



Effects of Proton Pump Inhibitors on Serum Calcium Level: A Study on Rabbit Model

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Proton Pump inhibitors (PPI) are widely used all over the world as therapeutic agents as well as prophylactic agent at different age groups for multiple gastrointestinal disorders etc. it inhibits the hydrogen potassium pump (H/K ATPase Pump). PPI interferes the calcium absorption and thus disturbs acid secretion which leads to decrease the calcium level in the body.

Objective: The present design is to evaluate the effects of PPI on serum calcium level in rabbit model.

Study Design: Randomized Control Trial/ Study on Rabbit Model.

Place and Duration of Study: This experimental study was done at Department of Pharmacology Isra Medical University Hyderabad (November 2020 to March 2021)

Material & Methods: A total 20 healthy male rabbits with weight between 1-2kg were included in this study. While female rabbits, ill rabbits and rabbits with weight less than 1kg were excluded from study. Ten rabbits were given omeprazole sachet of 20mg orally dissolve in water once a day and 10 rabbits were given sachet of esomeprazole of 20mg dissolve in water once a day upto 90 days regularly. At different levels of study blood samples were obtained from vein near ear of rabbits and samples were centrifuged for 10minutes to obtain the serum. Then serum was sent to Isra Diagnostic Laboratory for analysis of serum calcium levels of all samples at different levels of study.

Results: Serum calcium levels of all rabbits were analyzed at three different levels of study, at zero level before starting of experiment, at level I after completion of one month of experiment and level II after the completion of three months of experiment. The normal serum calcium level in rabbits is 13-15mg/dl.⁸There was a significant decline in serum calcium level in Group A (Omeprazole Group), while in Group B (Esomeprazole Group) there was no significant relation between decreased serum calcium levels.

Conclusion: The study concluded that there is significant relation of longterm usage of PPI on serum calcium level.

Keywords: PPI; calcium levels; blood serum; calcium absorption.

1. INTRODUCTION

Proton Pump inhibitors (PPI) are widely used all over the world as therapeutic agent as well as prophylactic agent at different age groups for multiple gastrointestinal disorders etc [1].PPI basically is a pro drug[2] which inhibits the hydrogen potassium pump (H/K ATPase Pump) [3]. PPI block the gastric H/K-ATPase, inhibiting gastric acid secretion. This effect enables healing of peptic ulcers, gastroesophageal reflux disease (GERD), Barrett's esophagus, and Zollinger-Ellison syndrome, as well as the eradication of *Helicobacter pylori* as part of combination regimens [4]. The gastric H/K-ATPase is composed of two subunits: a catalytic α subunit and a β subunit [5]. "The primary structure of the gastric H,K-ATPase α subunit was elucidated in the rat [6] and then in the hog [7], rabbit [8], and human [9]. This catalytic subunit consists of 1033 or 1034 amino acids with transmembrane segments in all species. Functional studies demonstrated that ATP catalyzed an electroneutral exchange of H for K, with a variable stoichiometry of 2H/2K/ATP at pH 6.1, which fell to 1H/1K/ATP as luminal pH fell below 3.0 [10,11]. The β subunit consists of 291 amino acids and contains six or seven N-linked glycosylation sites with one trans-membrane segment [12]. The gastric H/K-ATPase is fully assembled during biosynthesis in the endoplasmic reticulum and is delivered to the

apical membrane as a heterodimeric oligomer. N-glycosylation of the β subunit was identified as being responsible for trafficking to the canalicular membrane"[12].

There are different groups of PPI's use clinically like Omeprazole, Esomeprazole, Pantoprazole, Lansoprazole etc [13]. The Omeprazole group of PPI is commonly using world wide [14]. The PPI interfere with the absorption of calcium[15] and disturbed acidic secretion also decreased the intestinal absorption of calcium [16]. The present study designed to evaluate the effects of PPI in serum calcium level in rabbit model.

2. METHODOLOGY

This experimental study was done at the Department of Pharmacology of Isra Medical University Hyderabad. Rabbits were purchased from Hyderabad city and Animal House of Agriculture university of Tando Jam Sindh. Total twenty healthy male rabbits with weight between 1-2 kg were included in this study while female rabbits, ill rabbits and rabbits with weight less than 1kg or more than 2 kg were excluded from study, ten rabbits were given 20mg of omeprazole given orally dissolve in water once a day and ten rabbits were given 20 mg of Esomeprazole dissolve in water once a day up to 90 days regularly. At different levels of study blood samples were obtained from vein near ear of

rabbit and samples were centrifuged for 10 minutes to obtain the serum then serum was sent to Isra Diagnostic Laboratory for analysis of serum calcium levels of all samples at different levels of study. The Statistical data was analyzed by SPSS version 21 by applying student dependent t test and Microsoft word and excel 2020 used for generating graphs and tables.

3. RESULTS

The 20 rabbits model were divided in to two groups as group a and Group B, each group contained 10 rabbits. The Omeprazole group of drug was given to group a rabbits while Esomeprazole group of drug was given to group B rabbits. Serum Calcium levels of all rabbits were analyzed at three different levels of study, at zero level before start of experiment, at Level-

I after completion of one month of experiment and level-II after the completion of three months experiment. The normal serum calcium level in rabbits is 13-15mg/dl.[8]The serum calcium level is normally raised in rabbits as compared other species of mammals. Table No: 01 & 02 shown the mean serum calcium levels at different three levels of experiment of group A and group B respectively.

After the completion of three months of experiment our result shown that there was a significant decline in serum calcium levels in group A which were use omeprazole group of PPI while in group B there was no significant relation between decreased serum calcium levels with esomeprazole group of PPI. From above result it can be suggested that there is effects of PPI on serum calcium level.

Table 1. The mean serum calcium levels of rabbits of group a (omeprazole group given) at all levels of experiment

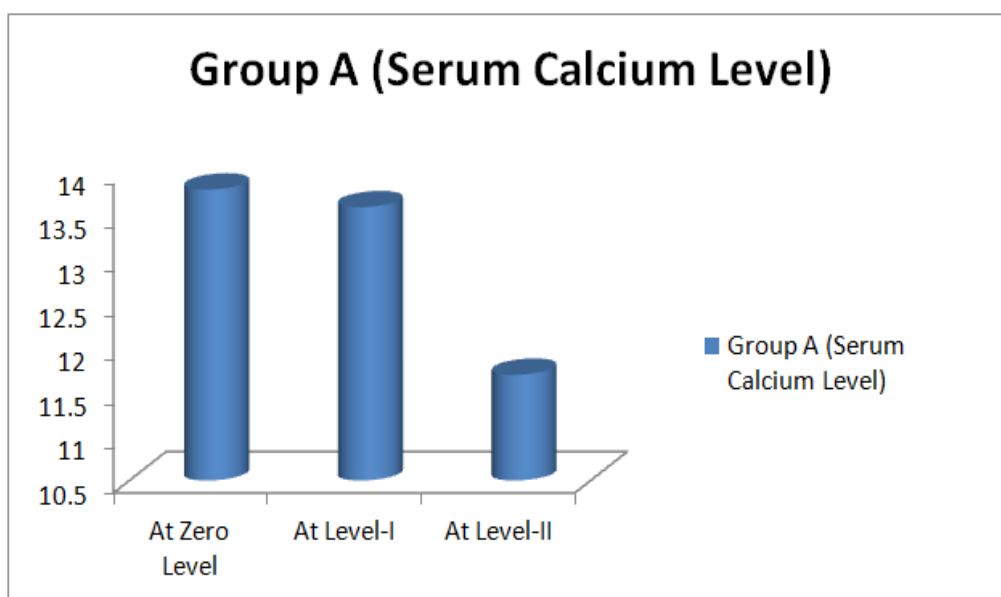
Parameter	At Zero Level	Level-I	Level-II	p.Value
Serum Calcium (mg/dl)	13.8+ 0.13	13.6+ 0.9	11.7+ 1.35*	<0.05

(* = p.value<0.05 by applying student t test)

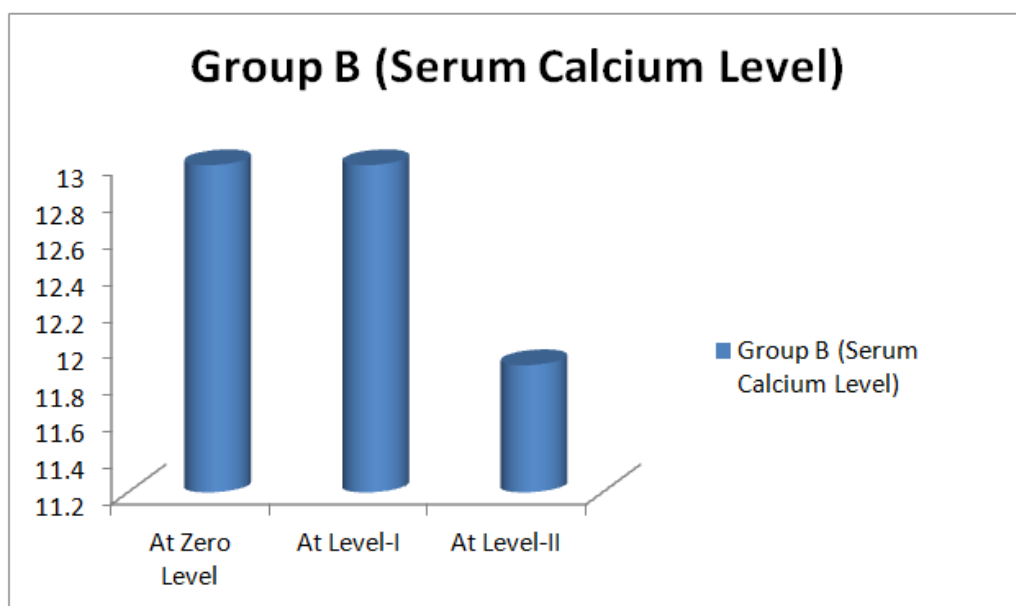
Table 2. The mean serum calcium levels of rabbits of group b (esomeprazole group given) at all levels of experiment

Parameter	At Zero Level	Level-I	Level-II	p.Value
Serum Calcium (mg/dl)	13.7 + 0.34	13.6 + 0.75	11.9 + 1.01	0.0413

(For analyze the significance student t test was applied)



Graph 1. Serum calcium levels of group



Graph 2. Serum calcium levels of group B

4. DISCUSSION

The PPI are the inhibitor of H/K ATPase pump and worldwide used for the treatment of different gastrointestinal disorder. Omeprazole commonly prescribed in clinical setup for treatment of gastro esophageal reflux, acidity due usage of NSAID's drugs, peptic ulcer [17,18]. Some studies observed there is relation between long term usage of PPI with bone mineralization, calcium absorption [19]. Prolong usage of PPI also alter the bone and calcium hemostasis [20].

Our study supported by O'Connell et al [21] reported that PPI especially omeprazole suppress the absorption of calcium so it will lead decreased level in blood. Our study also correlate with Hardey et al[22] that he concluded that PPI used in patients of renal dialysis with gastric ulcer disturbed the calcium hemostasis so use carefully in patients of renal dialysis. But Serfaty-Lacrosnier et al [23] suggested that there was no link or effect of PPI on calcium metabolism and absorption. But our study concluded that there was decreased level of serum calcium level by using of PPI continuous for three months especially significant result observed with usage of omeprazole group as compared to esomeprazole group.

There is limitation in our study need more research with extended sample size and different groups of PPI's like pantoprazole, lansoprazole, dexlanzaprazole etc along with long duration of study up to 6 months to 12 months.

5. CONCLUSION

The study concluded that there is significant relation of long term usage of PPI on serum calcium level.

CONSENT

Not applicable.

ETHICAL APPROVAL

Animal Ethic committee approval has been taken to carry out this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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