MEDICAL CHANNEL

Original Article

CHOLESTEROL, TRIGLYCERIDES AND LDL LOWERING EFFECTS OF GENERIC PRODUCTS OF SIMVASTATIN AND HDL EFFECT AS COMPARED TO ORIGINAL BRAND OF SIMVASTATIN IN HYPERCHOLESTEROLEMIC SUBJECTS – A RANDOMIZED STUDY

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ABSTRACT:

Lipids have an important role virtually in all aspects of life- serving as hormone or hormone precursors, aiding in digestion, providing energy storage and metabolic fuels, acting as functional and structural components in cell membranes and forming insulations to allow nerve conduction or to prevent heat loss. Increased cholesterol is a causative factor in the etiology of atherosclerotic diseases.

About 60% of plasma cholesterol is normally found in LDL fraction; 25% in the HDL fraction; while the rest of Cholesterol is present in VLDL variety. High density lipoproteins are also mainly Cholesterol esters. They are scavengers of Cholesterol and their function is to transport Cholesterol from the tissues to the Liver.

HMG-co A reductase inhibitors are widely used in the treatment of hypercholesterolemia due to their efficacy in reducing blood LDL- Cholesterol. Here we report the Cholesterol lowering effect of generic Simvastatin products in comparison with the Original brand Zocor.

Method: The generic drugs used in the present study were Atcol & Limitrol of Atco & Pharmevo laboratories respectively. The serial blood samples were collected after drug administration every 4weeks for 12 weeks.

Results: After the administration of drugs for 12 weeks; there was no significant difference statistically between the Original brand Zocor and the Atcol & Limitrol treated groups. All the drugs were well tolerated and only minor side effects nausea & dizziness were observed in some patients.

Conclusion: It can be concluded from this study that no significant difference can be observed as regards the efficacy & safety of these drugs. The efficacy & safety of the generic & brand drugs is almost the same & there is no statistical difference between them.

Key words: Cholesterol, Simvastatin, HMG-co- reductase inhibitors, Triglycerides.

INTRODUCTION:

The search for the causes of atherosclerosis is being carried out since long. The scientists have known for more than a century that that people who eat diet high in animal fat tend to have high levels of cholesterol in their blood stream; it has been well established that elevated Cholesterol in the blood stream is very likely to lead to atherosclerosis and the health dangers that come with it. In the last two decades however scientists have begun to unravel exactly how the Cholesterol traveling around in the blood leads to the

FIGURE - 1
Parameter-wise Observations of All Groups
On Day-0 and Day-90
SERUM
CHOLESTEROL (mg/dl)

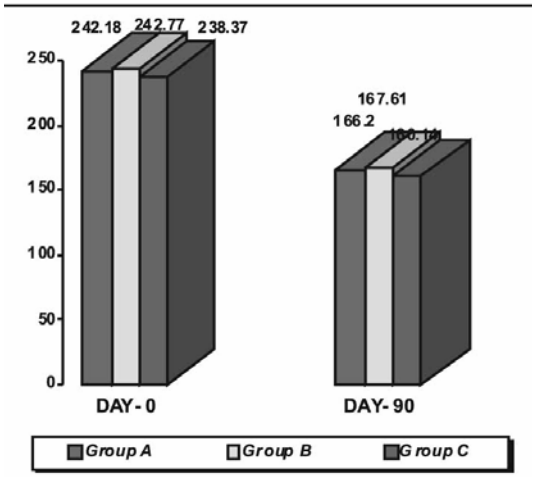


FIGURE - 2
PARAMETER-WISE OBSERVATIONS OF ALL GROUPS
ON DAY-0 AND DAY-90
SERUM
TRIGLYCERIDES (MG/DL)

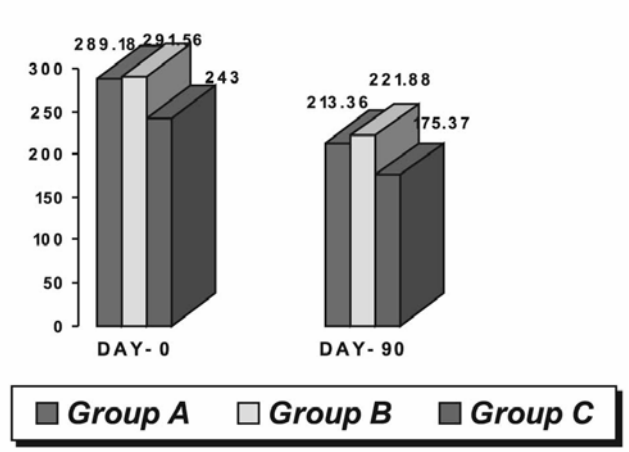


FIGURE – 3
Parameter-wise Observations of All Groups
On Day-0 and Day-90
SERUM
LDL-C (mg/dl)

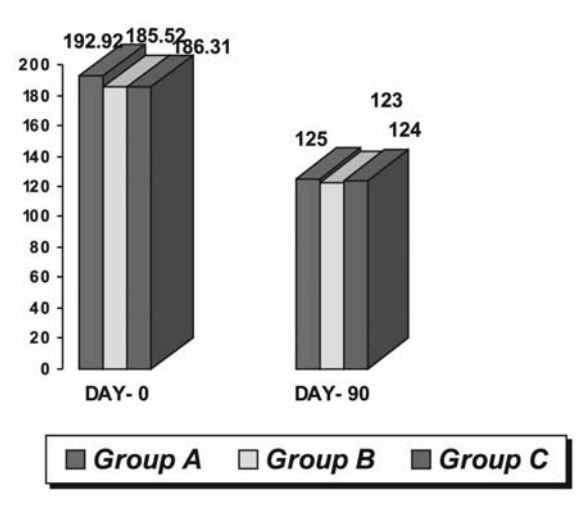
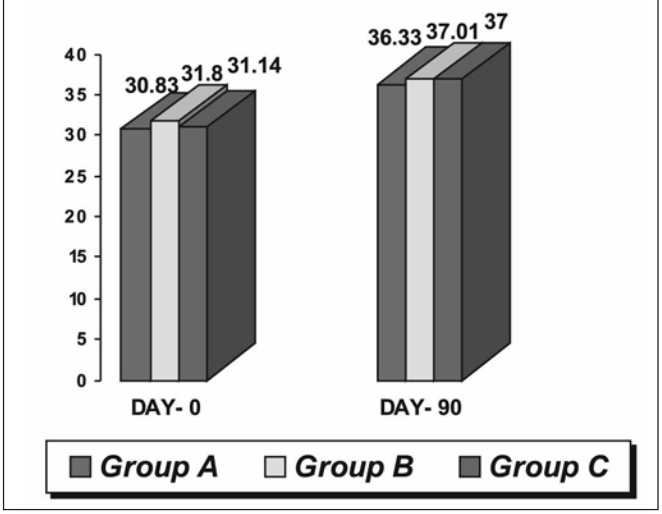


FIGURE - 4
Parameter-wise Observations of All Groups
On Day-0 and Day-90
SERUM
HDL-C (mg/dl)



development of a fibrous plaque and blood clots that block the artery 1,2. The statins block the rate limiting enzyme for endogenous Cholesterol synthesis, hydroxymethyl-glutaryl Co-enzyme A (HMG-CoA) reductase. This results in increase synthesis of LDL-receptors (upregulation)in the liver and increased clearance of LDL from the circulation ; plasma total Cholesterol and LDL-cholesterol fall to attain a maximum effect after commencing therapy 3.

Drug treatment to lower plasma lipoproteins and / or Cholesterol is primarily aimed at reducing the risk of atherosclerosis and subsequent coronary artery disease that exists in patients with elevated circulating lipids. Drug therapy usually is considered as an option only if non Pharmacologic interventions (altered diet & exercise) have failed to lower plasma lipids 4.

As with all things truly evil, the very essence of plaque that claims the lives of millions continues to elude us. However on the basis of reported sightings, the composite sketch of the serial killer is slowly coming up in to focus 5.

Saturated Vs unsaturated fat: Fat has a lot of bad press and for many people; just a mention of the word can evoke misery. You can try to lose it, try to hide it, try to avoid it, but your body

still needs it! Did you know that fat helps to insulate our nerve cell, keeps us warm balances our hormones, keeps skin and arteries supple, lubricates joints and is a component in every cell.
The key issue here is recognizing which type fat your body needs, how much your body requires and which type is your enemy. Armed with right information, you can focus on getting more of the good fats and less of bad fats into your daily diet 15.

AIMS OF STUDY:

The purpose of study was to help alleviate the rising cost of important drugs. In view of the rising cost of the drugs, one strategy of the National Drug Policy is to promote the usage of locally made generic products. Simvastatin is the drug of which the local production and utilization are strongly encouraged, provided it can give equal safety and efficacy to that of the original product. In the present study here we report the outcome of the first randomized study conducted in Pakistan on the LDL – cholesterol lowering effect of locally manufactured generic Simvastatin products in comparison with the innovators products Zocor.
The purpose of this study was to find out the comparative efficacy and safety of two generic brands of Simvastatin i.e Atcol and Limitrol with that of the original brand of Simvastatin i.e Zocor.

PATIENTS & METHODS:

This study was conducted at the department of Cardiology, Dow University of health sciences , Karachi. The patients were selected from out patients department. in all 264 patients were included. The generic products used were Atcol & Limitrol where as brand was Zocor. The drugs were administered as 20 mg oral doses. The blood samples were collected every 4 weeks for 12 weeks. After giving a written informed consent, each volunteer received physical examination and laboratory screening (complete blood count, fasting blood sugar, glucose, BUN, creatinine , electrolyte, liver function test, CPK, total Cholesterol , HDL, LDL Cholesterol and triglycerides.
Selection criteria:
Patients between the age of 28-68 years with fasting plasma LDL-Cholesterol > 160 mg /dl , no previous history of using any antilipidemic drug . Male & non pregnant females were included in the study.
Exclusion criteria : Individuals with a history of allergy to HMG-co A-reductase inhibitors, pregnancy or lactation , peri-menopause or menopause, having illness such as diabetes m ellitus, liver diseases , ischemic heart disease or epilepsy , past & present use of cyclosporine , digoxin, erythromycin, gemfibrozil, niacin vit B3, warfarin, immuosuppressive agents or other drugs having reported interaction with Simvastatin, heavy drinking habit of tea & Coffee> 1000 ml/ day; heavy smoking (> 20 cigarettes/ day) serum aminotransferase more than three times of normal were excluded.

RESULTS:

The results of this study show that all the drugs; Zocor; Atcol & Limitrol significantly reduced the total cholesterol; the serum triglycerides and the low density lipoproteins cholesterol (LDL-C); High density lipoproteins (HDL-C), however increased significantly in all the three groups (Tables 1, 2, 3 and 4) & (figures 1, 2, 3 and 4).
The results of this study show that Zocor; Atcol as well as Limitrol caused no serious adverse effects. Only a few patients showed side effects. The side effects were not serious to discontinue the treatment.

DISCUSSION:

Simvastatin therapy reduced LDL-Cholesterol level by an average 35%. Coronary heart disease mortality by 42%, non fatal coronary heart disease events by 40% & total mortality rate by 30% 6. Low density lipoproteins (LDLs) & their oxidized derivatives initiate & promote the atherosclerotic artery process leading to the development of coronary artery disease 7. Increased plasma levels of LDL- Cholesterol are significant predictors of the development of coronary artery disease 8 and 9.
Management of patients with lipid disorders is of two types. One is population based approach, which is intended to lower blood cholesterol by dietary recommendations (NCEP1990). The 2nd is the patient approach described in 2001 report of NCEP.
The adult treatment Panel III guidelines for the management of adults 20 years & older recommend a complete lipoprotein profile, total Cholesterol ; LDL; HDL; & triglycerides rather than screening for total Cholesterol & HDL-C alone.
In the present study no significant no significant differences in therapeutic effect & safety were demonstrated between the generic & the brand of Simvastatin products. Decrease in the blood LDL-Cholesterol can slow down & reduce the incidence of CAD & thus mortality rate associated with the disease (Rackley 2000). Recent studies provide clear & convincing evidence that psychological factors contribute significantly to the pathogenesis & expression of CHD (Nishter, s2002).

CONCLUSION:

It can be suggested that avoiding saturated fats ; increasing physical activity and adopting religious means i.e offering regular prayers certainly have an extremely significant effect in the management of hypercholesterolemia.

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