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Case Review

H2 Blockers and PPI: Review of Cases causing Adverse Drug Reactions

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Abstract: Proton pump inhibitors (PPIs) are a group of drugs that reduce the secretion of gastric acid. They act by binding with the enzyme H+ K+ ATPase and H2 Blockers are antihistaminics commonly used for inhibition of acid secretion. Mainly used for peptic ulcers and other hyperacidity conditions. Now a days its seem to be prescribed non rationally where it is not required. They are taught to be safe drugs and are now available over-the-counter. As we have reviewed and collected some cases showing wide range of adverse drug reactions due to proton pump inhibitors. Pharmacovigilance is concerned with identifying the hazards associated with pharmaceutical products and with minimizing the risk of any harm that may come to patients. Companies must conduct a comprehensive drug safety and pharmacovigilance audit to assess their compliance with worldwide laws, regulations, and guidance.

Keywords: Proton pump inhibitors (PPIs), H2 Blockers, Pharmacovigilance, Adverse Drug Reactions.

INTRODUCTION

Proton pump inhibitors (PPIs) are among the most widely used drugs worldwide. They are the used for the treatment for acid-related disorders, such as peptic ulcer disease, gastro esophageal reflux disease, Zollinger-Ellison syndrome and idiopathic hyper secretion. PPIs are useful in the eradication of Helicobacter Pylori infection as well as for prevention of peptic ulcers and upper gastrointestinal bleeding in patients taking non-steroidal anti-inflammatory drugs (e.g. aspirin) or antiplatelet agents. (Ali, T *et al.*, 2009).

PPIs are considered to be the safe drugs when used as directed, and are now available over-the-counter. However, PPIs were approved by the FDA for short-term use.

Side effect is an undesirable symptom caused by taking a drug or undergoing a therapy. Side effects can range from relatively minor symptoms such as drowsiness or an upset stomach, to serious effects such as liver damage, and sometimes even life-threatening or potentially fatal kidney damage effects. (Lazarus, B *et al*, 2016).

Nevertheless, proton pump inhibitors generally are well tolerated. PPIs may increase the risk of *Clostridium difficile* infection of the colon. High doses and long-term use (1 year or longer) may increase the risk of osteoporosis-related fractures of the hip, wrist, or spine. Prolonged use also reduces absorption of vitamin B12 (cyanocobalamin). Long-term use of PPIs has also been associated with low levels of magnesium (hypomagnesemia). Analysis of patients taking PPIs for long periods of time showed an increased risk of heart attacks.

Therefore, it is important to use the lowest doses and shortest duration of treatment necessary for the condition being treated.

CASE REVIEWS

Nishant Gupta *et al*, (2009) studied Case on Hepatitis induced famotidine**.** A 47 year old male with a past history of asymptomatic chronic Hepatitis C diagnosed 4 years ago, on no home medications, came to the hospital with chief complaints of right upper quadrant abdominal pain and vomiting for one day. An ultrasound of the abdomen done at the time of admission showed a stone in the gallbladder neck with pericholecystic fluid consistent with clinical diagnosis of acute cholecystitis. Started on Morphine, Cefoxitin and Famotidine and subsequently underwent laparoscopic cholecystectomy the next day. The sudden elevation in liver enzymes within a couple of days of hospitalization made them think of a possible

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medication induced adverse reaction. The patient's medications at that time were cefoxitin, morphine and famotidine. Famotidine was discontinued at that time and serial measurements of liver enzymes were done. The liver enzymes started improving from the next day and were back to normal within the next 7 days. The acute rise in liver enzymes made them as consider an adverse drug reaction and famotidine was discontinued. Thus in this case report concluded that famotidine induced hepatitis as a possible etiology of acute liver function.

Raj K *et al.* (2018) studied a case of Rabeprazole-induced Acute Interstitial Nephritis(AIN). Here they reported a case of 47-year-old male patient, admitted of peptic ulcer disease since 2 months and admitted with chief complaints of nausea and abdominal pain. The patient was on treatment with rabeprazole. At the time of admission, his serum creatinine level and blood urea nitrogen were elevated. Ultrasonography showed changes in the renal parenchymal cells, and renal biopsy report was also suggestive of AIN. So, they reported that this is a case of Rabeprazole-induced AIN and thus, the drug therapy was stopped on the day four. Patient was symptomatically and clinically better after discontinuation of the drug. Thus, in these case report it is concluded that the probability of the incidence of AIN being induced by rabeprazole.

Berna Aksoy *et al.* (2010) studied a case of Anaphylactic Reaction to Lansoprazole. Here they reported a case of 57-year-old woman admitted to emergency unit with facial redness and difficulty of breathing after patient swallowed a 30 mg lansoprazole capsule 15 minutes ago. Patient was agitated and had dyspnea. Patient blood pressure was raised. Rate of breathing was 30/minute, and pulse rate was 88/minute with an oxygen saturation of 96%. On dermatologic examination there were conjunctively hyperemia, slight eyelid edema and erythema involving face, neck and upper anterior trunk. Patient was diagnosed to have an anaphylactic reaction to lansoprazole. Patient was treated with slow intravenous Inj. of 100mg pheniramine-maleat and 250mg methylprednisolone immediately. Nasal oxygen was given at a rate of 6 lit/min. As patient complained of pressure and burning sensation in her epigastric area, intravenous 100mg ranitidine HCl and 10mg metochloropramide were administered. As dyspnea got worse, subcutaneous 1 mL adrenaline 1:1000 was administered and inj. was repeated with 20 min interval for three times. Additionally 2.5mg salbutamole-sulphate was administered with nebulizer. patient was followed up in the emergency unit for seven hours with intravenous pheniramine-maleat infusions and salbutamale sulphate nebulizer administration. At the end of seven hours of follow-up and disappearance of laryngeal edema patient was discharged with prescribed oral antihistamine. Past medical history revealed that the patient had duodenal ulcer, chronic pharyngitis, hypertension and diabetes mellitus. Patient was using telmisartan+hydrochlorothiazide for hypertension and glimepiride for diabetes mellitus. The patient had a history of milder similar allergic reaction to lansoprazole three years ago and applied to an emergency unit for treatment. Patient used rabeprazole without any allergic reaction before and there action was against lansoprazole. Patient had no family history of atopy. So in this case they reported patient was allergic to lansoprazole,in the place lansoprazole they gave rabeprazole for the treatment of duodenal ulcer.

Sabyasachi Ray (1989) studied case on Female Breast Engorgement on Ranitidine. Here they reported, A 60 year old female was referred by a psychiatrist for management of her chronic recurrent dyspepsia. Patient had a long history and strong family history of duodenal ulcer, confirmed on a number of occasions by barium meal study, the last being two years ago. Since then, she was on long term Cimetidine therapy. Patient was treated by psychiatrist for her agitated depression. Her antidepressant was changed from Doxepin (Sinequan) to Miauserin (Bolvidon) as her depression deteriorated recently. On examination, she had epigastric tenderness. Systemic examination and all screening tests were normal. Patient treatment with Cimetidine was stopped and Ranitidine was commenced on clinical grounds. During her follow up a month later, improvement of her dyspeptic symptoms were noted but patient felt heaviness and pain in both breasts about two weeks following therapy. Clinically, patient had bilateral swelling of breast particularly tense in the areolar and periareolar regions with tenderness. Patient had no history of chronic mastitis and she received no other new drugs. The patient felt very strongly that this complication was due to Ranitidine but we thought that was unlikely. Mianserin was stopped and patient was advised not to go back on Doxepin. As both drugs have been reported to cause similar breast problems though rarely. In view of her symptomatic improvement, Ranitidine was continued. Unfortunately, within a few days patient breast symptoms worsened progressly and became so unbearable that she discontinued Ranitidine herself. The breasts became normal within a week. During her attendance in the psychiatric clinic, as patient had considerable symptoms of peptic ulcer, the psychiatrist decided to try Ranitidine again. No other drug was prescribed from psychiatric or medical clinic. Patient breast swelling and tenderness came back within six hours and deteriorated further within a few days. Therefore, the treatment had to be discontinued and the breast problems subsided again completely. When she came for review, they decided to reassess the diagnosis by endoscopy before considering any further definitive therapy. Gastroscopy showed deformed duodenum but no ulcer. She had a small hiatus hernia and mild esophagitis for which she was treated with regular antacids only. On subsequent follow up in medical

clinic for next two years her symptoms were reasonably controlled. She was discharged from the clinic to the care of her general practitioner where she has been on regular follow up. Since then, she had no further recurrence of the breast symptoms after stopping Ranitidine. So in this case they reported that a 60 year old woman with chronic duodenal ulcer not responding to Cimetidine was changed to Ranitidine. She had symptomatic improvement, but had bilateral breast engorgement and tenderness for which treatment was discontinued.

Zheng Yu1 *et al*. (2018) studied case on Neutropenia and Thrombocytopenia Induced by Proton Pump Inhibitors.

Here they reported, an 85-year-old Chinese man was admitted to hospital because of dysphagia. Patient medical history included transurethral resection of prostate for benign prostatic hyperplasia and percutaneous vertebroplasty for lumbar vertebral compression fracture. Patient did not take any medicine when he was at home. The patient underwent endoscopic multi-band mucosectomy for resection of an early squamous cell carcinoma of the esophagus at 21 months previously in another hospital, and subsequently developed progressive dysphagia. Patient received four endoscopic dilations, and the dysphagia recurred soon after dilation each time. The exact results of examination and the details of treatment in the other hospital were unclear. Patient was able to swallow only liquids when he admitted to hospital. After admission to their hospital, a physical examination revealed that he weighed 60 kg, with a body mass index of 18.4, and had Stable vital signs No superficial lymph nodes were palpable. Abdominal examination revealed a soft, non-tender abdomen without hepatosplenomegaly. A complete blood count showed mild anemia with slightly reduced serum ferritin and iron concentrations. Iron deficiency anemia caused by malnutrition was suspected. Iron sucrose was administered intravenously and intermittently (100 mg, three times a week, intravenous infusion). Iron sucrose was stopped due to short hospital stay and shortage of medicine in the nursing home, with a total dose of 300 mg. An esophagoscopy and esophagogram revealed a 2mm long benign scar stricture. A stent was placed after dilation. Dysphagia was alleviated, and the patient was discharged from the hospital. The stent was dislodged from its proper location after 1 month, and dysphagia had recurred. The stent was removed and additional balloon dilation was performed. Dysphagia was improved markedly, but repeated half to 1 month after each dilation. Patient was hospitalized later two months for another two dilations. Pantoprazole sodium (80 mg, twice daily, intravenous infusion) was administered each time when he was in hospital, while esomeprazole (20 mg/day, orally) was administered intermittently when he was at home. patient came back to their hospital for the fourth balloon dilation. Pantoprazole sodium was given again from hospital day 3. A relatively obvious decrease in platelets was found on hospital day 5. After 4 days of pantoprazole administration, neutropenia was observed on hospital day 7. In a review of his previous medical history, they found a trend of slight decrease in white blood cells and neutrophils since his first admission to their hospital. Further examinations were performed. A bone marrow aspiration smear showed few nucleated cells, fat droplets, and scattered non-hemopoietic islands. A bone marrow biopsy indicated hypoplastic hematopoiesis. Helper T cells were in the normal range. Genetic detection of Wnt1 by reverse transcription polymerase chain reaction (RTPCR) was within the normal range. Antinuclear antibody (ANA) test was positive (1:1000, speckled pattern), while anti-dsDNA, anti-SS-A, anti-SS-B, anti-SM, anti-SCL-70, and anti-Jo-1 antibodies were all negative. Bone marrow suppression caused by PPI use was suspected due to lack of another cause. They stopped pantoprazole sodium treatment on hospital day 7 and subsequently found rebounds in white blood cell, neutrophil, and platelet counts; these values returned to normal on hospital day 15.

So, in this case report they reported a case of neutropenia and thrombocytopenia induced by proton pump inhibitors. Reductions in both white blood cells and platelets were noticed about 4 months after proton pump inhibitors were introduced. Bone marrow suppression induced by proton pump inhibitors was diagnosed as proven by bone marrow biopsy. White blood cell, neutrophil, and platelet counts went back to the normal range after proton pump inhibitors were stopped.

Anjan Adhikari *et al*. (2017) studied case on Proton Pump Inhibitor-induced Hypersensitivity Reaction.

Here they reported**,** a 27-years old female patient was admitted to hospital for cesarean delivery. Previous history of the patient reported allergy to ‘Ranitidine’. Through LUCS (Lower Uterine Cesarean Section) baby was delivered with vertex with the help of forceps. Placenta was delivered by Controlled Cord Traction (CCT). Uterus was repaired in two layers. Homeostasis was secured.

For post-operative treatment, patient was prescribed Ceftriaxone (1gm, i.v), Metronidazole (100, i.v), Tramadol (1 amp, i.m), Metoclopramide and Pantoprazole (i.v). Pantoprazole was prescribed as the patient was reactive to Ranitidine, H2 receptor antagonists. But immediately after post-operative medication, patient suddenly started suffering from severe bronchospasm, cyanosis, edematous face and skin. patient lost her consciousness and her extremities were cold and clammy. patient heart rate was increased; blood pressure and Oxygen saturation were decreased. A probable diagnosis predicted it as a case of ‘drug-

induced anaphylactic shock'. Immediate treatment started with mask ventilation, followed by intubation with 7mm ID (internal diameter), endotracheal tube (ETT). Intravenous injections of Adrenaline, Hydro-cortisone (200mg), Dexamethasone (8 mg), Atropine (1 amp), Promethazine (1 amp) were administered. She was under continuous monitoring. She regained her consciousness after about 24 hours. Her heart rate, blood pressure and Oxygen saturation were normal. She was kept under observation for three more days before discharge.

So, thus in this they reported a case of proton pump inhibitor induced hypersensitivity reaction t. A 27-years old female patient, with a history of drug allergy to ranitidine, experienced severe anaphylactic shock immediately after cesarean delivery. Therefore, instead of ranitidine, pantoprazole was used for this patient.

Filipa Ferreira *et al*. (2016) studied case on Pantoprazole-Related Symptomatic Hyponatremia. Here they reported, an 83-year-old man was admitted to the Emergency Room (ER) with symptoms of dizziness, nausea, vomiting and anorexia, progressively evident in the previous 3 weeks. Patient denied other associated symptoms, such as fever, mental state alteration, cough, pain, palpitations, dysuria, pollakiuria, diarrhea, vomiting or abdominal pain. Patient had a known history of arterial hypertension; type 2 diabetes; dyslipidemia; gastro esophageal reflux; and a hemorrhagic stroke (caused by the rupture of a brain aneurism at the age of 62, which resulted in sequelar mild left hemiparesis). Patient medicated with carvedilol 6.25mg bid, indapamide 1.5 mg id, metformin 500 mg and vildagliptin 50 mg id, sinvastatin 40 mg and ezetimibe 10 mg id, ticlopidine 250 mg id and pantoprazole 20 mg id. Clinical examination revealed a mild lentification and disorientation. The remainder of the physical examination showed no other relevant alterations and the neurologic exam did not show any findings other than sequelar left hemiparesis. Patient blood analysis revealed serum sodium and serum magnesium were slightly decreased with normal serum potassium; serum osmolarity and urinary osmolarity were decreased with urinary sodium of 58 mmol/L. The electrocardiogram was in sinus rhythm, with cardiac frequency of 79 bpm. A brain computerized tomography (CT) scan did not show any acute lesions. Serum sodium was corrected with the administration of hypertonic sodium chloride (3%) and slow infusion of normotonic fluid (0.9%) and magnesium sulfate for 3 days, reaching a normal concentration of serum sodium. At this point, the patient was asymptomatic and was discharged from the ER, with the indication to maintain his medication, including pantoprazole.

After 1 month, the patient was re-evaluated and was again found to be hyponatremic. At this point, he was admitted to an Internal Medicine ward for etiologic investigation. The possibility of Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) associated with pantoprazole was considered and pantoprazole was suspended. A slow infusion of normotonic saline and magnesium sulfate was initiated to correct hyponatremia and hypomagnesaemia.

So in this case they reported a case of pantaprazole related symptomatic hyponatremia an 83-year-old man with symptomatic severe hyponatremia due to Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) related to pantoprazole. Pantoprazole was discontinued and serum sodium levels reached normal values in two months.

TAO PENG *et al*. (2018) studied case on Pantoprazole-Induced Acute Kidney Injury.A 50-year-old woman with a less than 5 year history of diabetes mellitus presented with pantoprazole-induced acute kidney disease in Hospital. Blood glucose was usually controlled within the normal range and there was no prior medical history of hypertension, hematuria, proteinuria or other kidney disease. patient had a history of chronic gastritis, which was not treated. There was no history of treatment with and pharmacological agents or Chinese herbal medicine with the exception of long-acting insulin by subcutaneous injection once per day.

Prior to admission to the emergency department, the patient had elevated serum glucose for 1 day and complained of mild nausea without vomiting, abdominal pain or diarrhea. The results of laboratory tests revealed serum creatinine, blood urea nitrogen, hemoglobin and 24 h urine volume were in normal range. Serum glucose was increased. All relative indicators were measured from venous blood drawn 8 h after fasting and centrifuged at 11,000 x g for 15 min at 25˚C. Due to the patient's mild nausea and history of chronic gastritis, the patient was treated with pantoprazole (40 mg once a day, intravenous infusion) and intermediate acting insulin (12 U at 8 a.m. and 10 U at 5 p.m., subcutaneous injection) for 2 days. Following treatment, serum glucose was regained normal; however, the patient reported increased nausea, 24 h urine output was significantly reduced to 300 ml, Serum creatinine and Blood urea nitrogen were increased followed by first report. The patient was admitted to the Department of Nephrology.

Upon admission a physical examination revealed mild edema in bilateral eyelids and lower limbs without malar rash, oral ulcers or diffuse alopecia. Pertinent laboratory findings included serum creatinine and blood urea nitrogen were highly increased; hemoglobin was slightly high and 24 h urine volume 170 ml. White blood cell and platelet counts were normal. Parathyroid hormone, Calcium and Potassium levels were normal. Tests for anti-glomerular

basement membrane antibody and anti-neutrophil antibody were negative. Glycosylated hemoglobin was increased and the brain natriuretic peptide (BNP) concentration was very high. A urinary β2 microglobulin concentration was slightly decreased and the urinary albumin creatinine ratio was 0.01 g/gCr. Anti-nuclear antibody spectrum, tumor markers, thyroid function, immunoglobulin, complement C3 and C4, hepatitis B virus quantification and coagulation results were all within the normal range. Serum immune fixation electrophoresis was negative. Renal ultrasonography revealed that the kidney volume was above normal. Lung X-rays revealed no evidence of inflammation. Following admission to the Department of Nephrology, the patient immediately underwent renal biopsy. A total of two renal biopsy specimens ~1.5 cm in length were obtained containing 100% cortex. Specimens were stained with hematoxylin and eosin at 25˚C for 40 min. Microscopy revealed 17 glomeruli in each section without complete or peribulbar fibrosis. No proliferation was observed in the mesangial cells and matrix and no glomerular capillary thickening was reported. Masson staining was performed at 25˚C for 60 min and no immune complex deposition in the capillary walls was observed. Periodic acid-silver methenamine staining was performed at 25˚C for 30 min and revealed no atrophy in the tubules and only a few tubules were dilated with flat epithelial cells. Severe edema with multifocal lymphocyte, monocyte and eosinophil infiltration was observed in the renal interstitium; however, there was no thickening of arterial walls. All samples were observed using a light microscope (magnification, x400).

So in this case they reported Pantoprazole-induced acute kidney injury is commonly misdiagnosed and late diagnosis results in poor patient prognoses. Misdiagnosis leads to the administration of treatments that may exacerbate the condition, so appropriate diagnosis and treatment for pantoprazole-induced acute kidney injury is necessary.

Ankit Gaur *et al*. (2018) studied case on ranitidine induced thrombocytopenia. A 60-year-old female, a case of psoriasis, presented in Dermatology department of tertiary care hospital with multiple pustules over lower extremities, associated with fever and vomiting. The patient had diabetes mellitus type-2 and hypertension as co-morbidity from the past six years. Routine Hemogram on admission revealed WBC and platelet count was normal. Hemoglobin was decreased. Patient was started on azithromycin 250mg BD, Paracetamol 500 mg BD, IV ranitidine 50 mg BD and IV Domperidone. Hematological investigations repeated after 3 days revealed thrombocytopenia with platelet count, hemoglobin and WBC count were decreased with neutropenia. Important causes of pancytopenia like malaria, leptospirosis, dengue, autoimmune disorders, and sepsis were ruled out. Repeated blood picture showed further decrease in platelet count and White Blood Cell count; however, there was no spontaneous bleeding. Bleeding time, clotting time and INR were normal. With other causes ruled out realistically and the patient being clinically asymptomatic, it was concluded that a drug may be the possible cause of thrombocytopenia. Ranitidine-induced thrombocytopenia in critically ill patients has been reported. The drug was without delay withdrawn and after 48 hours a considerable improvement in the blood picture was noticed Hemoglobin, WBC count and platelet count were started to increase. The patient had recovery without incident and was discharged ten days later with normal blood counts.

So, in this case they reported Ranitidine induced thrombocytopenia by an idiosyncratic reaction.

Aryal E *et al*. (2017) studied case on Lansoprazole – Induce Black Hairy Tongue. A healthy 75 year old male presented to dermatology OPD with chief complaints of burning sensation, discomfort and bad breath from oral cavity for 8 weeks. He, smoker for last 20 years, had abdominal discomfort along with heartburn and bloating since last 2 years. He had been taking Lansoprazole, on and off, for last the 12 months and since the last 2 months, he has been taking it regularly from local chemist as over the counter (OTC) drug without consulting the physician. He was of normal built with vitals within normal limits. On intra oral examination, there was poor oral hygiene with stains on teeth with superficial black to brown hairy like growth on dorsum of tongue that appeared as an elongation of fillliform papillae almost 3 mm in growth. There was no history of pain, itching and bleeding from oral cavity.

Culture of the dorsal surface of tongue was negative for bacterial and fungal outgrowth after 48 and 72 hours. Routine blood investigations were within normal limit along with negative HIV test. A 4 mm punch biopsy was taken under sterile condition, with consent from patient, from the dorsum of tongue. Histopathological study showed elongation and hyperparakeratosis of the filliform papillae. Clinically and histopathologically diagnosis of BHT was made. Patient was advised to stop lansoprazole along with cessation of smoking along with gentle tongue debridement with soft toothbrush and was referred to dental department for assessment and management of oral cavity. On follow up after 8 weeks, there was resolving BHT with almost normal texture. Hence final diagnosis was Black Hairy Tongue (Clinically: Lansoprazole induced).

So, in this case they reported a case of lansoprazole –induced black hairy tounge. A 75 year man presented with black hairy fine growth from tongue along with discomfort, burning and halitosis from oral cavity after taking lansoprazole for acute peptic disease (APD) from over the counter and after

discontinuation of lansoprazole, black hairy tongue was resolving.

Subhajit Mukherjee *et al*. (2018) studied case on Adverse Effects of Proton Pump Inhibitors on Platelet Count. A 35-year-old Hispanic female was admitted for worsening upper abdominal pain, nausea, and vomiting. Patient had a past medical history of heartburn which was being treated with PPI. She was initially seen in the emergency department for worsening epigastric abdominal pain and was discharged home on daily omeprazole. She returned to her primary care clinic 2 months later complaining of similar symptoms while being on omeprazole. Since omeprazole was not effective, she was switched to esomeprazole. Two months later, she visited her home country and was evaluated for abdominal pain. Due to her persistent symptoms, cholecystectomy was performed, without much relief of her symptoms. Patient reported that she was unable to take the initially prescribed esomeprazole secondary to financial issues and was not on any acid-suppressing medications in the previous 2months.Upper endoscopy was then performed and it showed multiple gastric ulcers. She was then started on pantoprazole. After returning to the United States, she continued to have pain and started taking no steroidal anti-inflammatory drugs (NSAIDs) for relief. Subsequently, she visited her primary care office with worsening of her pain associated with nausea and vomiting. During this clinic visit, she was switched to dexlansoprazole and was asked to come to the emergency department if she continued to have symptoms. She returned to the emergency department the next day for further evaluation of her worsening symptoms. On initial evaluation in the emergency department, she was afebrile and had stable hemodynamics. She endorsed severe abdominal pain and a 30-pound weight loss over the last year, but denied any hematemesis, melena, or hematochezia.

Laboratory evaluation revealed white blood cell count was increased; platelet count was decreased with normal hemoglobin. On review of laboratory data, patient's last platelet count checked 6months priorly was normal and had been obtained before the patient was started on a PPI for the first time. No other laboratory tests had been obtained until this recent emergency department visit. Therefore, the effect of PPI on the platelet count for the next 6 months after initiation of therapy was not available to them. Chemistry panel, liver function, urinalysis, and blood/urine cultures were negative. CT imaging of the abdomen and pelvis showed diffuse steatosis but was otherwise normal.

Gastroenterology was consulted and due to refractory abdominal pain, weight loss, and NSAID use, an upper endoscope was recommended. Additionally, intravenous esomeprazole twice daily was started. patient platelet count continued to drop, falling to the next day and continued the day after. Hematology was consulted for the rapid drop in platelet count and the etiology was thought to be secondary to drug-induced thrombocytopenia, infection, or idiopathic thrombocytopenic purpura. They noted, the patient did not have any history of bleeding or clotting disorders. Additionally, there was no evidence of hemolysis on the peripheral blood smear and the patient was not coagulopathic. On review of medications, since there were no other drugs (except for one prophylactic dose of heparin) that could be attributed to thrombocytopenia, it was recommended to hold the PPI. The PPI was then stopped, and platelet count recovered within two days. Upper endoscope performed at that time revealed nonspecific gastritis. Biopsies were found to be negative for *Helicobacter pylori* infection. Due to the spontaneously improved platelet count, antibodies to heparin-platelet factor 4 complexes were not checked to rule out heparin-induced thrombocytopenia. Since the patient's platelet count normalized after stopping PPI, this current episode of thrombocytopenia was deemed likely secondary to PPI use.

The patient was subsequently discharged home, but continued to have persistent epigastric pain. She tried a H2 (histamine 2) receptor antagonist with minimal symptom relief. She was next seen in the Gastroenterology Clinic. At that time, the platelet count was decreased. During that visit, the question of whether patient's thrombocytopenia was truly related to PPI use was revisited, given that heparin induced thrombocytopenia was not ruled out. Since a PPI was warranted due to her persistent symptoms, the decision was made to restart Dexlansoprazole with close follow-up. She ultimately got readmitted to the hospital 7 days later for persistent epigastric pain (while on PPI). This time the platelet count was found to be decreased. The platelet count continued to drop, similar to her prior admission while on PPI, with the lowest count. PPI was held because of prior concern for PPI-induced thrombocytopenia. On that admission, the patient did not receive any heparin products and peripheral blood smear was not consistent with hemolysis. She did not receive any medications known to cause thrombocytopenia. Platelet count was improved while off PPI and she was discharged home. Patient's symptoms improved on H2 antagonist, sucralfate, and pain control with morphine. On that admission, PPIs were listed as a drug allergy and documented in the patient's medical record. She was seen in the Gastroenterology Clinic after hospital discharge and it was noted that her symptoms were partially controlled onH2 antagonist, sucralfate, and scopolamine (which she received from her home country for control of nausea). Platelet count was ultimately improved.

So, this they reported a case of PPI-induced thrombocytopenia. In this case patient, thrombocytopenia immediately developed after the

initiation of PPI on two separate occasions and resolved after its discontinuation.

Ranakishore Pelluri *et al*. (2016) studied case on Pantoprazole Induced Vit.B12 Deficiency. A 40 years old male patient who developed vitaminB12 deficiency while being treated with Pantoprazole. The patient had been treated with pantoprazole 40 mg for gastro esophageal reflux disease with gastric ulcer for 15 days. After this, the patient consulted his physician about uncharacteristic symptoms including periodic dizziness. Blood examinations revealed Vitamin B12 deficiency. The patient was examined, and no other causes were found that could explain the inability to absorb vitamin B12. After Pantoprazole was discontinued, serum B12 levels normalized.

So, in this they reported a case of pantaprazole induced vitamin B12 deficiency long term use of proton pump inhibitors cause vitamin B12 deficiency.

YI Kim *et al*. (2010) studied case on Famotidine-Induced Anaphylaxis. A 23-year-old man was admitted to the urology department for operation of left varicocele. Patient had no past history of other medications, illnesses, or allergic diseases. On the operation day, cefazedone 1g and famotidine 20 mg were administrated intravenously for preoperative preparation. Immediately after the injection of famotidine, the patient complained of dyspnea, showed seizure-like activities, and became comatose. Cardio-pulmonary-coronary resuscitation was performed immediately with epinephrine, fluid replacement, and corticosteroids because blood pressure was not detected. Recovery was complete and there were no sequelae. Complete blood counts, liver functions, renal functions, and serum electrolytes were within normal limits. To exclude cardiac problems such as arrhythmias, we performed electrocardiography, 2D-echocardiography, and 24-hourHolter monitoring, but they showed no abnormal findings. The total serum immunoglobulin (Ig) E level was 93.8 IU/mL. Specific serum IgE levels to penicilloyl G, penicilloyl V, ampicilloyl, amoxycilloyl, and cefaclor were not detected with Immuno CAP.

About 1 month later, skin prick tests with the following drugs were performed on the patient's back: cefazedone, ß-lactam antibiotics (penicillin G potassium crystal, ampicillin-sulbactam, and amoxicillin sodium), H2-receptor antagonists (famotidine, nizatidine, ranitidine hydrochloride, and cimetidine), and proton pump inhibitors (pantoprazole and lansoprazole). The results were all negative. Intradermal skin tests with all the above drugs were subsequently performed on the back, with positive reactions to famotidine, nizatidine, and ranitidine and negative reactions to all the other drugs, including cefazedone and cimetidine. The maximal concentration of all the drugs used in the prick and intradermal skin tests was 3 mg/mL.

Additionally, they performed intradermal tests with famotidine, nizatidine, ranitidine, and cimetidine on the forearm of the patient and 6male controls (mean [SD] age, 27.2 [1.0] years). Clear positive reactions to famotidine, nizatidine, and ranitidine were again observed in the patient, but not in the controls. The tests were performed with close monitoring of blood pressure and cardiac rhythm. There were no adverse cardiac events following the test dose of famotidine.

To determine famotidine-specific serum IgE, enzyme linked immuno- assay (ELISA) was performed. Unfortunately, however, they failed to detect famotidine-specific serum IgE. They used to detect specific IgE in serum using ELISA. Thirteen healthy controls with negative skin prick tests to famotidine were included. The final absorbance value was determined by subtracting the HSA-coated value from that of the famotidine-HSA-coated value. The positive cutoff for specific IgE (0.04) was determined using the mean + 2 SD of the absorbance values observed in the controls. The patient had no detectable specific IgE level to famotidine-HSA conjugate (0.00).

To find safe alternatives to the H2-receptor antagonists tested, which showed clear positive skin reactions, oral challenge tests with pantoprazole, lansoprazole, and cimetidine were performed after written informed consent was obtained. Oral challenge tests with ampicillin trihydrate and cefixime were also carried out. The patient tolerated those drugs well. However, he refused to undergo additional oral challenge tests with famotidine, nizatidine, or ranitidine due to fear of another severe anaphylactic episode. They also recommended that the patient underwent an intravenous challenge test with cefazedone due to the unavailability of oral forms of cefazedone but he also refused to undergo this test.

On the basis of the skin test and oral challenge test results, they recommended that the patient took proton pump inhibitors and cimetidine, but not famotidine, nizatidine, or ranitidine due to the risk of anaphylaxis. The baseline level of total tryptase in serum was determined using ImmunoCAP due to the severe anaphylactic reaction. The result, however, 2.2l µg/L, was in the normal range (<11.4 µg/L).

So, in this case report suggests that famotidine may induce immunoglobulin E–mediated anaphylaxis and have cross-reactivity with nizatidine and ranitidine. Clinicians should therefore be aware of possible lifethreatening adverse reactions to commonly used H2-receptor antagonists such as famotidine.

Srikanth KP *et al*. (2015) studied case on Anaphylactic Reaction to Omeprazole. A 64-year-old woman received a prescription for omeprazole 20 mg capsules from her general practitioner for peptic symptoms. About 55 minutes after taking the first

capsule, she developed malaise, periorbital edema, erythema of the skin, pruritus, nausea, and vomiting. On presentation to hospital her pulse was feeble and blood pressure was not recordable. After treatment with injection adrenaline (1:1000dilution) 0.5mg subcutaneously, injection hydrocortisone intravenously, injection pheniramine intravenously, injection normal saline infusion, she recovered uneventfully. The acute onset of urticaria, edema, and hypotension and a close temporal association of these clinical signs with the ingestion of the tablet in their patient allow this reaction to be classified as anaphylactic shock, according to the Council for International Organizations of Medical Sciences.

So, they reported in this case that the PPI can cause anaphylactic reactions and that one should be aware of its life threatening adverse reaction while prescribing PPIs.

Ebru Tekbaş *et al*. (2012) studied a case on Famotidine-Induced Acquired Long QT Syndrome. A 59-year-old woman was admitted to hospital with unstable angina pectoris. Past medical history included hypertension. Patient had been using silazapril for hypertension. Also patient had been using famotidine for gastritis for two months. patient ECG revealed that T-wave inversion at all derivation except aVR and V1 and QTc was slightly longer. It was calculated as 464 ms. Physical examination on admission revealed blood

Pressure was increased with normal pulse rate. Cardiac and lung auscultation were normal. Cardiac enzymes and other routine laboratory tests were within normal range. Transthoracic echocardiography showed mild left ventricular hypertrophy, diastolic dysfunction and mild mitral regurgitation. The patient was treated with aspirin (300 mg/day), clopidogrel (75 mg/day), subcutaneous enoxaparine (0.6 ml twice a day), intravenous nitroglycerin, metoprolol (100 mg/day), silazapril (2.5mg/day) and intravenous famotidine (20 mg twice a day). Coronary angiography revealed normal coronary artery. Approximately 12 hours after receiving the first dose famotidine the QTc became markedly prolonged at 624 ms. Serum potassium, magnesium, and calcium levels were normal. Two days after famotidine was stopped, the QTc returned to baseline at 460 ms. So, in this case they reported a case of famotidine associated with acquired long QT syndrome.

Ulfin Rethnam *et al.* (2007) studied a case on Anaphylactic Reaction Associated with Ranitidine in a Patient with Acute Pancreatitis. A 56-year-old female with acute pancreatitis was admitted to hospital. Patient was known to suffer from diverticular disease and had a myocardial infarction in the past. Patient was allergic to metronidazole and buscopan. Patient had no family history of drug allergies.

During the initial course of management patient was given 50mg of ranitidine as a slow intravenous bolus for epigastric discomfort. Few minutes after the injection, the patient complained of itching at the injection site that spread to involve the entire upper limb. patient also complained of swelling of her tongue and difficulty in breathing. Within Minutes her level of consciousness deteriorated and patient became comatose. The initial examination revealed the following features: GCS 6/15, a grossly edematous face, neck and extremities, a grossly swollen tongue, congested conjunctivae, cyanosis, diffuse rhonchi over both lung fields. Despite immediate administration of intramuscular adrenaline, intravenous hydrocortisone and high flow oxygen the patient progressed into a cardio respiratory arrest. Cardiopulmonary resuscitation was commenced. Patient was intubated with difficulty and was resuscitated successfully. She was transferred to the Intensive Care Unit for ventilatory and inotropic support. Two days later she was weaned off the ventilator and by then patient was haemodynamically stable without inotropic support. Patient made a full recovery in 3 days. A skin sensitivity test prior to the patient's discharge revealed the patient's sensitivity to Ranitidine.

So, this case they report a case of severe anaphylactic reaction associated with ranitidine in a patient with acute pancreatitis.

Antonio Oliva *et al*. (2008) studied case on Fatal Injection of Ranitidine. A 51-year-old man was admitted to the hospital for treatment of benign prostatic hyperplasia (BPH). The patient's anamnesis was negative for allergic events. Before hospitalization patient was being treated with alfuzosin, which belongs to a group of medications known as alpha-1Areceptor antagonists used to treat the symptoms of enlarged prostate and BPH. On admission to the hospital alfuzosin treatment was suspended and the patient underwent transurethral resection of the prostate under epidural anesthesia, followed by post-surgical administration of antibiotics (modivid) and lactated Ringer's solution. Twenty-four hours after surgery, routine prophylaxis for stress ulcer (one phial of Zantac® 50 mg, intravenous, in normal saline solution) was prescribed. Within minutes of the injection of ranitidine, the patient developed a combination of wheezing, dyspnea and hypotension followed by loss of consciousness. Despite intensive resuscitation attempts, no cardiac activity reappeared and death was certified 30 minutes later. As the circumstances of death appeared suspicious to the treating emergency physician, a forensic investigation was initiated and the public prosecutor ordered a forensic necropsy.

The autopsy revealed pulmonary congestion with widespread upper airway edema, the presence of petechial hemorrhages and brain swelling with diffuse petechial hemorrhages. There was no evidence of recent

myocardial infarction or other structural heart diseases. The rest of the organs were unremarkable. Histological sections confirmed the presence of widespread hypo laryngeal and pharyngeal mucosal and sub mucosal edema with inflammatory cells and an abundance of mast cells. Testing for specific IgE antibodies and mast cell tryptase was not performed because of post-mortem degradation of the serum.

Toxicological analyses on blood performed using a gas chromatography-mass spectrometry technique revealed the presence of ranitidine at lessthan 10 ng/ml (limit of quantitation). No other drugs were found. Death was attributed to anaphylactic shock due to an adverse reaction caused by intravenous injection of ranitidine, suggestive of a pathogenic mechanism of immediate- type hypersensitivity reaction type I, according to the Gell and Coombs Classification System.

So, in this they reported a case of fatal injection of ranitidine. they present the clinical history, histological and toxicological data of a 51- year-old man with negative anamnesis for allergic events, who died suddenly after the intravenous administration of one phial of Zantac® 50 mg prescribed as a routine post-surgical prophylaxis for stress ulcer.

Abdul Jabbar *et al*. (2010) studied case on Hyperprolactinaemia Induced by Proton Pump Inhibitor. A 13 year old girl admitted to her hospital with a history of migranous headache and was prescribed mefenamic acid. Other than these bouts of headache for last 3 months, patient had no active medical issues. On taking mefenamic acid patient developed dyspeptic symptoms and was found helicobacter antibody positive and was prescribed Omeprazole.

After 4 Days of treatment with Omeprazole 20mg BD, patient developed bilateral galactorrhea. Patient prolactin level was found high. On detailed interrogation patient refused to have taken any other drugs in particular antiemetics or H2 receptor antagonists. An MRI of hypothalamo-pituitary area revealed a bulky pituitary probably due to pubertal change. Patient was given a course of anti-helicobacter regimen and Omeprazole was discontinued. The galactorrhea resolved and three weeks later her serum prolactin levels returned to normal.

Considering the temporal relationship with omeprazole, with the patient and parent's consent, patient was re-challenged with omeprazole after six weeks and her serum prolactin level was checked again. The serum prolactin level was increased and returned back to normal in 2 weeks after withdrawal.

As part of laboratory work up, serum calcium, phosphorus, gastrin was reported normal. Later, patient reported with a bout of headache to some other center and was given injection Domperidone and tablets for nausea as take home medication. Forty eight hours later she again developed galactorrhea and her domperidone was discontinued. This time her prolactin level was normal. Patient remained normal with episodes of headache and nausea, which used to settle with acetaminophen and NSAID, along with antacids, sucralfate and ranitidine which were tolerated well.

After about six months patient again developed a severe bout of headache with nausea, vomiting and dizziness and attended a nearby medical center where patient was given injection diclofenac. On insistence by her parents about the past medical history of galactorrhea induced by omeprazole (lo sec), this time patient was prescribed lansoprazole instead of omeprazole. Three days later patient again developed galactorrhea and her serum prolactin was increased which returned to normal in a week after stopping lansoprazole.

So, in this ase they reported a case of hyperprolactinemia induced by omeprazole. (A 13 year old girl who manifested hyperprolactinaemia and galactorrhea induced by Omeprazole).

MEILING YU *et al*. (2016) studied case on severe Adverse Reactions Caused by Omeprazole. A 61-year-old female was admitted to Hospital as a result of experiencing a whole-body rash for 10 days, diarrhea for 7 days, and unconsciousness and oliguria for 1 day. The patient had been diagnosed with hyperthyroidism 30 years ago, but was not administered a formal treatment or monitored. The patient had been experiencing arthritic pain for >1 month and had received an intra-articular injection and oral administration of non-steroidal anti-inflammatory drugs (NSAIDs), but the exact drug was unknown. The patient was prescribed 20 mg twice daily and orally of omeprazole enteric-coated tablets to treat the stomach discomfort caused by these NSAIDs. However, the patient developed a whole-body rash 7 days after omeprazole administration, which was 10 days before admission. This rash did not disappear following anti-allergy treatment at a local clinic. The patient also experienced diarrhea >10 times a day, and nausea and vomiting from 7 days prior to admission. The patient's diarrhea was treated with an infusion of unknown drugs 2 days prior to admission at the local Hospital but demonstrated no marked improvement in symptoms. The patient developed a high fever reaching 40˚C, 1 day prior to admission, and was transferred the Intensive Care Unit (ICU) to continue treatment for low blood pressure and oliguria. The patient was treated with 20 mg norepinephrine intravenously once per day to treat low blood pressure, and furosemide injection (40 mg) was administered intravenously once per day to cure oliguria. Norepinephrine activates the alpha receptor, then induces the small artery and vein blood vessel to

contract and thus increases the blood pressure. The patient lost consciousness and her condition did not improve following treatment for allergies and a fluid infusion of 20 mg norepinephrine was pumped into the blood intravenously once per day in order to increase blood pressure. Norepinephrine activates the α-receptor, then induces the small artery and small vein blood vessel to contract and finally increases the blood pressure.

The patient was then transferred to the ICU department for further treatment. A tracheal intubation with mechanical ventilation was performed due to the patient's loss of consciousness and dyspnea. Blood gas analysis revealed severe metabolic acidosis and electrolyte disturbance of pH 6.86, PaCO2 41 mmHg, PaO2 120 mmHg, HCO3-7.1 mmol/l, BE-26.1 mmol/l, sodium 134.7 mmol/l, potassium 2.26 mmol/l and Calcium 0.93 mmol/l. Fluid infusion, correcting acid-base disturbance (by sodium bicarbonate injection) and other treatment, including calcium and potassium supplements, calcium gluconate injection and potassium chloride injection. Admission examination results were as follows: Temperature was afebrile; pulse and respiratory rate were increased; blood pressure was decreased; and Glasgow score, 3 (19, 20). The patient maintained a whole-body rash and did not respond to loud noise or physical stimuli, but did respond to pain stimulation induced by piercing with a needle, meaning that the central nervous system functioned normally. The patient's pupils measured 1 mm and did not react to light. The patient's breath sounded rough and rale upon lung auscultation as determined by a stethoscope, but was not obviously dry. Electrocardiogram monitoring showed a regular sinus rhythm (heart rate was increased) and no cardiac murmur. The abdomen was soft and the patient demonstrated no presence of pain when it was pressed. The liver and spleen were small enough to feel by doctors, implying that their function is normal, and bowel movement sounds could be heard. No obvious edema was observed in the four limbs, but the patient presented with oliguria. A routine blood test indicated that the patient's white blood cell (WBC) count had increased, and neutrophils (NEUTs) were not measured (WBC was increased with in normal values of hemoglobin, hematocrit and platelets count. The results led to the following symptom identification: i) Allergic shock; ii) pulmonary infection and respiratory failure; iii) acute kidney injury; iv)metabolic acidosis; v) electrolyte disturbance, hypokalemia and hypocalcemia; vi) hyperthyroidism; and vii) diarrhea.

The patient was administered 500 ml glucose and sodium chloride injection and 500 ml polygeline injection both intravenously. A total of 20 mg norepinephrine was also administered intravenously by a drip once per day in order to maintain blood pressure. 2.25 g Piperacillin sodium and Tazobactam sodium were both administered intravenously three times per day for antibiotic treatment upon admission to the ICU. In addition, blood filtration was performed for acute kidney injury, 3.0 g calcium gluconate injection once daily and 6.0 g 10% potassium chloride injection once daily were administered to treat electrolyte disturbance, hypokalemia and hypocalcemia. Furthermore, 6.0 g montmorillonite powder was injected through the nose three times a day and 2.0 g triple viable *Bifidobacterium lactobacillus* were administered through the npse three times a day in order to treat diarrhea and regulate intestinal flora. Loperamide hydrochloride capsules at 4.0 g were administered through the nose once per day to inhibit intestinal motility, as the patient was experiencing diarrhea >10 times a day. Furthermore, an injection of 80 mg methylprednisolone sodium succinate was administered intravenously once per day and 80 mg compound ammonium glycyrrhetate S was administered intravenously once per day for anti-allergy treatment. The patient was diagnosed with diarrhea, allergic shock caused by omeprazole, and omeprazole enteric-coated tablet-induced rash following a consultation between the Departments of Pharmacy and Gastroenterology. Blood gas analysis demonstrated a blood pH 7.48, PaCO2 35.5 mmHg, PaO2 61.5 mmHg, BE 2.9 mmol/l, sodium 142.3 mmol/l, potassium 3.42 mol/l and LAC 2.3 mmol/l. The patient's metabolic acidosis had been treated, but lactic acid levels remained high, which highlighted that there remained an obstruction to circulatory function, and a poor oxygenation index of ~100 mmHg. A routine blood test was done 2 days later returned the following results: WBC and hemoglobin were normal; NEUT slightly increased; red blood cell count, hematocrit and platelet count were decreased. The routine blood test and body temperature (37.0˚C) revealed a significant attenuation of the infection; a sputum smear revealed dysbacteriosis, and diarrhea, and the patient was administered norvancomycin by a nasal tube. On May 8th, the patient demonstrated marked deflorescence and a normal urine output, which indicated a significant improvement in kidney function. The patient stopped experiencing diarrhea on May 13th, after which her condition began to stabilize. Genetic screening revealed that the patient had a poor metabolism of omeprazole.

So in this they reported a case the severe adverse reactions (omeprazole enteric-coated tablet-induced rash, diarrhea and allergic shock).

Hiroaki Kitamura *et al*. (2016) studied case on Reactive Plasmacytosis and Generalized Lymphadenopathy Induced by Famotidine. A 53-year-old woman referred to hospital with chief complaints of fever, fatigue, and cough. Patient past medical history was unremarkable. Six days prior to admission, the patient visited her family physician because of dry cough. Despite the administration of antibiotic (cefcapene pivoxil), the patient’s symptoms were not resolved.

On admission, patient body weight and height were 60 kg and 160 cm, respectively. The patient was pyrexial with normotensive, although her pulse rate was slightly elevated. patient room air pulse oximetry was normal. A physical examination revealed generalized lymphadenopathy with no palpable hepatosplenomegaly. A chest examination revealed no rales and regular heart sounds without murmurs or gallops. Laboratory tests on admission revealed a leukocyte count increased consisting of abnormal differential count and 28% plasma cells that had a large and immature morphology. The hemoglobin concentration and the platelet count were normal. Blood chemistry analysis revealed mild liver dysfunction [aspartate aminotransferase was increased and alanine aminotransferase was remained normal; lactate dehydrogenase and alkaline phosphatase were very high] and a serum C-reactive protein concentration was increased. Bone marrow aspiration revealed a normocellular marrow with 33% plasma cells of small to medium size and a hyperbasophilic cytoplasm. Serum protein electrophoresis exhibited a polyclonal pattern with increased amounts of IgM and IgE; the κ/λ free light-chain concentration ratio was normal. The patient had increased serum levels of soluble interleukin-2 receptor and interleukin 6. Serological tests for hepatitis B virus and hepatitis C virus were negative. Antibody tests for Epstein-Barr virus and cytomegalovirus showed patterns of past infection. The cell surface phenotype of the plasma cells on flow cytometry was CD38+CD138+/- CD19+CD56-. Chest radiography did not detect any abnormalities. Computed tomography (CT) indicated multiple lymphadenopathy that included the supraclavicular fossa, the mediastinum, the bilateral hilum of lungs, and the para-aortic, mesenteric, and inguinal regions. Neoplasms such as angioimmunoblastic T-cell lymphoma (AITL) were also suspected, and an inguinal lymph node biopsy was performed. Histological examination showed reactive lymphoid hyperplasia. Monoclonal rearrangement of the T-cell receptor (TCR)-γ chain or immunoglobulin heavy chain (IgH) genes was not observed. On the basis of these findings, a clinical diagnosis of reactive plasmacytosis was made.

The marked increase in IgE levels suggested that the etiology of the plasmacytosis was a drug-induced reaction. Therefore, a drug-induced lymphocyte stimulation test (DLST) was performed for the drugs the patient had been prescribed with before admission, namely, loratadine, famotidine, cefcapene pivoxil hydrochloride hydrate, LAC-B granular powder N, ogikenchuto, by akkokaninjinto, and saikokei-shito. Only the test for famotidine was positive: the stimulation index was 2.2. The patient did not have anti-dengue IgM antibodies.

In the absence of additional treatment, the plasmacytosis of the patient improved soon after the prescribed medications were ceased. In parallel, the serum IgE and sIL-2R levels dropped and the multiple lymphadenopathy disappeared.

Maiko Taura, *et al*. (2017) studied case on Drug Eruption Caused by Esomeprazole. A 69-year-old woman was referred to hospital for consultation regarding generalized pruritic papules and erythema. They did not observe any other general symptoms, such as fever, lymph node swelling, liver dysfunction, or kidney dysfunction. Patient had a history of rheumatoid arthritis, hypertension, and gastric ulcer, and have received a 2-month treatment using iguratimod, salazosulfapyridine, nifedipine, and esomeprazole. Because they suspected drug eruption, all drugs were discontinued and the eruption subsequently disappeared within 1month.They restarted treatment using esomeprazole and celecoxib, although the skin eruption recurred soon after restarting treatment. Thus, they suspected drug eruption caused by esomeprazole, and performed a skin biopsy, patch test (using esomeprazole, omeprazole and lansoprazole), and a drug lymphocyte stimulation test (DLST) using esomeprazole. Histological examination of a punch biopsy specimen from the right chest revealed superficial perivascular lymphocytic infiltrates with severe vacuolar alteration, which was consistent with drug eruption.

So in this they reported a case of Drug Eruption caused by Esomeprazole.

Pramendra Prasad Gupta *et al.* (2018) studied case on Anaphylactic Reactions Due To Pantoprazole. A 32-year-old female presented in the emergency ward with chief complaints of rashes all over her body, itching on the whole body, and swollen lips and eyes. Patient was immediately evaluated. Patient history showed that she had taken a pantoprazole 40mg tablet 30minutes prior to the development of signs and symptoms. Patient's examination revealed that BP, pulse rate and respiratory rate (RR) were normal and SPO2 98% in room air with normal body temperature. Patient was given tab avil (pheniramine maleate) 25 mg orally, cetirizine HCL 10mg, and hydrocortisone 200 mg. patient was then kept under observation. In the next 1 hour, patient signs and symptoms improved, and patient felt comfortable, with no rashes and no pruritus, and patient lips and eyes returned to normal. patient was kept under further observation for 12 hours and then discharged. In this case, it was confirmed that other medication was not taken (apart from pantoprazole).

CONCLUSION

We can say in conclusion that physician and clinical pharmacist should work together to increase appropriate use of PPIs. The inappropriate use of PPIs must be prevented through proper interventions. The development of guidelines for PPI usage will avoid irrational prescription of PPIs. The need for PPI use in the individual patient must be evaluated by the clinical

pharmacist and if any possible alternatives are found to be effective the same can be reported to the physician.

The appropriate use of PPIs will ensure the patient safety by reducing the risks associated with unnecessary prescription of PPIs. The regular monitoring of prescription of PPI by clinical pharmacist is the need of the hour.

REFRENCES

1. Gupta, P. P., Bhandari, R., Mishra, D. R., Agrawal, K. K., Bhandari, R., Jirel, S., & Malla, G. (2018). Anaphylactic reactions due to pantoprazole: case report. *International medical case reports journal*, *11*, 125.
2. Ali, T., Roberts, D. N., & Tierney, W. M. (2009). Long-term safety concerns with proton pump inhibitors. *The American journal of medicine*, *122*(10), 896-903.
3. Lazarus, B., Chen, Y., Wilson, F. P., Sang, Y., Chang, A. R., Coresh, J., & Grams, M. E. (2016). Proton pump inhibitor use and the risk of chronic kidney disease. *JAMA internal medicine*, *176*(2), 238-246.
4. Gupta, N., Patel, C., & Panda, M. (2009). Hepatitis following famotidine: a case report. *Cases journal*, *2*(1), 89.
5. Raj, K., Raj, S., & Lakshmi, R., (2018). Rabeprazole-induced acute interstitial nephritis: A case report. *National Journal of Physiology, Pharmacy and Pharmacology*. 8(2), 295-296
6. Aksoy, B., AKAR, T., & Aksoy, H. M. (2010). Anaphylactic Reaction to Lansoprazole: Case Report. *Turkiye Klinikleri Journal of Medical Sciences*, *30*(1), 404-405.
7. Ray, S. (1989) Female breast engorgement on ranitidine; A case report *Med. J. Malaysia* Vol. 44 No. 4]
8. Yu, Z., Hu, J., & Hu, Y. (2018). Neutropenia and Thrombocytopenia Induced by Proton Pump Inhibitors: A Case Report. *Drug safety-case reports*, *5*(1), 28.
9. Adhikari, A., Indu, R., Ray, M., Bhattacharya, S., Biswas, R., & Das, A. K. (2017). Proton Pump Inhibitor-induced Hypersensitivity Reaction: A Case Report. *Journal of Young Pharmacists*, *9*(1), 137.
10. [Ferreira, F., Mateus, S., Santos, A. R., Moreira, H., & Ferreira, N. R. (2016). Pantoprazole-related Symptomatic Hyponatremia. *European Journal of Case Reports in Internal Medicine*, *3*(2).]
11. Peng, T., Hu, Z., Zheng, H., Zhen, J., Ma, C., & Yang, X. (2018). Pantoprazole-induced acute kidney injury: A case report. *Experimental and therapeutic medicine*, *15*(6), 5302-5306.
12. *Gaur A,Chhabra M (2018)* ranitidine induced thrombocytopenia: a case report**;** Volume 7, Issue 8, 1003-1007**.**
13. Aryal, E., Rajbhandari, M., & Bhattarai, S. (2017). Lansoprazole–Induce Black Hairy Tongue-A Case Report. *Nepal Journal of Dermatology, Venereology & Leprology*, *15*(1), 52-54.
14. Mukherjee, S., Jana, T., & Pan, J. J. (2018). Adverse Effects of Proton Pump Inhibitors on Platelet Count: A Case Report and Review of the Literature. *Case reports in gastrointestinal medicine*, *2018*.
15. Pelluri, R., Begum, S. S., Sowmya, N., Jyothsna, M., Prathyusha, S., Divya, Y., ... & Ramarao, N. (2016). A Case Report on Pantoprazole Induced VIT. B. *Indian Journal of Pharmacy Practice*, *9*(1), 63.
16. Kim, Y. I., Park, C. K., Park, D. J., Wi, J. O., Han, E. R., & Koh, Y. I. (2010). A case of famotidine-induced anaphylaxis. *J Investig Allergol Clin Immunol*, *20*(2), 166-169.
17. SRIKANTH, K.P.,THAPA, B.R.,SADHNA., LAL, B., MENON, P., SODHI, K ., VAIPHEI,RAO KLN, K., (2015). Anaphylactic reaction to omeprazole. *Tropical Gastroenterology,36(2),137–139*.
18. Tekbaş, E., ARUTÜRK, Z., Habib, Ç. İ. L., & İslamoğlu, Y. (2012). Famotidine-induced acquired long QT syndrome: a case report. *Gaziantep Medical Journal*, *18*(1), 48-50.
19. Rethnam, U., & Yesupalan, R. S. (2007). Anaphylactic reaction associated with Ranitidine in a patient with acute pancreatitis: a case report. *Journal of medical case reports*, *1*(1), 75.
20. Oliva, A., Partemi, S., Arena, V., De Giorgio, F., Colecchi, C., Fucci, N., & Pascali, V. L. (2008). Fatal injection of ranitidine: a case report. *Journal of medical case reports*, *2*(1), 232.
21. Jabbar, A., Khan, R., & Farrukh, S. N. (2010). Hyperprolactinaemia induced by proton pump inhibitor. *Journal of the Pakistan Medical Association*, *60*(8), 689.
22. Yu, M., Qian, J., Guo, D., Li, L., & Liu, X. (2016). Severe adverse reactions caused by omeprazole: A case report. *Experimental and therapeutic medicine*, *12*(2), 1103-1106.
23. Kitamura, H., Kubota, Y., Fukushima, N., Ichinohe, T., Hayasaka, D., Kamachi, K., ... & Sueoka, E. (2016). Case Report Famotidine-induced reactive plasmacytosis and generalized lymphadenopathy: a case report and review of the literature. *Int J Clin Exp Pathol*, *9*(7), 7680-7685.
24. Taura, M., Asai, J., Wakabayashi, Y., Masuda, K., & Katoh, N. (2017). Drug eruption caused by esomeprazole: A case report and mini-review. *Allergology International*, *66*(3), 499-500.