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EFFECT OF OMEPRAZOLE ON BIOCHEMICAL HAEMATOLOGICAL AND HORMONAL PARAMETERS

On chronic omeprazole used in patient at al Quranah city

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Contents

Abstract

Objective : To assess the effect of proton pump inhibitor on body functions by looking at the results for patients and comparing them with the rest of the research , Because of the widely use as over counter drug or prescriptions , the vitamin D level, calcium in the serum ferritin level, liver function, kidney function, blood components, lipids and sex hormones

Patients and Methods : Patients were received and interviewed in Al-Qurna Hospital, outpatient clinic, medical section and were selected according to certain criteria , 20 patients on long-term omeprazole therapy .

Result : show decrease in level of vitD3 and calcium and showed significant , Patient use PPIs drug than at control, The results also showed on the lipid profile Triglycerides and VLDL are significantly decreased than normal concentrations , while LDL increased significantly than control. The liver function tests only AST showed significant alterations than control.

Conclusion : it is clear that PPIs are currently being both overused and misused. probability of misuse and abuse increases exponentially. Although a safe and very effective class of pharmaceutical agent, proton pump inhibitors should be used only when there is documented evidence of a GI disorder that cannot be treated with an H2-receptor antagonist, and where a PPI use is clinically justified. Increased Clinician awareness on appropriate PPI prescription will lead to better patient outcome at lower cost.

Introduction

Omeprazole is a member of class of substituted benzimidazoles. These agents inhibit the proton pump in the gastric parietal cell, blocking the final step in the gastric acid secretory pathway , Omeprazole has a broad spectrum Use especially in the treatment of gastroesophageal reflux Disease ، Peptic ulcers caused By stress, non steroidal anti-inflammatory drugs and infection Of Helicobacter pylori have been treated by using omepra -zole . The prolonged inhibition of gastric acid secretion allowed for once-daily dosing in patients with peptic ulcer disease and gastroesophageal reflux, and once- or twice-daily dosing in patients with Zollinger-Ellison syndrome. Compared with currently available therapies, omeprazole is well tolerated and demonstrates a more rapid ulcer healing rate. It is superior to conventional therapies in the treatment of Zollinger-Ellison syndrome. Side effects are infrequent when the drug is used for the short-term management of ulcer

Long-term PPI therapy especially omeprazole may reduce Red Blood Cells (RBC) and White Blood Cell (WBC) counts as well as hemoglobin levels, leading to iron deficiency. It may also affect concentrations of some micronutrients, although the underlying mechanism of this association is not fully clear [2] .The most frequent laboratory haematology test is the complete blood count (CBC). The CBC provides important information about the patient's blood counts, clotting ability, and blood content. The CBC includes the RBC count, haem-oglobin (Hb), hematocrits (Het), the total WBC count, and at least an estimate of the platelet count. Various types of anemia (e.g., iron deficiency, pernicious anemia, and sickle cell anemia) are all diagnosed by visual examination of the peripheral blood smear[3] Reductions in both white blood cells and platelets were noticed about 4 months after proton pump inhibitors were introduced .White blood cell, neutrophil, and platelet counts when back to the normal range after proton pump inhibitors were stopped [4]

Omparazole for acidity

Available dosage 10mg, 20mg

Precaution: To br taken before meal

Available types: Tablet , injection

Omeprazole in clinical practice is unlikely to cause any significant interference in endocrine function.[5] urea is the major excretory product of our biochemical metabolism, while creatinine is a more specialized product of the breakdown of protein. Analysis of U&Es focuses on raised (hyper-) and reduced (hypo-) levels of these products and electrolytes. In both pre- and post-renal disease, there is nothing intrinsically wrong with the kidney itself or its functioning. However, failure to correct pre- or post-renal disease will lead to renal disease.

Chronic kidney disease (CKD) can be plotted by the relative rise in urea compared with the rise in creatinine. In contrast to Acute kidney Injury (AKI) , in CKD there is a greater incr-ease in creatinine and a slower rise in urea. [6] , PPI is a cause Acute Kidney Injury (AKI) due to acute tubulointerstitial nephritis (AIN), especially in the elderly. Additionally, two recent independent studies associated PPI consumption to an excess risk for CKD , and a recent prospective, double-blinded cohort study disclosed that omeprazole prophylaxis was associated to increased serum creatinine among patients admitted to hospital . However, the cellular and molecular mechanisms of PPI nephrotoxicity in general and specifically of omeprazole, have not been characterised, thus hampering prevention and therapy efforts[7]

Methodology

We enrolled 20 patients treated with omeprazole and another 20 control group without omeprazole treatment , their ages range from (18 _ 55) in Iraq , Basra , alqurna , In each group, complete blood count, and sex hormone, ferrtin , creatinine and urea clearnes , vitamin D3, thyroid hormone, lipid profile, liver functions by using analysis systems. There are some things that were overlooked during examinations and statistics that some patients taking PPI for intermittent long periods and Some take it for a very short time And also the age difference. Unless otherwise stated, all tests were performed at Dr. Ali's maknes Laboratory, in Basra Al_Qurna. We measured the CBC by using EMERALD system （abbotte company, in USA） , chemical analyzer smart __150 （Gento TEK company, in USA) use for all chemical analysis full automatid like solutions for measure the liver function and lipid profile, mini vidas (Biomerieux) company, France) for measure Vitamin D3 and hormones, spotchem EZsp_4430 (Arkray company, Japanese) for lipid profile, liver functions, renal functions and for all dry chemical analysis. It took us to work to conduct analyzes and statistics one month, from 2/2 to 4/3

The results

Table 1: comparison between some of hormones, vitamins and minerals of omeprazole treated patients and control non-treated group

Normal range of hormones, vitamins and minerals	Omeprazole Group	Control Group	Significance (p<0.05)
TSH (0.38 - 4.31mlU/ml)	2.629231±1.945578	1.7675±0.847707	NS
T4 (4.9 -11 ug/ dl)	7.46±2.627642	9.096±5.763664	NS
T3 (0.79 -1.58 ng/ml)	1.346±0.358119	1.427±0.876281	NS
prolactin fem (4.1-28.9ng/ml)	30.11±29.19361	23.15±8.572164	NS
testosterone fem (0.23-2.6)	1.825±1.285635	0.653333±0.388158	NS
FSH (4.5 to 21.5 IU/L)	15.3875±15.09526	12.81333±6.027161	NS
Progestron (5-20 ng/ml)	7.87±5.345083	9.74± 6.889296	NS
vitamin D3 (30 -100 ng/ml)	17.3095±11.14448	25.02824±13.47998	S
s. calcium (8.4 -10.4 mg/dl)	7.810909±0.860296	9.303±1.784887	S
ferritin fem (20-250 mg/dl)	18.19333±16.39169	69.85±106.7043	NS

S significant <0.05; NS non-significant >0.05

Table 2: the comparison of biochemical tests between control and Omeprazole treated group

Normal range of biochemical tests	Omeprazole Group	Control Group	Significance (p<0.05)
cholesterol (150-200 mg/dl)	223.4545455±53.4833874	205.6923077±47.15821706	NS
triglyceride (60 -165 mg /dl)	158.8181818±48.16600083	215.4615385±85.98315279	S
HDL (>40 mg/ dl)	43.1±14.7380837	50.57692308±19.05895038	NS
D. LDL (< 130 mg/d)l	152.6±49.82681117	120.9230769±35.46468088	S
VLDL (< 32 mg/dl)	33.2±8.625543461	47.96923077±14.7392551	S
ALP (44-147 U/ L)	72.2375±20.77119554	87.47272727±63.78521915	NS
ALT (3 -55 U/ L)	27.62625±14.76613107	23.54545455±26.87141097	NS
AST (5 - 34 U/L)	23.32125±9.48705349	14.73125±8.959469751	S
T P (10-14)	9.133333333±3.821430797	12.48±5.271337591	NS
total bilirubin (0.2-1.2mg/dl)	0.761428571±0.320542695	1.333333333±1.175868473	NS
direct bilibrubin (0-0.5mg/dl)	0.26±0.15513435	0.858333333±1.0022059	NS
indirect bilibrubin <8	0.471428571±0.233054255	0.883333333±0.627779154	NS
urea (15-40 mg/dl)	45.759±14.22719341	26.27813±14.77416	S
creatinine (0.5-0.9 mg/ dl)	1.399±0.45412798	0.783571429±0.259751572	S

S significant <0.05; NS non-significant >0.05

The results also showed on the lipid profile Triglycerides and VLDL are significantly decreased than normal concentrations; while LDL increased significantly than control. The liver function tests; only AST showed significant alterations than control as illustrated on table 2.

Table 3: measurement of complete blood picture at both control and Omeprazole treated group

Normal range	Omeprazole	control	Significance (p<0.05)
WBCs	7.86±2.672747	8.952±2.791912	NS
LYM (20% -40%)	33.93 ±11.57539	37.23333±12.08508	NS
MID (15%-1%)	9.115 ±1.768816	8.833333±2.347608	NS
GRAN (70%-50%)	57.045±12.84722	52.53333±13.61433	NS
RBC (5.5-3.5)	4.723± 0.904131	4.468333±0.662363	NS
HGB(15-11g/dl)	11.135±1.950783	11.38±1.769161	NS
HCT (26-38 g/dl)	36.725±5.497164	38.95667±9.263003	NS
MCV (99-80 Fl)	78.715±10.2914	82.49667±12.75654	S
MCH (32-26 pq)	24.26±3.7832	25.7633±1.8406*	NS
MCHC (36 -32 g/dl)	30.325±1.572753	29.20667±5.214101	NS
RDW-CV (14% -11%)	14.693±9.617891	12.34545±1.03958	NS
RDW-SD (46-39 Fl)	36.21±13.43192	39.34545±4.652604	NS
PLT (300-100 ^9/L)	304.4±70.74223	272.9±65.67703	NS
MPV (10.4-10 Fl)	9.27±1.303881	8.986667±1.207658	NS
PDW (14.-10 f L)	13.38±2.632309	13.58667±2.397518	NS
PCL (0.28 -0.10 f L)	0.45375±0.54298	0.20625±0.053168	NS
P-LCR (43% -13%)	24.325±9.409532	28.4125±8.541736	NS
P-LCC (129 -13^9 /L)	56.0875±11.84175	58.7125±14.49743	NS

The data exhibited that only MCV showed significant decreased than control group

Discussion

Proton Pump Inhibitors (PPI's) such as omeprazole are known for drug reduce gastric fluid PH, to treat heartburn, reflux disease (GERD), and ulcers. PPIs is They act by inhibiting the H+-K+-ATPase enzyme (proton pump) present in the parietal cells of the gastric mucosa. These drugs are the most potent blockers of gastric acid secretion, as they block the secretion irreversibly Their efficacy has been estimated to be better than that of histamine-2 receptor blockers It will use for stomach when taking NSAIDS to relive stomach side effect . Even if you've been taking for a long term administration of PPI has been incriminated as a risk factor in the body by effect on hormone, mineral, enzyme and other substance in body that effect of daily activity on the body ، The omparazole and PPI have many side effects , Enteric infections associated diarrhea , Pneumonia , Altered anti platelet metabolism e.g. Clopidogrel , Osteoporosis related fractures , Deshpande, et al. Also to Vitamins and minerals deficiencies : Vitamin B12 , Vitamin C , Calcium , Iron and Magnesium . [8] In this study, we study the effect of PPI on body functions by looking at the results for patients and comparing them with the rest of the research ، The level of vitamin D, calcium in the serum, ferritin level, liver function, kidney function, blood components, lipids and sex hormones were discussed.

Effect of omeprazole on vitamin D : Evaluate the effect of proton pump inhibitors on vitamin D levels in patients who are treated for vitamin D deficiency or insufficiency , Vitamin D very important because deficiency will cases Rickets, Muscle weakness and fall,Osteoporosis and fractures,Hypertension(HTN) and Left ventricular hypertrophy ,Diabetes mellitus, DM , Increased risk preeclampsia [9] The statistical analysis was done by comparing the mean change in Vitamin D in each group with the use of the Student test. In our data study show significant deficiency vitamin D in patient taken PPI for long time period in the range (17.3095 ± 11.14448) comparison to control group of patient that value range from (25.02824±13.47998) In another study show the mean improvement in 25 (OH) vitamin D levels for the "PPI" group was 40% with a mean raw difference of 9.5 . No PPI" group demonstrated a mean improvement of 60 % with a mean difference of 14.2 (95% CI 12.3-16.2)

Rani Hanna his study: The improvement in 25 (OH) vitamin D levels in the '"no PPI "cohort was 49% greater than those taking a PPI. In April 2012 that done study for two year to known the Change in 25-OH Vitamin D in Blood over 60 days, The result this study on Chronic use of PPIs has been associated with increased fracture risk. The risk is increased with longer duration of therapy and increased patient age[10], This study revealed that there was an inconsistent measurement of vitamin D, with only half of chronic PPI users having a vitamin D level documented in their medical record. [11]Christian Roux has studied for Increase in vertebral fracture risk in postmenopausal women using omeprazole: Omeprazole use is associated with an increased risk of vertebral fractures in postmenopausal women

These findings are in agreement with previous studies, The absorption and transport of lipids of vitamin D in GIT seems to be a multistep process including physiochemical as well as enzymatic involvement , The acidic pH of gastric juice may affect the bioavailability of vitamin D. It is apparent that no data available on the susceptibility of major dietary forms of vitamin D to GIT pH conditions so result of taking PPi leads to a decrease in stomach acid, explaining its effect on vitamin[[13].

Effect of omparazole on calcium : in our study show that postprandial calcium concentration did not increase in subjects on PPI, whereas control subjects demonstrated an apparent increase in serum calcium , the results of decrease of calcium level in blood in range 7.810909±0.860296 compare to control patient 9.303±1.784887 , It has been attributed to the reduction in gastric acid production, This prolonged treatment is believed to hinder calcium absorption in the small intestine , The ability of the small intestine to absorb calcium salts is highly pH dependent, and since proton pump inhibitors cause an increase in gastric pH, calcium salts are rendered insoluble and cannot be absorbed. This inhibition of calcium absorption has a direct correlation to osteoporotic fractures in those individuals taking a PPI , these studies have attributed this observation to the fact that calcium absorption occurs in the small intestine where the pH of the contents is typically between 6 and 7, even without PPIs therapy .[15] Thus, regardless of the secretion of gastric acids, as the pH of the chyme in the duodenum remains relatively constant, PPI does not affect the absorption. In a study done on postmenopausal women, 30 days of continuous PPI therapy could not decrease intestinal calcium absorption. Even no change in parathyroid hormone (PTH), serum calcium was observed, providing further evidence that PPIS do not alter calcium absorption in the short term. Another mechanism that has been proposed was that PPI suppresses gastric acid production by inhibiting the hydrogen/potassium adenosine triphosphatase (H+/K+ ATPase) located on the parietal gastric cells [17]

These proton pumps are also found in the plasma membrane of osteoclasts, which decrease the osteoclast activity , that may be reduce bone turnover. In the current study, A study conducted in Canada determined that after seven years of continuous exposure to a PPI, there was a statistically significant increase in osteoporosis-related fractures, and an increase risk of hip fracture after five years, As bone mineralization and resorption takes many years, and because of the subtle effect that proton pump inhibitors have on bone mineralization, several years may be required before it has a measurable clinical outcome.
[18] , Our results are in agreement with previous study

Effect of omparazole on thyroid hormone
In the study group, the mean change in the TSH level from before and after initiation of PPI therapy, 2.629231±1.945578 IU/mL, was statistically significant . In the control group, the mean change in the TSH level during the study period, 1.7675±0.847707 IU/mL, was not statistically significant effect , Also another hormone T4 in PPIs therapy 7.46±2.627642 and control 9.096±5.763664 and T3 hormone show average 1.346±0.358119 and control patient show 1.427±0.876281, So that PPI show have weak effect on thyroid hormone, Centanni et al. investigated the effect ofPPIs on the bioavailability of levothyroxine, concluding that increased levothyroxine doses may be required inpatients exposed to omeprazole.In another Studies on the effects of omeprazole on thyroid function in the rat , The effects of omeprazole on thyroid parameters in rats have been examined. rats were dosed orally with omeprazole , Treatment for 7 or 14 days resulted in generally decreased plasma T3 concentrations in males (with little change or slight increases in females) and increased serum TSH concentrations (22%-68% increases). In-vitro studies showed omeprazole to be only a weak inhibitor of TSH-stimulated organification in cultured porcine thymocytes. It is concluded that omeprazole has weak effects on the pituitary-thyroid-liver axis, its main action being to inhibit the peripheral deiodination of thyroid hormones. [19]

In February 1998 that done study on proton pump inhibitors on thyroid hormone metabolism in rats show Pantoprazole and omeprazole treatment did not affect plasma T4 or T3 significantly, whereas lansoprazole treatment produced marked reductions in plasma T4 but did not affect plasma T3 significantly.[20] , We can take the study and consider it acceptable through its compatibility with several researches, taking into consideration , omeprazole to be only a weak inhibitor of TSH-stimulated , that Several factors might change the absorption of levothyroxine. For example, it is known that levothyroxine bioavailability is affected interfere with intestinal absorption of levothyroxine not effected by stomach acidity [21]

Effect of omparazole on ferritin value

In the study group, the mean change in the ferritin level from before and after initiation of PPI therapy,(18.19333±16.3916 9) was statistically significant , In the control group, the mean change in the ferritin level during the study period 69.85±106.7043, was not significant effect , Our study demonstrates that short duration of omeprazole use does not affect iron absorption in iron-replete healthy individuals who are on a normal diet. Although short-term omeprazole therapy does not appear to affect iron absorption, since PPIs are increasingly being used for longer durations . Iron is essential for the production of RBCS and the iron balance is maintained by the absorption of dietary iron in the GI tract. ([22] . There are two forms of dietary iron, heme iron and non-heme iron , Dietary non-heme iron is much less well absorbed than heme iron and its absorption is markedly improved in the presence of gastric acid [23]

That PPIs which effect on absorption than assists the absorption by dissociating the iron salts in the food and by increasing their solubility, allowing them to be reduced to ferrous form. Our study demonstrates that It can be considered the study and agree with the rest of the research because omeprazole is not an iron store, but rather an iron absorption , also Although short-term omeprazole therapy does not appear to affect iron absorption, in healthy individuals who are on a normal, no change in the values was observed, Hutchinson Show the use of PPIS may actually lead to iron deficiency anemia. No decrease in the body iron stores or iron deficiency was observed in patients who received continuous omeprazole therapy for up to 12.5 years On the contrary, in patients with hereditary hemochrombtosis PPIS were shown to reduce the frequency of therapeutic phlebotomy and the absorption of dietary non- heme iron However, these results cannot be applied to general PPI users. [24]In another study show Administration of omeprazole for a short duration does not affect absorption of orally administered iron in healthy individuals who are on a normal diet. Since

omeprazole's effect was shown in iron-depletion or iron-overload states, it is apparent that omeprazole may have an effect on iron absorption only in abnormal iron metabolic states. In 2010 show research Omeprazole and possibly all proton pump inhibitors seem to decrease the absorption of oral iron supplementation, to a level where either they may have to be continued for a long term or may have to be given the iron supplementation intravenously. (25) Some study show use Proton pump inhibitors (PPIs) for the long-term use of PPIs is considered safe, there are several reported cases of iron deficiency anemia and a community-based case control study reported that the risk of iron deficiency was increased among long-term PPI users However, the association between PPI use and iron deficiency anemia remains controversial and it is not yet known whether the extended use of PPIs is associated with iron deficiency anemia after a long latency period. ...(26) So , Patients who need to be on long term PPI, especially who may have ongoing occult blood loss should be checked regularly for iron deficiency anemia, as they most certainly also significantly decrease dietary iron absorption. And if found to be iron deficient, they should either be treated with high dose iron therapy or for susceptible patients with in iron therapy.

Effect of omparazole on sex hormone

for assess the effects of PPIs on sexual function and serum levels of testosterone, prolactin, follicle stimulating hormone (FSH), Progesterone diagnosed female patients , in comparison to healthy controls. In our study show the average of Progesterone 7.87±5.345083 in patient use PPIs and for control patient 9.74± 6.889296 , that show a weak effect on the level of Progesterone , prolactin fem the average (30.11±29.19361) for patient taken omeprazole and value (23.15±8.572164) for control result , the testosterone fem for patient use PPIs (1.825±1.285635) and for control group (0.653333±0.38815) and for FSH the level (15.3875±15.09526) and for control result 12.81333±6.02716 , All the result show no significant change in value than from normal range In another study show Long term Omeprazole therapy might cause a reduction in the level of testosterone hormone with insignificant effects on other sexual hormonal levels (prolactin, FSH) within significant effect on sexual function, in male patients with peptic ulcer disease.(27) Another report a case of a young female with symptoms of gastroesophageal reflux disease who developed galactorrhea after starting esomeprazole therapy.Resolution of galactorrhea after stopping the drug (28) Also It has been reported in the rat that a high dose of lansoprazole 150 mg/ Kg/d orally decreased the blood level of testosterone and produced an associated increase in luteotrophic hormone. Concluded from their study in male rats, that lansoprazole treatment for 14 days induced hepatic CYP-dependent testosterone metabolism in vitro and enhanced plasma clearance of radio labelled testosterone in vitro and that these effects might

contribute to depletion of circulating testosterone levels (29) , Lindquist and Edwards gives 15 reports of impotence and 15 reports of gynaecomastia associated with the use of omeprazole therapy Also Carvajal et al (1992) reported 3 patients who developed impotence with unilateral gynaecomastia in relation to omeprazole therapy.(30) some study referred that omparazole increase prolactin level, that suggasted on PPIs may have a mild inhibitory effect on CYP3A4, which leads to decreased metabolism of estrogen, thereby increasing serum estrogen levels. Estrogen causes stimulation and production of prolactin release, which results in development of galactorrhea. That interperation for PPI induced galactorrhea (31) This study needs more follow-up and larger groups of both sexes in order to consider it acceptable or no

Effect of omparazole on kidney function

The study biochemical values of the patients who developed Acute kidney injury AKI following PPI therapy. The normal values in our laboratory are as follows: Patients had abnormally elevated laboratory renal parameters (urea and creatinine) prior to after of PPI therapy; In the current study by Muller , 19 subjects were found to have developed AKI among the 175 patient records assessed. Thus, an incidence of 10.86% was estimated in the study. An incidence of 2.86% (6 cases out of 210) was found in a study done in Southeast England.(32) A study by Sampath kumar K et al., also showed that pantoprazole was the most commonly implicated PPI , Pantoprazole was the most common PPI responsible for the development of AKI in the current study but this could be because 82% of the study population had been prescribed pantoprazole, as opposed to the other PPIs. (33) However, there are several reports available, which report AKI with other PPIs . AKI is now considered as a class effect of PPIs . The dosage and duration of PPI therapy did not play a significant role in the development of AKI. Similar results were observed in previous studies as well (34) ، The duration of PPI therapy preceding the development of AKI varied from 7 to 21 days in the current study. Also, it has been assume that AKI could be secondary to oxidative stress, Further, the hypomagnesemic component associated with the use of PPIs could be another reason for development of AKI and (chronic kidney disease) CKD, especially in the older patient (35) , The study can be considered acceptable with research and results because there association between omeprazole use and progression of CKD stage was identified, showing a higher risk of disease evolution among omeprazole users (36) Effect of PPI on lipid profile: Cholesterol is considered both good and bad . At normal levels, it is an essential substance for the body, while when concentrations in the blood raised , it becomes a silent danger that puts people at risk of heart attack . In other handHigh levels of LDL can increase the risk of cardiovascular disease, clogged arteries, and other

heart health issues. (37) In our data research show clear difference in level Cholesterol, triglycerides, HDL, LDL and VLDL of patient take omeprazole for long time period, Cholesterol is slightly increase about (223.4545455±53.4833874), triglycerides , a borderline affected between (158.8181818±48.16600083), HDL has slightly increase in range (43.1±14.7380837),the D. LDL considered the most one has increasing in its level (152.6±49.82681117 (, VLDL showed slightly increased than normal value (33.2±8.625543461). Compare to control group of patient, the Cholesterol value range from (205.6923077±47.15821706), the triglycerides value range from (215.4615385± 85.98315279), HDL value about (50.57692308±19.05895038), D. LDL show its value in range (120.9230769±35.46468088), and VLDL in range about (47.96923077±14.7392551). Proton pump inhibitors use was accompanied with a significant increase in fasting low-density lipoprotein (LDL) levels and a limited increase in LDL's main structural protein apolipoprotein B , However, PPI use not associated with differences in fasting high-density lipoprotein (HDL) (p=0.24), fasting triglyceride levels (p=0.81) (37) , In another research the author found The long term use of Proton pump inhibitors results in increased levels of serum total lipids, cholesterol, LDL-C, Triglycerides and reduced level of serum HDL-C. (38) , Other researcher found the subjects receiving statin + PPI had a higher LDL-C reduction by 6.4% compared with those taking a statin alone (fully adjusted p =0.005). In contrast PPIs may modestly boost the statin mediated LDL-C reduction.this study needs more time and more patients

Effects of omparazole on blood picture :

The complete blood count (CBC with Differential) may be a broad screening test to work out a human general health status. It will be used to: Screen for a large range of conditions and diseases , Help diagnose various conditions, like anemia, infection, inflammation, bleeding disorder or leukemia, CBC may be a panel of tests that evaluates the three forms of cells that circulate within the blood and includes the following: Evaluation of white blood cells, the cells that are a part of the body’s defense system against infections and cancer and also play a role in allergies and: White blood cell count (WBC) could be a count of the full number of white blood cells in a person's sample of blood. White blood cell differential may or might not be included as a part of the panel of tests. It identifies and counts the amount of the assorted varieties of white blood cells present. The five types include lymphocytes (LYM), neutrophils, monocytes, eosinophils, and basophils (GRA). MID cells and percentage: (MID) cells include less frequently occurring and rare cells correlating to monocytes, eosinophils, basophils, blasts and other precursor white cells that fall in a very particular size range. % and absolute counts are determined for lymphocytes, neutrophil,

and a mid-size population of monocytes, basophils, eosinophils, blasts, and other immature cells. Evaluation of red blood cells, the cells that transport oxygen throughout the body: Red blood cell count (RBC) could be a count of the particular number of red blood cells during a person's sample of blood. Haemoglobin (HGB) measures the number of the oxygen-carrying protein within the blood. Hematocrits (HCT) measures the share of a person's blood that consists of red blood cells.

Red blood cell indices are calculations that provide information on the physical characteristics of the RBCs: Mean corpuscular or cell volume (MCV) could be a measurement of the common size of RBCs. Mean corpuscular or cell hemoglobins (MCH) may be a calculation of the typical amount of oxygen-carrying haemoglobin inside a red somatic cell. Mean corpuscular or cell hemoglobin concentration (MCHC) may be a calculation of the typical percentage of hemoglobin inside a red cell. Red cell distribution width (RDW) may be a calculation of the variation within the size of RBCs.

The CBC may include a reticulocyte count, which could be a measurement of absolutely the count or percentage of young red blood cells in blood. Evaluation of platelets, cell fragments that are vital for normal blood clotting: The platelet count (PLT) is that the number of platelets in a very person's sample of blood.

Mean platelet volume (MPV) may be a calculation of the common size of platelets. P-LCR assay: this is often the ratio of large platelets to cells & P-LCC test: this is often an abbreviation for platelet large cell count , The parameter is to be a target to be a thickness plane, within the early stages of its manufacture.

In study of proton pump inhibitors therapy that show effect on , In our data study show no effect on WBC, LYM, neutrophils, monocytes, eosinophils, and basophils , MID cells and percentage , Gran is short for granulocyte , RBC (Red blood cell), Haemoglobin (HGB) , Hematocrits (HCT) , Mean corpuscular or cell haemoglobin (MCH), Mean corpuscular or cell haemoglobin concentration (MCHC), RDW-CV (Red cell distribution width (RDW), RDW-SD , platelet count (PLT), Mean platelet volume MPV ,Platelet Distribution Width PDW , P-LCR (platelet large cell) , P-LCC (platelet large cell) in patients take omeprazole are normal and that change non significant effect, just decease in MCV value that indicates that the red blood cells are small, or microcytic and that causes Iron deficiency. compare to control group of patient that value , such as show little difference in data of RBC for patients take omeprazole in rang (4.723± 0.904131), compare to control group of patient in rang (4.468333±0.662363). As will as the haemoglobin (HB) level will decease in patients take omeprazole for long time period in rang (11.135±1.950783), compare to control group of patient in range (11.38±1.769161) , The platelet account in our data show slightly elevated in patients take omeprazole for long time period in rang (304.4±70.74223)

compare to control group of patient in rang (272.9±65.67703).in another study the author used in their research 37 patients on long term ppi therapy Their results appears as show Red blood cells and WBC counts were lower in the ppi group compared with controls).(39) In another research investigating the relationship between PPI use and iron deficiency is not consistent. (40) showed no effect on iron absorption with short-term PPI therapy, while in contrast some studies suggest that prolonged omeprazole use for at least 3 to 4 years is unlikely to cause iron and ferritin malabsorption (41) , whereas Sarzynski found that among adults on long-term PPI therapy, defined as >1 year, there was a significant decrease in hematologic indices from baseline.(42) In another research about the effect of PPI on platelet count, the author (43) found In their patient, the thrombocytopenia occurred after the initiation of PPI and resolved after its stopping . The causality of PPI with regard to thrombocytopenia in this particular case was further strengthened by the observation of another episode of thrombocytopenia when the PPI was reintroduced. Complete recovery of the platelet count only occurred when the PPI was discontented and, hence, the PPI was subsequently listed as a drug allergy for this patient., they are very few, recorded no significant effect of omeprazole on blood, mentioned that 22 haematological effects: leucopenia and agranulocytosis have been reported but Most studies indicate no significant effect of Omeprazole on blood, generally Excessive use of medicines can cause haematological effects . To study the results of this study, we need to study for a longer period, taking into account larger groups of patients and from specific groups to determine the acceptability of the study on blood.

Effect of omparazole on liver function :

in our data study show normal Significance in GPT (ALT) alanine aminotransferase(3 -55 U/L) in patient take omeprazole for long time period in rang(27.62625±14.76613107) while the ALP (44- 147 U/L) show reduce in rang (72.2375±20.77119554) , compare to control group of patient in rang (87.47272727±63.78521915) , as well as the TP show high decrase in patients take omeprazole for long time period in range (9.133333333±3.821430797),compare to control group of patient in rang (12.48±5.271337591) , and the AST (aspartate aminotransferase) (5 - 34 U/L) has no differences in patient take omeprazole (23.32125±9.48705349) compare with control patient (14.73125±8.959469751) , while the total bilirubin (0.2-1.2mg/dl) in patients take omeprazole show no differences with control Group in range (0.761428571± 0.320542695) .also indirect bilirubin <8 has no differences in patients take omeprazole(0.471428571±0.233054255) compare with control group(0.883333333± 0.627779154) , This conclusion is in line with the findings of many researchers, where

(Bian et al, 2017) (44) confirmed the existence of a significant link between acidity drugs and liver diseases . while the (Francavilla et al, 1989) (46) show there is no effect of omeprazole in liver ,(Cheng, 2013) show the presence of anti-inflammatory effects by inhibitors of acidity, but recommended researches to find out their other effects ,while (K INUTHIA, 2 017 said , Omeprazole can cause a defect in the liver.(45) When the drug administered at dose (20) mg, there is no significant effect on the the enzyme compared to the control group, But when the dose given is increased to (40) mg of omeprazole for three consecutive months lead to significant increase in the value of the ALT enzyme compared to the control group at $p< 0.05$. This means there is a very clear effect of this drug on the liver, which is expected after the knowledge of the side effects of medications such as omeprazole and PPIs on the organs of the body , especially the liver ,which metabolism. (48) he said there is also significant differences between the control patient and the patient treated with omeprazole when the patient take omeprazole for long time and in high dose this lead to increase the value of GOT (AST) enzymes , this enzyme is an important indicator to determine the health of liver in the body, any increase or decrease in enzyme value over its normal range is evidence of an inflammation or liver dysfunction.some of researcher show there is no effect of omeprazole on ALT, AST and total bilirubin levels. These findings are in agreement with previous studies,

Conclusion

At the present study the results showed significant differences at VitD3 and S.Ca concentrations and also significant abnormal urea and creatinine. At lipid profile increased in levels of LDL and triglycerides with no effects on HLD. While, there was no effects on blood pictures

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