



1: Lecturer, Department of Pharmacology, Shaheed Muhtarma Benazir Bhutto Medical University Larkana Sindh,

2: Professor; Department of Pharmacology, Bilawal Medical Collage LUMHS Jamshoro, Sindh.

3: Assistant professor; Department of Biochemistry, LUMHS Jamshoro.

4: Associate Professor, Department of Pharmacology, LUMHS Jamshoro, Sindh.

5: Lecturer, Department of Pharmacology, LUMHS Jamshoro, Sindh.

6: Lecturer, Department of Forensic Medicine LUMHS Jamshoro.

*=corresponding author

raza.memon@lumhs.edu.pk

Proton Pump Inhibitors: Pantoprazole is the safe drug as compared to Omeprazole drug during treatment of Dyslipidemia.

Fazeela Rizwan Memon¹, Nasreen Kazi², Ali Raza Memon^{3,*}, Muhammad Jamil Laghari⁴, Rizwan Ahmed Memon⁵, Jamshaid ul Qadir Memon⁶.

Abstract::

Introduction: Proton pump inhibitors (PPIs) are commonly used to manage retrosternal burning to peptic ulcer disease. Dyslipidemia is also very common in Asian population.

Objective: To evaluate the effects of different groups of PPIs like omeprazole, Pantoprazole, esomeprazole on lipid profile.

Methodology: This animal study conducted at the Department of Pharmacology with collaboration of Diagnostic & Research laboratory of Liaquat University of Medical & Health Sciences Jamshoro from 16 Nov to 30 Nov 2020. 24 male rabbit were divided in 3 equal groups. The sample for lipid profile were taken twice; first sample was collected before start of PPIs, while another sample was taken after six weeks of the treatment with different groups of PPIs. The lipid profile was analyzed by Cobass Auto analyzer (C-311) of Hitachi at Diagnostic & Research Laboratory LUMHS. The Statistical analysis was performed by student 't' test and chi square test by using SPSS version 21.

Result: The results found were statistically significant ($p < 0.05$) for omeprazole and esomeprazole while it was insignificant ($p = 0.247$) for pantoprazole. TG's was significantly more in group A and B animals as compare to group C animals. Low density Lipoprotein found raised among all groups but the rise was statistically insignificant.

Conclusion: Omeprazole exerts significant effects over all observed parameters of lipid profile, esomeprazole showed effects over few parameters, while pantoprazole showed insignificant effects over lipid profile.

Key words: Proton Pump Inhibitors, Low density Lipoprotein, Cholesterol.

Introduction:

The Proton Pump Inhibitors (PPIs) are widely used all over the world at different age groups for the treatment, curative and preventive purpose from different gastro-intestinal disorders.^{1,2} The burning sensation of upper GIT is common problem in Asian population due to different oily and spicy food items.³ Esophageal re-

flux, peptic ulcer also common in Asian population.^{4,5} Our population also commonly use pain killers for different pain at different times. NSAID group of drug commonly used for the pain relieving purpose which cause the peptic ulceration⁶ so PPIs are widely use for different purposes in our population.⁷ Dyslipidemia is one of the health disturbance issues in Asian popula-

tion.^{8,9} The 19% of Pakistani population is suffering from dyslipidemia.¹⁰ The Dyslipidemia is alarming signaling with association of major health issues in Asian population like Diabetes mellitus, Hypertension, Cerebrovascular accident, Cardiac manifestation like angina, myocardial infarction etc.^{11,12,13}

This animal study designed to evaluate the effects of different groups of PPIs like omeprazole, Pantoprazole, esomeprazole on lipid profile.

Methodology: This experimental animal study was done at Department of Pharmacology with collaboration of Diagnostic & Research laboratory of Liaquat University of Medical & Health Sciences Jamshoro, Sindh. from 16 Nov to 30 Nov 2020. Total 24 rabbits were selected from animal husbandry of Agricultural University of Tando Jam Sindh. They were divided in to three groups; group A, B and C; each group contained eight rabbits. Only male rabbits with weight between 1-2 kg were included in this research while female rabbits, ill rabbits, weight below 1kg or above 2kg were excluded from this study. Each rabbit put into separate cage with proper diet. The sample for lipid profile was taken from ear vein at zero level means before start of the treatment and at level-I means after six weeks of administration of different groups of PPIs. The lipid profile was analyzed by Cobass Auto analyzer (C-311) of Hitachi at Diagnostic & Research Laboratory LUMHS.

The Statistical analysis was performed by independent student 't' test and chi square test by SPSS version 21.

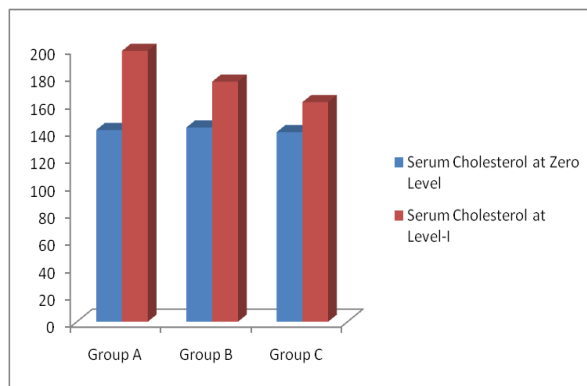
Results: Total 24 healthy male rabbits were selected for this study divided in to three groups; each group contained eight rabbits, group A rabbits was given omeprazole, group B was given Esomeprazole while group C was given Pantoprazole. All groups of PPIs were given by oral route. Lipid profile was analyzed at zero level (before start of experiment) and at level-I after six week of experiment.

Table No: 1 Serum Cholesterol (mg/dl) levels of all groups under Experiment.

Group	At Zero level	Level - I	p value
A	140.625	198.625	<0.05
B	142.5	176.075	<0.05
C	139.025	161	0.247

Table no 1 shows that the mean serum cholesterol levels of all three groups under experiment before and after experiment. As evident there was significant (p<0.05) incline in serum cholesterol level in groups of

omeprazole and esomeprazole drug experiment while pantoprazole had insignificant rise in serum cholesterol level.

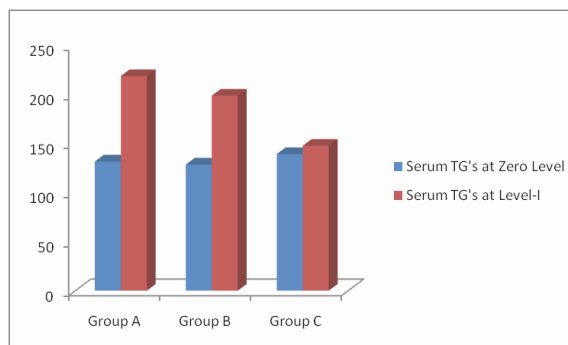


Graph No:01 Serum Cholesterol levels of all groups under Experiment

Table No: 02 shown the mean serum triglycerides levels (TG's) levels of all three groups under experiment before and after experiment. This table shows that there was more significant (p<0.001) incline in serum TG's level in group of omeprazole drug while in esomeprazole drug group also observed significant (<0.05) incline in esomeprazole drug group while pantoprazole had no significant effects on serum TG's level.

Table No: 2 Serum TG's (mg/dl) levels of all groups under Experiment.

Group	At Zero level	Level - I	p value
A	131.626	218.75	<0.001
B	128.5	198.75	<0.05
C	139.25	147.75	0.18



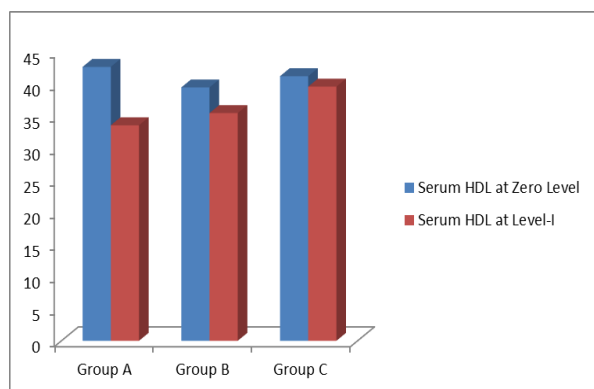
Graph No: 02 Serum TG's levels of all groups under Experiment

As shown in table no 3, the mean serum low density lipoprotein levels (LDL) of all three groups under experiment before and after experiment. There was significant

($p < 0.05$) rise in serum LDL level among animals from omeprazole drug while in esomeprazole drug group and pantoprazole drug groups, rise of LDL was statistically insignificant.

Table No: 3 Serum LDL (mg/dl) levels of all groups under Experiment.

Group	At Zero level	Level - I	p value
A	73.5	126.5	<0.05
B	77.25	95.5	0.319
C	74.075	84	0.01

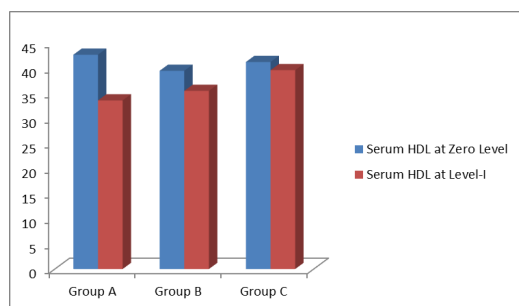


Graph No: 03 Serum LDL levels of all groups under Experiment

High density lipoprotein levels (HDL) of all three groups under experiment before and after experiment are shown in table no 4. The disturbance in HDL found insignificant among animals of all 3 groups.

Table No: 4 Serum HDL (mg/dl) levels of all groups under Experiment.

Group	At Zero level	Level - I	p value
A	42.7	33.6	0.12
B	39.5	35.5	0.193
C	41.25	39.625	0.02



Graph No: 04 Serum HDL levels of all groups under Experiment

The above findings suggested there were significant effects of omeprazole on examined parameters of lipid profile; while esomeprazole affects few and while pantoprazole is which has insignificant effect on lipid profile.

Discussion:

The Proton Pump inhibitors act as antacid by blocking the H/K ATPase pump at parietal cell of stomach, they are commonly using all over the world in different age groups with different gastric problems, to control the side effects of different drugs like NSAIDS, steroids, anti cancer drugs etc.^{2,6,14} In our population diabetes mellitus, hypertension, dyslipidemia then superimposed cardiac problems like angina and myocardial infarction etc.¹⁵ The analysis of lipid profile is the main indicator, prognostic test to evaluate the cardiac issues, diabetic atherosclerosis etc.¹⁶ This study was aimed to analyze the effects of different commonly using PPI in different clinical setups on lipid profile. Very little quantity of research was carried out on this research proposal earlier. On literature review we can not find a valid and recent study on this research proposal only Ashique Ali Arain et al¹⁷ reported omeprazole, esomeprazole and pantoprazole to reduce total cholesterol, LDL- cholesterol, HDL-cholesterol and triglycerides; we however found almost inverse result during this animal study. The findings of current study clearly shows that these agents do affect the lipid profile increasing the total lipids ,cholesterol and triglycerides while the protective cholesterol (HDL) is reduced that seems a possible mechanism behind the cardiac effects associated with PPIs. The mechanism of rise in lipids after PPIs requires more detailed investigations on the complex cholesterol synthesis pathway along with the various enzymes responsible for the same. Several recent studies have also shed light on PPIs and the cardiovascular system. PPI users have been shown to have a significantly greater risk of heart attack than those on other antacid medication.^{18,19} PPIs were also reported to reduce the production of NO (nitric oxide), so losing a natural protective agent for the blood vessels.¹⁹ PPIs were seen to damage the vascular endothelial cells quickly; these agents inhibit the cellular acidic nature compartment (lysosome) rendering its ability to clean up the waste products resulting into the accumulation of the same further inhibiting the lysosomal function.¹⁹ But the current research did not show the

significant effects on oxidative stress during study period but might be the study period was too short duration.

The current research must be viewed as pilot experimental study; however observations are thoughts provoking necessitating a large scale, multicenter study of larger duration to confirm findings in human subjects. As this animal study partly explain cardiac problems observed in patients taking PPIs, we assume that changes in lipids induced by PPIs prone the population to cardiovascular events; till prove or disprove after further research.

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