Original Article

Cardiovascular Risk Reduction Comparison of Felodipine and Propranolol in Patients of Essential Hypertension

Reduction of Cardiovascular Risk

1. Noor ul Huda Ansari 2. Nehal Naseer 3. Vardah Noor 4. Abira Nazir 5. Mushtaq Ahmed

1. Asstt. Prof. of Pharmacology, QAMC, Bahawalpur 2. MBBS 3. D.Pharm 4. Prof. of Pharmacology, NMC, Multan. 5. Assoc. Prof. of Pharmacology, QAMC, Bahawalpur

ABSTRACT

Objective: To compare the efficacy of felodipine versus propranolol in patients of essential hypertension for Serum cholesterol, LDL cholesterol and HDL cholesterol.

Study Design: Randomized controlled study.

Place and Duration of Study: This study was conducted at the Accident and Emergency Department, Bahawal Victoria Hospital, Bahawalpur and Ansari Private Clinic Model Town B Bahawalpur from 1st July 2015 to 30th September 2015.

Materials and Methods: Total 90 patients with essential hypertension having age range from 30 to 50 years were enrolled in this study for three months. Patient were randomly divided into three groups I, II and III, each group comprising 30 patients. Group I patients were treated with felodipine, Group II patients were treated with propranolol and group III patients were treated with placebo. Effects of these drugs on Lipid profile(Serum cholesterol, HDL cholesterol and LDL cholesterol)were compared.

Result: Felodipine, treated patients exhibited markedly significant fall in the serum cholesterol (P<0.01), highly significant fall at the level of LDL cholesterol (P<0.001) and non-significant effect in HDL cholesterol. Whereas propranolol treated patients showed highly significant increase of serum cholesterol (P<0.001), markedly significant increase in LDL cholesterol (P<0.01) and markedly significant decreased in HDL cholesterol (P<0.01).Whereas comparison of two drugs Felodipine and Propranolol displayed a highly increased (P<0.001) serum cholesterol, LDL cholesterol and markedly increased (P<0.01) HDL cholesterol.

Conclusion: Result of this study showing that comparing the two drugs felodipine had significantly decreased Serum cholesterol and LDL Cholesterol, whereas propranolol increased the Serum cholesterol, LDL cholesterol and decreased HDL cholesterol. So felodipine prove its merit over propranolol.

Key Words: Cardiovascular Risk, Felodipine and Propranolol, Hypertension

Citation of article: Ansari NH, Naseer N, Noor V, Nazir A, Ahmed M. Cardiovascular Risk Reduction Comparison of Felodipine and Propranolol in Patients of Essential Hypertension. Med Forum 2016;27(1): 37-40.

INTRODUCTION

Hypercholesterolemia, hypertension and cigarette smoking are three major risk factors responsible for ischemic heart disease.[1] Whereas obesity, physical inactivity, diabetes, personality-type, excessive alcohol intake, hypertriglyceridemia and hyperuricemia have been categorized as minor cause, because they are either relatively less powerful determinants of risk or less prevalent within the population[2].It was also noticed that 50% of all Coronary Heart Disease (CHD) deaths were associated with raised Serum cholesterol concentration; whereas 50% of these excess deaths were linked in cholesterol level above 85th percentile[3].

The treatment of hypertension has failed to show a definite preventive effect on the incidence of coronary heart disease which has aroused interest in lipid metabolism in hypertension therapy[4]. In 1983 Cutler[5] reported that dietary lipids are absorbed through the small intestine and reach the blood mainly in the form of chylomicron. Other lipid fractions are synthesized within the liver and gut from the primitive metabolites such as acetate. High density lipoprotein (HDL) and very low density lipoproteins (VLDL) are both synthesized in the liver. LDL is a lipoprotein which carries most of the serum cholesterol borne by the blood stream. The cholesterol rich LDL fraction from the liver apparently enters the coronary artery wall and deposits its cholesterol load in the intima where as it may initiate or perpetuate the process of atherosclerotic plaque formation. HDL fraction is also carried by the blood stream, when reaches the arterial wall, seems to play a protective role against the formation or progression of atherosclerosis by removing the cholesterol deposited by LDL. Levy[6] reported that a definite correlation existed between the increased serum LDL cholesterol concentrations and prevalence of CHD. Miller cited by Cutler[5] noted an inverse

Correspondence: Noor Ul Huda Ansari
Asstt. Prof. of Pharmacology, QAMC, Bahawalpur
Contact No.: 0300-9681788
E-mail: noorulhuda56@gmail.com

correlation between HDL cholesterol and coronary heart disease prevalence.

Among other antihypertensive drugs beta blockers and calcium channel antagonists are widely used in cases of essential hypertension. Propranolol, a non-selective beta blocker, is a standard drug to which other beta blockers are compared[7]. The beta blockers are known to produce unwanted metabolic effects such as dyslipidemia[8] and reduction in HDL-cholesterol level[9, 10].Propranolol is reported to have little effect on serum cholesterol and LDL-cholesterol[11, 12, 13,7]but produces a significant rise in serum cholesterol and LDL-cholesterol in an investigation carried out in smokers[14]. Beta blockers are said to inhibit adenylate cyclase activity, leading to a reduced activity of lipoprotein lipase (LPL) through beta 2-receptor antagonism which would retard VLDL catabolism. Propranolol and other beta blockers increase catecholamine levels, thereby increasing hepatic cholesterol production and decreasing lecithin- cholesterol-acyltransferase (LCAT) activity, thus suppressing the HDL-LCAT cycle and ultimately decreasing HDL cholesterol[15, 14].

Felodipine is the member of second generation of dihydropyrdine class of calcium antagonists and is insoluble in water[16, 17]. Calcium antagonists have little or beneficial effect on lipid profile[18, 19, 13]. In a study on hypertensive patients receiving calcium antagonists there was 10% reduction in total cholesterol. This decline resulted from LDL cholesterol fraction[20]. This is due to the fact that catecholamines suppress LDL receptor activity whereas calcium antagonists antagonise the catecholamine action, thereby increasing LDL receptor activity resulting in a decrease in LDL level [21] and non-significant effect on HDL cholesterol[22].

MATERIALS AND METHODS

This study was conducted at Accident and Emergency Department, Bahawal Victoria Hospital, Bahawalpur and Ansari Private Clinic, Model Town B, Bahawalpur from 1st July 2015 to 30th September 2015.Onehundred and thirty two patients of mild to moderate essential hypertension were initially registered in this study some of them were excluded because of noncompliance or other reasons and ninety patients were followed up for the full course of three months. The patients were divided randomly into three groups, each comprising of 30 patients. Group I was given felodipine tablets 5mg once daily, Group II was given propranolol tablets 40mg twice daily and group III was given placebo tablets once daily. All the patients were withheld from any anti-hypertensive medication for at least two weeks prior to their inclusion in the study. The fasting blood samples from all the patients were analyzed for serum cholesterol, LDL-cholesterol and HDL-cholesterol on the day of registration (day0) and repeated every month.

Methodology: Serum cholesterol and HDL-cholesterol were estimated by their respective enzymatic method using kit supplied by B.M whereas LDL-cholesterol was calculated according to the formula of Freidwald[23].

Statistics: SPSS Statistic Software (Version 22.0) was applied for analysis of acquired data. Values are given as mean ±SEM. group comparison was done by applying students t-test, and values within the same group at different time intervals were compared by paired t-test.

RESULTS

The felodipine, propranolol and placebo treated groups are I, II and III respectively. The levels of serum cholesterol, LDL-cholesterol and HDL-cholesterol for the patient treated with felodipine, propranolol and placebo were observed at day 0, 30, 60 and 90. The differences (as mean±SEM) in the level of serum cholesterol, LDL-cholesterol and HDL-cholesterol at different time intervals as affected by felodipine, propranolol and placebo were calculated.

Serum cholesterol: Felodipine treated patients exhibit a fall in the level of serum cholesterol, which was non-significant from day 0 to 30 , day 0 to 60 and markedly significant ($P<0.01$) between day 0 to 90. In contrast, propranolol increased the level of serum cholesterol, this increase was significant ($P<0.05$) between day 0 to 30 and highly significant ($P<0.001$) between day 0 to 60 and day 0 to 90 (table 2). When the mean values of the corresponding difference in the felodipine and propranolol groups were compared (table3) it showed a markedly significant difference for day 0 to 30 and day 0 to 60 ($P<0.01$), however the difference became highly significant ($P<0.001$) between day 0 to 90.

LDL cholesterol: Felodipine treated patients exhibit a fall in the level of LDL cholesterol, which was non-significant between day 0 to 30 , day 0 to 60 and highly significant ($P<0.001$) between day 0 to 90,whereas propranolol produced an increase in LDL cholesterol. This increase was non-significant between day 0 to 30, day 0 to 60 and became markedly significant ($P<0.01$) from day 0 to 90 (table 2).

When the mean values of corresponding differences in felodipine and propranolol groups were compared (table 3). This difference assumed non-significance between day 0 to 30, significance ($P<0.05$) between day 0 to 60 and high significance ($P<0.001$) between day 0 to 90.

HDL – cholesterol: In present study a non-significant change was noticed in the level of HDL cholesterol throughout the study with felodipine therapy (table2). The level of HDL cholesterol decreased along with the treatment in propranolol group; the decrease was non-significant between day 0 to 30 but became significant ($P<0.05$) between day 0 to 60 and markedly significant ($P<0.01$) from day 0 to 90 (table 2).

When the mean values of the corresponding differences in the felodipine and propranolol groups were compared it showed a non-significant difference between day 0 to 30 which became significant ($P<0.05$) between the 0 to 60 and markedly significant ($P<0.01$) between day0 to 90 (table 3).

Table No.1: Change in Level of Serum Cholesterol, LDL-Cholesterol and HDL-Cholesterol Before and During Treatment (Mean ± S.E.M)

Drugs	Serum Cholesterol level in mg/dl				LDL-Cholesterol in mg/dl				HDL-Cholesterol in mg/dl			
	Before treatment	During treatment			Before treatment	During treatment			Before treatment	During treatment		
	Day 0	Day 30	Day 60	Day 90	Day 0	Day 30	Day 60	Day 90	Day 0	Day 30	Day 60	Day 90
Felodipine (n=30)	187.13 ±6.29	182.83 ±6.32	180.40 ±5.98	171.76 ±4.86	124.40 ±5.75	121.83 ±6.19	116.90 ±5.71	105.70 ±3.87	37.33 ±1.30	36.83 ±1.51	38.53 ±1.89	39.53 ±1.46
Propranolol (n=30)	160.10 ±8.21	172.06 ±7.39	184.10 ±8.15	195.60 ±8.77	89.90 ±7.20	93.70 ±6.77	102.56 ±7.28	109.70 ±8.38	39.83 ±2.20	38.23 ±1.63	35.46 ±1.41	32.66 ±1.34
Placebo (n=30)	169.16 ±6.58	174.36 ±6.95	174.80 ±6.90	176.70 ±7.15	108.46 ±6.85	112.56 ±7.08	113,80 ±6.46	111.43 ±7.02	34.43 ±1.61	36.16 ±1.43	36.33 ±1.22	36.33 ±2.54
S.E.M:= Standard Error of Mean					n: =number of patients							

Table No.2: Effect of on serum cholesterol, LDL-Cholesterol and HDL-Cholesterol at different time intervals (d±S.E.M)

Drugs	Significance of Serum Cholesterol			Significance of LDL-Cholesterol			Significance of HDL-Cholesterol		
	Day 0-30	Day 0-60	Day 0-90	Day 0-30	Day 0-60	Day 0-90	Day 0-30	Day 0-60	Day 0-90
Felodipine vs Propranolol	P<0.01	P<0.01	P<0.001	N.S	P<0.05	P<0.001	N.S	P<0.05	P<0.01
Propranolol vs Placebo	P<0.05	P<0.05	P<0.001	N.S	P<0.05	P<0.01	N.S	N.S	N.S
Felodipine vs Placebo	N.S	P<0.05	P<0.001	N.S	N.S	P<0.05	N.S	P<0.05	P<0.05
N.S:= Non-significant									

Table No.3: Levels of significance of serum cholesterol, LDL-Cholesterol and HDL-Cholesterol on conversion of drugs at different time intervals

Drugs	Significance of Serum Cholesterol			Significance of LDL-Cholesterol			Significance of HDL-Cholesterol		
	Day 0-30	Day 0-60	Day 0-90	Day 0-30	Day 0-60	Day 0-90	Day 0-30	Day 0-60	Day 0-90
Felodipine vs Propranolol	P<0.01	P<0.01	P<0.001	N.S	P<0.05	P<0.001	N.S	P<0.05	P<0.01
Propranolol vs Placebo	P<0.05	P<0.05	P<0.001	N.S	P<0.05	P<0.01	N.S	N.S	N.S
Felodipine vs Placebo	N.S	P<0.05	P<0.001	N.S	N.S	P<0.05	N.S	P<0.05	P<0.05
N.S:= Non-significant									

DISCUSSION

In the present study felodipine reduced the level of serum cholesterol; though non-significant initially, this effect became markedly significant (P<0.01) by the end of three month time. On the other hand, propranolol increased the level of serum cholesterol which was highly significant (P<0.001) by the end of therapy. The action of felodipine and propranolol on comparison exhibited highly significant risk reduction with felodipine but not with propranolol. The rise in serum cholesterol by propranolol in the present study contradicts the report of Day[11] and Shanks[7], it is however, in consensus with the observation of Vyssoulis[14] hence upholding the statement of Lardinois[24] and Vyssoulis[14] that beta blockers increase the hepatic production of cholesterol.

The present study revealed that during felodipine therapy there was a non-significant reduction in the level of LDL cholesterol initially ,i.e. day 0 to 30 and day 0 to 60 but a highly significant reduction in LDL cholesterol level at the end of therapy i.e. day 0 to 90 (P<0.001). On the other hand propranolol increased its level, which assumed marked significance after the third month of therapy (P<0.01).The results of felodipine agree with those reported by Walldius cited by Scheon[20]. However, the results of propranolol in this study disagree with the finding of Day[11] and Shanks[7]and agree with the observations of Vyssoulis[14] who observed a significant rise in LDL cholesterol with propranolol therapy.

It is reported that propranolol significantly decreased HDL cholesterol [13, 14, 15, 18]. A similar decrease was also observed in the present study (P<0.01).On the other hand, felodipine raises the level of HDL cholesterol but not to the level of significance matching the findings of Capewell and Maninder Kaur[22].

Comparing the two drugs, felodipine versus propranolol, effect on serum cholesterol was markedly significant (P<0.01) between day0-30, day0-60 and

highly significant (P<0.001) between day0-90. Comparative effect on LDL cholesterol were non-significant between day0-30, significant (P<0.05) between day 0-60 and markedly significant (P<0.001) between day0-90. Comparative effect on HDL cholesterol was non-significant between day0-30, significant (P<0.05) between day 0-60 and markedly significant (P<0.01) between day 0-90.Thus it can be concluded from the present investigation that felodipine reduces the cardiovascular risk factor, in comparison to propranolol and has a beneficial effect on serum cholesterol, LDL-cholesterol and HDL-cholesterol thus proving its merit over propranolol.

CONCLUSION

Comparing the two drugs, felodipine had significantly reduced the various cardiovascular risk factors, as assessed in this study. Thus felodipine has proved its merits over propranolol not only causing beneficial effects on lipid profile i.e. serum cholesterol, LDL-cholesterol and HDL-cholesterol but reducing the cardiovascular risk factors in patients of essential hypertension.

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Dollery CT. Risk predictors, risk indicators and benefit factors in hypertension. Am J Med1987;82 (Suppl IA): 2-8.
2. Kaplan WM. Coronary heart disease risk factors and antihypertensive drug selection. J Cardiovas Pharmacol 1982;4 (Suppl2): s187-9.
3. Martin MJ, Hulley SB, Browner WS, Kuller LH, Wentworth D. Serum cholesterol, blood pressure and mortality: implications from a cohort of 361662 men. The Lancet 1986;II:933-6.
4. Editorial. Antihypertensive drugs, plasma lipids and coronary disease.Lancet1980;ii:19-20
5. Cutler R. Effect of antihypertensive agents on lipid metabolism. Am J Cardiol 1983;51:628-31.
6. Levy RI. Cholesterol, lipoproteins, apoproteins and heart disease: present status and future prospects. Clin Chem1981;27(5): 653-62.
7. Shanks RG. Clinical pharmacology of vasodilatory Beta blocking drugs. Am Heart J1991;121: 1006-11.
8. Vivian A. Fonseca. Effects of β blocker on glucose and lipid metabolism. Zurrent Medical Research and Opinion 2010;26(3):615-629.
9. Birnbaum J, Dibianco R, Becker KL, Muesing R, CosTello RB, Singh SN, et al. Glucose and lipid metabolism during acebulolol and propranolol therapy of angina in non-diabetic patients. Clin Phar Ther 1983;33: 294-300.
10. Dujovne CA, Decoursey S, Krehbiel P, Jackson B, Chemoff S. Serum lipids in normo and hyperlipidemics after methyldopa and propranolol. Clin Pharmacol Ther1984;36:157-62.
11. Day JL, Metcalfe J, Simpson CN. Adrenergic mechanisms in control of plasma lipid concentration. Br Med J 1982;284:1145-8.
12. Johnson BF. The emerging problem of plasma lipid changes during antihypertensive therapy. J Cardiovas Pharmacol1982;4 (Suppl2): S213-221.
13. Lehtonen A. Effect of beta blockers on blood lipid profile. Am Heart J1985;109,5(2):1192-96.
14. Vyssoulis GP, Karpanou EA, Pitsavos CF, Toutouza MA, Paleologos AA, Toutouzas PK. Dislipidemic effect of cigarette smoking on beta-blocker- induced serum lipid changes in systemic hypertension. Am J Cardiol1991;67: 987-92.
15. Leren P, Helgeland A, Holme I, Foss PO, Sjermann I, Lund-Larsen PG. Effects of propranolol and prazosin on blood lipids. The Oslo study. Lancet1980;II: 4-6.
16. Suryakanta N, Dibyasunadar P, Kumar AP. Nanosuspension- Prepration, In Vitro and Ex Vivo Evaluations of Felodipine hydrochloride. Research J Pharm and Technol2015;8(1):38-43.
17. Shah U, Joshi G, Sawant K. Improvement in antihypertensive and antianginal effects of felodipine by enhancing absorption from PLGA Nanoparticles optimized by fractional design. Material Science and Engineering2014;35: 153-63
18. Capewell S, Collier A, Matthews D, Hajducka C, Collier R, Clarke BF, et al. A trial of the calcium antagonist felodipine in hypertensive type 2 diabetic patients, Diabetic Med1989;6: 809-12.
19. Sudhir K, Jennings GL, Bruce A. Cardiovascular risk reduction: initial diuretic therapy compared with calcium antagonist (felodipine) therapy for primary hypertension. Med J Aust 1989;151: 277-279.
20. Scheon RE, Frishman WH, Shamoon H. Hormonal and metabolic effects on calcium channel antagonists in man. Am J Med1988;84:492-504.
21. Krone W, Nagele H. Effects of antihypertensive on plasma and lipoprotein metabolism. Am Heart J 1988;116:1729-34.
22. Kaur M, Kaur KJ, Bedi GK, Sidhu GS, Sikand R. Effects of felodipine on serum lipid profile of patients with hypertension. Ind J Clin Biochemistry 2000;15(2):63-67.
23. Friedwald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein Cholesterol in plasma, without use of preparative ultracentrifuge. Clin Chem1972;18(6): 499-502.
24. Lardinois CK, Neuman SL. The effect of antihypertensive agent on serum lipids and lipoprotein. Arch InternMed1988;148:12808.
25. Hunninghake DB, Ninn N. The effects of cardioselective vasodilating beta blockers on lipid. Am Heart1991;121:1029-32.