects on cell-membrane and myocardial function (3).

Many available antihypertensive drugs are reported to affect lipid levels and worsen glycemic control. Comparable data to guide on the suitability of these drugs is scanty. In a new therapeutic approach to the treatment of hypertension, the ideal agent should not only be efficacious and well-tolerated but also should reverse hypertension induced cardiovascular disease and should induce positive alteration of serum lipids.

The present work was undertaken to study the comparative effects of widely used antihypertensives, atenolol and nifedipine, on lipid profile and other biochemical parameters in non-diabetic essential hypertensive and diabetic hypertensive patients.

METHODS

The study was a controlled open clinical

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trial. It was approved by the Local Ethical Committee.

Qualifying criteria: Patients visiting the Shukla General Hospital's OPD were selected for the study. They had mild to moderate essential hypertension, defined as a mean diastolic blood pressure of more than 90 to less than 110 mm Hg after 2-3 weeks of placebo treatment. Men and women were between the ages of 45 and 70 years, and within 15 to 25% of ideal body weight. Patients with severe retinopathy, cardiac, renal or neurological disease were excluded.

Treatment period: The selected patients from the hospital's OPD were fully explained about the procedures and a written consent was obtained from them. Those who met the eligibility criteria were admitted to the Shukla General Hospital for one day, and underwent a physical examination and received placebo treatment for 2-3 weeks. For follow up, patients attended the OPD of Shukla Hospital.

Diabetic patients were maintained of their usual diet and treatment for control of diabetes. At the end of placebo period, if they still met qualifying requirements, both non-diabetic essential hypertensive and diabetic hypertensive patients were randomised to receive either atenolol, 50 mg per day or nifedipine, 10 mg per day. After 4 weeks of active treatment, patients whose mean diastolic blood pressure was less than 90 mm Hg were instructed to continue taking the same dose (50 mg of atenolol or 10 mg of nifedipine). Patients whose diastolic blood pressure was more than 90 mm Hg were instructed to increase their dose to 100 mg per day atenolol or 20 mg per day nifedipine for the remaining period of the study.

Data collection: Supine blood pressure and pulse were measured every month and blood samples were collected for serum lipids, glucose, urea and creatinine levels after completion of the placebo period and the treatment of 3 and 9 months.

At each visit, blood pressure recording was done using a Sphygmomanometer on the same arm and, whenever possible, by the same nurse or physician. Blood samples obtained after a 12 hours fast, were analysed for total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, glucose, urea and creatining levels by standard diagnostic kits.

Life-styles monitoring: No specific dietary prescription was provided to avoid diet fluctuation. Patients were required to continue their usual diet habits throughout the study. Patients were asked not to make changes in physical exercise or smoking habits during the course of the study. Drug compliance was assessed by pill counts.

Statistical methods: Statistical analysis was performed using one way analysis of variance. A value of P less than 5% was considered as significant.

RESULTS

Baseline demographics: A total of 65 patients (30 female and 35 male) ranging from 45 to 70 years, participated in the study. The gender, age, race, weight and height distribution were similar in all the groups. Out of the 31 patients who received atenolol (50-100 mg per day), 16 (10 males/6 females) were diabetic hypertensive patients and 15 (8 males/7 females) were essential hypertensive patients. The remaining 34 patients who received nifedipine (10-20 mg per day) 18 (8 males/10 females) diabetic hypertensive patients and 16 (9 males/7 females) non-diabetic essential hypertensive patients.

Effect on blood pressure: The antihypertensive effect was similar with both the drugs (Table I). In diabetic as well as non-diabetic hypertensive patients, atenolol as well as nifedipine effectively reduced the mean blood pressure within a month. Overall control of blood pressure was maintained in 24 of 31 (77.4%) and 28 of 34 (82.3%) patients receiving atenolol and nifedipine, respectively during 9 months of therapy.

Effects on lipid levels: Atenolol therapy slightly increased the triglyceride level after 3 months and this was not significant (P>0.05).

TABLE I : Effect of Atenolol and Nifedipine on blood pressure.

Group / Treatment		Duration				
		Initial	*1st month*	*3rd month*	*6th month*	*8th month*
Diabetic hypertensive						
Nifedipine	SBP	178 ± 2.6	150 ± 2.1	146 ± 4.8	152 ± 4.8	154 ± 2.8
	DBP	105 ± 2.3	89 ± 3.2	89 ± 5.1	86 ± 3.6	86 ± 3.8
Atenolol	SBP	174 ± 3.6	158 ± 2.7	158 ± 4.2	164 ± 4.6	154 ± 4.0
	DBP	108 ± 1.4	91 ± 2.2	90 ± 4.6	92 ± 5.2	88 ± 3.6
Non-diabetic hypertensive						
Nifedipine	SBP	172 ± 1.8	158 ± 1.7	148 ± 3.2	15 ± 4.1	148 ± 2.8
	DBP	106 ± 2.8	87 ± .4	90 ± 2.6	96 ± 2.3	88 ± 1.8
Atenolol	SBP	168 ± 2.4	156 ± 2.9	158 ± 3.7	160 ± 2.8	156 ± 3.2
	DBP	104 ± 1.8	90 ± 1.5	98 ± 2.6	92 ± 3.3	87 ± 2.3

However, there was a significant ($P<0.05$) increase in triglyceride levels and decrease in HDL-cholesterol levels after 9 months of treatment in both diabetic hypertensive and non-diabetic essential hypertensive patients (Table II). Further, atenolol treatment did not affect the total cholesterol and LDL-cholesterol levels throughout the study period. However, nifedipine therapy in diabetic hypertensives and non-diabetic essential hypertensive patients did not produce any significant change in lipid levels through out the study period.

Effects on other biochemical parameters: In diabetic hypertensive and essential hypertensive patients, the fasting blood glucose levels were slightly but not significantly increased after 3 months and 9 months with both the drugs

TABLE II : Effects of Atenolol and Nifedipine on lipid profile.

	Diabetic hypertensive		*Non-diabetic hypertensive*	
	Atenolol (n=16)	*Nifedipine (n=18)*	*Atenolol (n=15)*	*Nifedipine (n=16)*
Total cholesterol (mg/dl)				
Initial	239.32 ± 8.25	201.83 ± 7.44	211.40 ± 7.15	210.67 ± 8.87
3 months	235.81 ± 7.28	205.28 ± 6.81	210.23 ± 7.59	214.28 ± 9.78
9 months	220.96 ± 6.56	200.25 ± 6.95	201.92 ± 6.90	206.11 ± 9.45
Triglycerides (mg/dl)				
Initial	164.81 ± 18.75	119.79 ± 8.73	127.29 ± 5.93	124.22 ± 7.53
3 months	176.88 ± 8.78	125.44 ± 7.62	135.18 ± 5.66	125.13 ± 7.46
9 months	192.8 ± 8.52*	126.83 ± 7.07	158.85 ± 6.53*	120.83 ± 6.30
LDL-Cholesterol (mg/dl)				
Initial	158.44 ± 17.20	126.89 ± 5.84	136.90 ± 7.27	136.91 ± 7.54
3 months	155.67 ± 6.83	131.30 ± 5.98	135.67 ± 7.28	140.11 ± 8.38
9 months	142.20 ± 5.32	124.93 ± 6.66	129.25 ± 7.04	132.46 ± 8.11
HDL-Cholesterol (mg/dl)				
Initial	47.70 ± 1.30	49.18 ± 1.70	49.04 ± 1.20	48.91 ± 1.19
3 months	46.93 ± 1.10	50.11 ± 1.27	47.53 ± 1.05	49.53 ± 0.94
9 months	41.03 ± 1.08*	49.29 ± 1.73	42.73 ± 0.74*	49.31 ± 1.05

*Significantly different from initial ($P < 0.05$).

(Table III). Serum creatinine and blood urea were also not significantly altered with atenolol and nifedipine in diabetic hypertensive and non-diabetic essential hypertensive patients (Table III).

Several experiments in animal models especially cholesterol fed rabbits, have indicated that nifedipine may reduce accumulation of atherosclerotic components and therefore, slow the progression of atherosclerotic lessions (11).

TABLE III : Effects of Atenolol and Nifedipine on blood glucose, serum creatinine and blood urea.

	Atenolol			*Nifedipine*		
	Initial	*After 3 months*	*After 9 months*	*Intiial*	*After 3 months*	*After 9 months*
Fasting blood glucose (mg/dl)						
DM-HT	164.00 ± 7.79	170.00 ± 6.92	171.00 ± 8.34	163.00 ± 11.20	172.00 ± 9.20	174.00 ± 8.70
EH	88.62 ± 5.13	94.50 ± 6.20	95.68 ± 5.21	90.00 ± 4.07	101.00 ± 5.20	104.00 ± 4.56
Serum creatinine (mg/dl)						
DM-HT	1.38 ± 0.112	1.32 ± 0.12	1.40 ± 0.107	1.36 ± 0.077	1.42 ± 0.09	1.51 ± 0.081
EH	1.13 ± 0.07	1.14 ± 0.09	1.19 ± 0.07	1.14 ± 0.072	1.16 ± 0.08	1.04 ± 0.050
Blood urea (mg/dl)						
DM-HT	27.70 ± 1.80	26.80 ± 1.66	28.64 ± 1.90	31.13 ± 1.91	31.60 ± 1.82	32.76 ± 1.80
EH	27.66 ± 1.81	27.60 ± 1.51	28.43 ± 1.37	8.96 ± 1.78	27.90 ± 1.60	28.14 ± 1.52

All values show Mean ± SEM; DM-HT : Diabetic hypertensive patients; EH : Non-diabetic hypertensive patients

DISCUSSION

Different beta blockers may show different effects of serum lipoprotein levels in diabetic hypertensive subjects. Non-selective beta-blockers have been shown to affect serum lipid levels adversely (4-7). Non-selective β-blockers do not alter plasma total cholesterol concentration (8). Triglyceride concentration is increased by 20-30% (8), possibly as a result of unopposed alpha-effect inhibiting lipoprotein lipase (9). Plasma HDL concentration tends to decrease with non-selective β-blocker (8).

Selective β_1-adrenoceptor blockers like atenolol and metoprolol do not affect plasma cholesterol. It was postulated that selective beta-blockers such as atenolol and metoprolol are likely to affect adversely the serum lipid levels to a lesser extent than non-selective ones such as propranolol. The results of our study support the previous finding (10) that atenolol can affect serum lipid levels to an extent quantitatively similar to non-selective β-blockers.

However, conflicting data is available as far as the influence of nifedipine on lipid profile in patients with non-diabetic or diabetic hypertension is concerned. Several studies have shown that nifedipine does not produce any significant effect on lipid parameters (12, 13). In contrast, Huston and associates (14) reported a significant increase in HDL, HDL-2 and apolipoprotein A-I and A-II levels after the administration of nifepidine. Our previous studies with streptozotocin diabetic rats (15) reported that nifedipine prevented diabetes induced hyperlipidemia, cardiac dysfunction and cardiomyopathy. In the present study, however, nifedipine was not found to produce any significant alteration in total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides levels in either diabetic or non-diabetic hypertensive patients.

Plasma lipoprotein changes that would constitute a coronary heart disease risk factor in an untreated population might have the significant effect when such changes are induced

by atenolol. As far as renal functions are concerned, our data confirm those previously reported (16, 17) that atenolol and nifedipine did not produce any consistent changes in creatinine and urea level in patients with normal renal function.

It has been postulated that adverse changes in blood lipids by antihypertensive drugs are transient, however, extended trials have shown that derangement of blood lipid levels may persist indefinitely or at least for several years (18-20).

Because of the proven risk potentiation between hypertension, diabetes and dyslipidemia, and considering the concept that equally effective antihypertensive drugs for any given patients can be directed by its beneficial or atleast neutral effects on metabolism. It may be suggested from the present study that nifedipine is preferred over atenolol in the diabetic or non-diabetic hypertensive patients.

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