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Effect Of Omperazole On Kidney

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بسم الله الرحمن الرحيم

In the name of Allah

{يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ ۚ}
المجادلة / ١١

Allah raises those among you who have believed and those who have been given knowledge degrees.

Dedication

Thank God who helped us with his success, and thanks to him first and foremost ...

The path ended only with giving, and we went through a long path, we exceeded the obstacles in our way and displaced some of them so that the path of giving would be wide, full of success stories and support for loved ones for us in times when we thought that it would only pass with fatigue, staying up late and heavy moments, and with the support of God, we depended and displaced, For those who helped us in secret with words and deeds, our mothers, fathers, loved ones and Friends of the years, and the educational staff transferred knowledge and gained skills and printed in our memory beautiful, happy and influential moments.

We thank you and give you the fruit of our efforts.

Thanks and gratitude

Oh God, praise and thanks as it should be for the majesty of your face and the greatness of your authority and the weight of your throne when you have blessed us and preferred.

And after...
As we finish our research, we extend our thanks and great appreciation and gratitude to (Dr. Mohammed Kamel Hassani) for the scientific care that we have included throughout his supervision of this research through continuous follow-up, valuable observations and good opinions that were good help in sorging this work and helping to accomplish it in this way and content.

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The Content

Introduction

In recent years, the use of proton pump inhibitors (PPI), especially omeprazole, has been associated with development of chronic kidney disease (CKD). These drugs are widely used worldwide. Although some studies have found an association between the use of PPI and the onset of acute renal failure and CKD. This study aims to analyze the association between the continuous use of omeprazole and the progression of CKD in adult and elderly individuals.
(Barreto *et al*., 2010).

Chronic kidney disease (CKD), characterized by progressive deterioration of biochemical and physiological functions of the body systems, can be defined as a syndrome caused by the progressive decrease in renal function (Franco *et al*., 2005).

Recently, parallel to the classical causes of development and progression of CKD, Diabetes Mellitus (DM) and Systemic Arterial Hypertension (SAH), the use of drugs which were once considered safe have been identified as possible causes of renal damage. Among these drugs, proton pump inhibitors (PPI), highly prescribed worldwide to treat gastroesophageal reflux and peptic ulcers through inhibition of gastric acid synthesis, have shown to be closely associated with acute interstitial nephritis (AIN), reduction of glomerular filtration rate (GFR) and the development of CKD(Schoenfeld *et al*.,1993)

Initially it was believed that these drugs were associated with the development of recurrent acute renal injury, generating an AIN process that could be chronic and cause loss of renal function by successive renal tissue regeneration.
However, recent studies found that loss of renal function is not necessarily caused by sequential acute lesions, as the use of PPI has been associated with CKD regardless of the occurrence of previous acute episodes
(Lazarus *et al* .,2010) .

The association between PPI use and CKD development is a recent and not fully understood topic. Only a few studies evaluating the impact generated by the use of these drugs, specifically on CKD progression and staging, have been performed. In addition, considering the high consumption of PPI in Brazil
(Costa *et al*., 2015) .

and in the world population, as well their adverse effects, it is necessary to conduct researches to better elucidate this association. Such research may favor the creation of clinical protocols to promote the rational use of PPI, without disregarding the cost and benefit of this therapeutic approach. In this sense, the present study aims to analyze the association between the regular use of PPI and CKD progression in adult and elderly individuals, as well to analyze the survival of these patients.

Chronic kidney disease (CKD) has been recognized as a leading public health problem worldwide .The global estimated prevalence of CKD is 13.4%, and patients with kidney failure needing renal replacement therapy are estimated between 5 and 7 million.(Zhang ,2019) .

Procedures used in the management of kidney disease include chemical and microscopic examination of the urine (urinalysis), measurement of kidney function by calculating the estimated glomerular filtration rate(EGFR) using the serum creatinine; and kidney biopsy and CT scan to evaluate for abnormal anatomy. Dialysis and kidney transplantation are used to treat kidney failure; one (or both sequentially) of these are almost always used when renal function drops below 15%. Nephrectomy is frequently used to cure renal cell carcinoma .
(Cotran *et al*.,2005).

Renal physiology is the study of kidney function. Nephrology is the medical specialty which addresses diseases of kidney function: these include CKD, nephritic and nephrotic syndromes, acute kidney injury, and pyelonephritis. Urology addresses diseases of kidney (and urinary tract) anatomy: these include cancer, renal cysts, kidney stones and ureteral stones, and urinary tract obstruction. The word “renal” is an adjective meaning “relating to the kidneys”, and its roots are French or late Latin. Whereas according to some opinions, "renal" should be replaced with "kidney" in scientific writings such as "kidney artery", other experts have advocated preserving the use of renal as appropriate including in "renal artery".(Kalantar *et al*.,2021) .

CHAPTER ONE

1- Kidney:

The kidneys are two reddish-brown bean-shaped organs found in vertebrates. They are located on the left and right in the retroperitoneal space, and in adult humans are about 12 centimeter's (4+1⁄2 inches) in length. They receive blood from the paired renal arteries; blood exits into the paired renal veins. Each kidney is attached to a ureter, a tube that carries excreted urine to the bladder.
(Lote ,2012).

The kidneys lie in the retroperitoneal space behind the abdomen, and act to filter blood to create urine. The kidney participates in the control of the volume of various body fluids, fluidosmolality,acid–base balance, variouselectrolyteconcentrations, and removal of toxins. Filtration occurs in the glomerulus: one-fifth of the blood volume that enters the kidneys is filtered. Examples of substances reabsorbed are solute- free water, sodium, bicarbonate, glucose, and amino acids.
Examples of substances secreted are hydrogen, ammonium, potassium and uric acid.(Mescher, 2016) .

The nephron is the structural and functional unit of the kidney. Each adult human kidney contains around 1 million nephrons, while a mouse kidney contains only about 12,500 nephrons. The kidneys also carry out functions independent of the nephrons. For example, they convert a precursor of vitamin D to its active form, calcitriol; and synthesize the hormones Erythropoiten and renin.

The positioning rusted Source of the kidneys is just below the rib cage, with one on each side of the spine. The right kidney is generally slightly lower than the left kidney to make space for the liver.

Each kidney is approximately 3 centimeters (cm) thick, 6 cm wide, and 12 cm long. In males, the average weightTrusted Source of the kidneys is roughly 129 grams (g) for the right one and 137 g for the left. In females, the average weightTrusted Source of these organs is 108 g for the right kidney and 116 g for the left kidney. (Gupta *et al* 2017) .

1.1 Structure:

The kidneys are two bean-shaped organs that are roughly the size of a fist. A tough, fibrous renal capsule surrounds each kidney and provides support for the soft tissue inside. Beyond that, two layers of fat serve as further protection. The adrenal glands lie on top of the kidneys(Hamm, *et al*.,2015)

Inside the kidneys are a number of pyramid-shaped lobes. Each consists of an outer renal cortex and an inner renal medulla. Nephrons flow between these sections. Each nephron includes a filter, called the glomerulus, and a tubule. The glomerulus filters blood, which enters the kidneys through the renal arteries and leaves through the renal veins. The kidneys are relatively small organs, but they receive 20–25%Trusted Source of the heart's output.
The tubule returns necessary substances to the blood and removes waste that then becomes urine. The kidneys excrete urine through the ureter, a tube that leads to the bladder. (Kaufman *et al*.,2021)

The kidney produce urine by removing toxic waste products and excess water from the body. Urine formed in each kidney passes through the ureter, flows into bladder before finally being excreted through the urethra. Most people (males and females) have two kidneys.(Nagami *et al*.,2017)

•The kidneys are located at upper and back side of the abdomen, on either side of the spine, They are protected from damage by the lower ribs.
•The kidneys lie deep inside the abdomen so normally one cannot feel them.
•The kidneys are a pair of bean shaped organs. In adults, a kidney is about 10 cm long, 6 cm wide and 4 cm thick. Each kidney weighs approximately 150-170 grams.
•Urine formed in the kidneys flow down to urinary bladder and then through the ureters. Each ureter is about 25 cm long and is a hollow tube- like structure made up of special muscles.
•The urinary bladder is a hollow organ made up of muscles, which lie in the lower and anterior part of the abdomen. It acts as a reservoir of urine
•The adult urinary bladder hold about 400-500 ml of urine; when filled to near capacity, a person feels the urge to pass urine.
•The urine in the bladder is excreted through the urethra during the process of urination. In females, the urethra is relatively short, while it is much longer in males. (Hydronephrosi, 2018)

1.2 Function:

The main role of the kidneys is maintaining-homeostasis. They manage fluid levels, electrolyte balance, and other factors that keep the internal environment of the body consistent and comfortable. (Molina, *et al*.,2012)

The kidneys perform a variety of important functions:

1.) They regulate the osmotic pressure (osmolality) of the body fluids by excreting osmotically dilute or concen- trated urine.
2.) They regulate the concentrations of numerous ions in blood plasma, including Na+, K+, Ca2+, Mg2+, Cl, bi- carbonate (HCO3), phosphate, and sulfate.
3.) They play an essential role in acid-base balance by excreting H+, when there is excess acid, or $HCO3^{-}$, when there is excess base
4.) They regulate the volume of the ECF by controlling Nat and water excretion.
5.) They help regulate arterial blood pressure by adjust- ing Na+ excretion and producing various substances (e.g., renin) that can affect blood pressure.
6.) They eliminate the waste products of metabolism, including urea(the main nitrogen- containing end-product of protein metabolism in humans), uric acid (an end-prod- uct of purine metabolism), and creatinine (an end-product of muscle metabolism)
7.) They remove many drugs (e.g., penicillin) and for- eign or toxic compounds.
8.) They are the major production sites of certain hormones, including erythropoietin and 1,25-dihydroxy vitamin D3.
9.) They degrade several polypeptide hormones, including insulin, glucagon, and parathyroid hormone
10.) They synthesize ammonia, which plays a role in acid-base balance.
11.) They synthesize substances that affect renal blood flow and Na+ excretion, including arachidonic acid derivatives (prostaglandins, thromboxane A2) and kallikrein (a proteolytic enzyme that results in the production of kinins.(George, 2012).

These organs carry out a wide range of bodily functions.
The kidneys are essential organs that perform several vital functions that are necessary for survival, including waste excretion, reabsorption of nutrients, maintaining pH, regulating blood pressure, osmolality regulation, and secretion of active compounds.
Waste excretion The kidneys remove waste products from the blood and eliminate them in the urine. This includes compounds like urea, uric acid, and drugs, which can be harmful if they accumulate in the body. The kidneys filter these waste products from the blood and excrete them in the urine, helping to maintain the body's internal environment and preventing the buildup of harmful compounds(Ogobuiro *et al*.,2021) .

Reabsorption of nutrients the kidneys also play a crucial role in the reabsorption of nutrients from the blood.
The kidneys reabsorb important nutrients like glucose, amino acids, bicarbonate, water, and electrolytes like sodium and potassium from the urine and return them to the bloodstream. This ensures that the body has a constant supply of essential nutrients and helps maintain overall health.(Cotran *et al*.,2015) .

Maintaining pH the kidneys help regulate the body's pH by reabsorbing and producing bicarbonate from urine to neutralize acids. This is important because the body's pH needs to be within a specific range to ensure that enzymes and proteins can function properly. The kidneys can retain bicarbonate if the pH is tolerable and release it if acid levels rise. This helps maintain the body's internal environment and ensures that enzymes and proteins can function properly.
(Nagami et al.,2017) .

Regulating blood pressure the kidneys play a crucial role in regulating blood pressure. Hormones like angiotensin II play a role in increasing the kidneys' absorption of sodium chloride, which effectively increases the size of the extracellular fluid compartment and raises blood pressure. The kidneys also release renin, which helps manage the expansion of arteries and the volumes of blood plasma, lymph, and interstitial fluid. This helps regulate blood pressure and ensures that the body's internal environment is maintained.
(Molina *et al* , 2015).

In summary, the different functions of the kidneys are interconnected and work together to ensure that the body's internal environment is maintained. The kidneys perform several vital functions, including waste excretion, reabsorption of nutrients, maintaining pH, regulating blood pressure, osmolality regulation, and secretion of active compounds. These functions are essential for maintaining overall health and ensuring that the body functions properly.

1.3 Diseases:

A range of diseases can affect the kidneys. Environmental or medical factors may lead to kidney disease, and they can cause functional and structural problems from birth in some people. (Kalantar et al, 2021).

In people with diabetic nephropathy, damage occurs to the capillaries of the kidney as a result of long-term diabetes. The symptoms may not become apparent until years after the damage starts to develop.
(Glodny *et al*,. 2009).

They can include:
- fluid buildup
- sleep difficulty
- poor appetite
- upset stomach
- weakness
- difficulty concentrating

1.3.1 Kidney stones:

Stones can form as a solid buildup of minerals in the kidneys.
They can cause intense pain and might affect kidney function if they block the ureter (Molina *et al* 2012) .

1.3.2 Kidney infections:

Kidney infections tend to result from bacteria in the bladder that transfer to the kidneys.
The symptoms can include lower back pain, painful urination, and, sometimes, fever. Changes in the urine may include the presence of blood, cloudiness, and an unusual odor.

Kidney infections are more common Trusted Source in females than in males and more likely to affect those who are pregnant. The infection often responds well to antibiotics(Molina *et al*,.2015).

1.3.3 Renal failure:

In people with renal failure, the kidneys become unable to filter out waste products from the blood effectively.
If an injury or another factor, such as the overuse of medication, causes kidney failure, the condition may be reversible with treatment. If the cause is a disease, however, kidney failure often does not have a full cure.(Emamian *et al* ,1993)

1.3.4 Kidney hydronephrosis:

Hydronephrosis means “water on the kidney”.
It usually occurs when an obstruction prevents urine from leaving the kidney, causing intense pain.
In time, untreated hydronephrosis can put pressure on a person’s kidneys and may result in kidney damage.(Boron ,2004) .

1.3.5 Interstitial nephritis:

A reaction to medications or infection can cause inflammation of the nephrons.
The treatment usually involves addressing the cause of inflammation or changing a course of medication.(Clapp ,2009)

1.3.6 Acute Interstitial nephritis:

Acute renal failure, Poor blood flow, interstitial renal, This effect results from the patient's hypersensitivity to painkillers and anti- inflammatory drugs. What does it look like in the case? cause interstitial swelling of heart tissue; due to sedimentation of white blood cells.
This type of kidney can be treated with nephrotherapy in acute interstitial inflammation. (Winkelmayer, 2004)

1.3.7 Chronic interstitial nephritis:

Chronic interstitial nephritis is caused by a combination of analgesics and non-steroidal anti-inflammatory drugs.

How to take medicine in return in a long translation? Interstitial tissue gradually begins to deteriorate, and then its function, in addition to microtubule atrophy, reabsorption of minerals, solids, and then lost in the urine, the amount of urine increases, Different types of painkillers that have an effect on the kidneys include:

Non-steroidal anti-inflammatory drugs, such as: aspirin, ibuprofen, iProfenide, naproxen, diclofenac.

Painkillers, such as: paracetamol.(Naito *et al*.,2003)

1.3.8 Kidney damage:

Diabetes mellitus is the most common cause of chronic renal failure, and this is due to the fact that high blood sugar damages the kidneys, and over time this leads to a weakening of the kidney's ability to get rid of excess fluids and body waste, and to clarify the mechanism by which diabetes causes damage Kidneys In a simple way.

it can be said that chronic high blood sugar harms the kidneys in several ways, perhaps the most important of which is that it can lead to narrowing and hardening of the blood vessels emerging from the kidneys, and this impedes the path of blood through filters or renal glomeruli (Glomeruli); They are the tiny blood vessels responsible for filtering the particles carried in the blood through the kidneys, and with this obstruction in the blood path from the filters to the outside of the kidneys, the pressure inside them increases, and they are exposed to damage, which usually allows proteins to pass through the kidneys filters into the urine, and therefore the high protein in urine strongly indicates that diabetes is one of the major potential causes of chronic kidney disease in an individual. [Primary Causes of End-Stage Renal Disease].

In addition, diabetes can cause damage to the nerves in various parts of the body, which may lead to difficulty in emptying the bladder of urine, and the reflux of urine from the bladder to the kidneys, and the presence of urine in the bladder for a long time increases the chance of urinary infection, which also increases the risk of damage to the bladder. The kidneys.] But it must be noted that good control of diabetes readings and follow-up with a specialist doctor on a regular basis reduces the risk of chronic kidney disease and kidney failure to a large extent. High blood pressure is the second most common cause of kidney failure after diabetes. , as chronic high blood pressure can damage blood vessels in various parts of the body in general, and in the kidney in particular, which leads to a decrease in the functional characteristics of the kidneys over time, and increases the accumulation of harmful substances and excess fluids in the body;

In order to clarify the mechanism by which blood pressure causes damage to the kidneys, it can be explained in a simple way that the continuous increase in blood pressure may cause an increase in the thickness of the blood vessels .

that supply the kidneys with blood, and thus narrowing of these vessels, and a decrease in the amount of blood reaching the kidneys, specifically the renal glomeruli, and these glomeruli are exposed to damage With the passage of time and their walls begin to harden, which impedes their ability to filter particles from the blood to form urine, and in addition to that, chronic damage to the kidneys makes matters worse. This is because it causes an additional increase in blood pressure as a result of a decrease in the ability of the kidneys to help regulate blood pressure, which is one of its main functions as mentioned above, and this would also increase damage to the kidneys. (Lupus, 2019)

is the case in patients with diabetes., the same applies to pressure patients, as good control of pressure readings and follow- up with a specialist doctor on a regular basis reduces the risk of chronic kidney disease and kidney failure to a large extent.

In the event of an autoimmune disease, the body also mistakenly attacks one or more parts of the body's healthy cells, which leads to a weakening of their functions, and at other times the damage caused by the autoimmune disease can be life-threatening, and it is worth noting that there are many Types of autoimmune diseases, and these types depend on the different areas in the human body that they affect,] For example, an autoimmune disease can affect one part of the kidney and expose it to damage and damage, so It was in the glomeruli of the kidneys (: Glomerular), or blood vessels, small kidney tubules, and it should be noted that immune diseases are considered the third most common cause of chronic renal disease and kidney failure after diabetes and high blood pressure, and examples of immune diseases that are The following can cause kidney failure .

Good pasture syndrome is an autoimmune disease that affects the human body. In this case, the immune system attacks the collagen protein present in the filters or glomeruli of the kidneys and lungs, but the greatest damage is to the kidneys ,which leads to glomerulonephritis and damage. Systemic lupus erythematous It is one of the immune diseases that can affect many parts of the body, including the kidneys, where the immune system can attack the kidneys in the event of this disease, specifically the filters

or glomeruli of the kidneys, causing inflammation and damage as well.
IgA nephropathy: IgA nephropathy is a form of glomerulonephritis, which is caused by an abnormal accumulation of IgA in the glomeruli, which can lead to inflammation and damage in some cases. But fortunately, 50% of people with this syndrome do not develop serious kidney damage.] Some diseases and genetic disorders There are many kidney diseases that occur due to genetic and hereditary mutations, and examples of these diseases include the following: Polycystic kidney disease: (Polycystic kidney disease is a disorder of the kidneys and other organs in which cysts, which are groups of fluid-filled sacs, develop in the kidneys and interfere with their ability to filter waste from the blood. As these cysts grow, the kidneys swell and can lead to kidney failure.

Fabry disease: It is a genetic disorder caused by the accumulation of a certain type of fat in the cells of the body. This disease occurs in childhood, as the accumulation of fat causes signs and symptoms that affect many parts of the body, such as the heart and kidneys.
There are several drugs that can affect the kidneys and cause kidney damage, both in the short term and over time. Here are some examples :
Non-steroidal anti-inflammatory drugs (NSAIDs): NSAIDs like ibuprofen and naproxen are commonly used to treat pain and inflammation, but they can also cause kidney damage, especially if taken in high doses or over a long period of time. NSAIDs can reduce blood flow to the kidneys and cause damage to the kidney tubules.

Certain antibiotics: Some antibiotics, such as amino-glycosides, can be toxic to the kidneys and cause kidney damage. These drugs are often used to treat serious infections, but they can cause damage to the kidney tubules and lead to acute kidney injury.
Contrast dyes: Contrast dyes are sometimes used in medical imaging procedures like CT scans and angiograms. These dyes can be toxic to the kidneys and cause kidney damage, especially in people with pre-existing kidney disease or diabetes.

Chemotherapy drugs: Some chemotherapy drugs can be toxic to the kidneys and cause kidney damage. This is especially true for drugs like cisplatin and methotrexate, which are commonly used to treat cancer.
Antiviral drugs: Certain antiviral drugs, such as acyclovir and tenofovir, can be toxic to the kidneys and cause kidney damage, especially if taken in high doses or over a long period of time.

Lithium: Lithium is a drug used to treat bipolar disorder, but it can also be toxic to the kidneys and cause kidney damage, especially if taken in high doses or over a long period of time.

Diuretics: Diuretics are drugs that increase urine output and are commonly used to treat conditions like high blood pressure and heart failure. However, some diuretics can cause kidney damage, especially if taken in high doses or over a long period of time.

It's important to note that not everyone who takes these drugs will experience kidney damage, and the risk varies depending on factors like age, pre-existing kidney disease or diabetes, and the dose and duration of the drug treatment. If you have concerns about a drug you are taking and its potential effects on your kidneys, it's important to talk to your healthcare provider .

CHAPTER TWO

Stomach drug:

Medications for gastrointestinal diseases and symptoms include prescription and nonprescription drugs, conventional and unconventional agents, simple small molecules, complex macromolecules and large recombinant proteins. These medications are can be classified based upon their use: drugs for nausea and vomiting (anti emetics), pro-kinetic agents, laxatives, antidiarrheal agents, drugs for acid peptic disease, drugs for irritable bowel syndrome, inflammatory bowel disease and, of course, miscellaneous.

Agents used for gastrointestinal disease rarely cause liver injury. One reason for this is that they are often locally active and result in little systemic exposure. The immune modulatory agents used to treat inflammatory bowel disease are an exception, being given systemically, often intravenously and capable of causing liver injury, although not very frequently(Zimmerman ,2018) .

Antidiarrheal agents include bulk forming agents, hydroscopic agents, bile acid resins, bismuth, inhibitors of intestinal motility, non-absorbed antibiotics and hormones. Bulk forming agents include methyl-cellulose; hydroscopic agents include pectin and kaolin; bile acid resins are cholestyramine, cholesterol and colesevelam; inhibitors of intestinal motility include opioids such as diphenoxylate and loperamide. Antibiotics include rifamycin and rifaximin which are non-absorbed and are used for travelers 'diarrhea.

Hormones with antidiarrheal activity include octretide and somatostatin. Most antidiarrheal agents are active locally in the small intestine and colon and are largely not absorbed. Some, however, have been implicated in rare causes of liver injury (senna, cascara, cholestyramine)

Telotristat is a relatively new agent that inhibits the synthesis of serotonin and is used specifically for the diarrhea of carcinoid syndrome. Agents discussed in LiverTox include the following, which are linked to the specific drug record(Reuben, 2011)

•Bismuth
•Cholestyramine
•Colesevelam
•Colestipol
•Crofelemer
•Difenoxin
•Diphenoxylate
•Kaolin
•Loperamide
•Methyl-cellulose
•Octreotide
•Pectin
•Rifamycin
•Rifaximin
•Somatostatin
•Telotristat

Anti emetics are a diverse group of medications that act at different points in the pathways that regulate nausea and vomiting. These include antihistamines, anticholinergic agents, phenothiazines, serotonin type 3 receptor blockers, centrally acting benzamides, cannabinoid receptor agonists, substance P antagonists and miscellaneous. Agents discussed in LiverTox include the following, which have links to the specific drug record:

•Anticholinergic Agents:
o Hyoscyamine, Methscopolamine, Scopolamine.

•Antihistamines:
o Cyclizine, Dimenhydrinate, Hydroxyzine, Meclizine, Promethazine.

•Cannabinoid Receptor Agonists:
o Dronabinol, Nabilone, Tetrahydrocannabinol • Phenothiazines.
o Chlorpromazine, Prochlorperazine • Serotonin 5-HT3 Receptor Antagonists.
o Alosetron, Dolasetron, Granisetron, Ondansetron, Pal onosetron.

•Substance P/Neurokinin 1 Receptor Antagonists:
o Aprepitant, Fosaprepitant, Rolapitant.

•Miscellaneous
o Dexamethasone, Metoclopramide, Trimethobenzamide.(Reuben, 2011).

Acid peptic disease/antiulcer agents that include antacids, the histamine type 2 receptor blockers (H2 blockers), and the proton pump inhibitors (PPIs). These agents are some of the most commonly taken medications and are very well tolerated, most being available both by prescription and over-the-counter. While many of these drugs are approved for use in duodenal and gastric ulcer disease, their major use is for acid reflux and indigestion. Agents discussed in LiverTox include the following, which are linked to the specific drug record:

• Histamine H2 Receptor Antagonists (H2 Blockers) :
o Cimetidine, Famotidine, Nizatidine, Ranitidine.

• Proton Pump Inhibitors:
o Dexlansoprazole, Esomeprazole, Lansoprazole, Omperazole, Pantoprazole, Rabeprazole.

Cathartics, laxatives or agents for constipation include bulk forming agents, osmotic agents, stool wetting agents, nonspecific stimulants, prokinetic agents and agents that increase fluid secretion. Many of these therapies are not systemically absorbed and none are considered particularly hepatotoxic. Naldemedine and naloxegol are opioid antagonists and are used to treat the constipation associated with opioid use. Not all of these agents are discussed in LiverTox, but those that are have links to the specific drug record:

•Bisacodyl
•Cascara Sagrada
•Castor Oil
•Docusate
•Fiber, Bran
•Lactulose
•Magnesium Sulfate
•Methyl-cellulose
•Naldemedine (Opioid Antagonist)
•Naloxegol (Opioid Antagonist)
•Plecanatide (for Chronic Idiopathic Constipation)
•Prucalopride (for Chronic Idiopathic Constipation)
•Senna

Inflammatory bowel disease encompasses several disorders, most commonly ulcerative colitis and Crohn colitis. Agents can be classified as 5-aminosalicyclic acid (5-ASA) based agents, immunosuppressive drugs, antitumor necrosis factor agents, corticosteroids, antibiotics and miscellaneous. Agents discussed in Liver Tox include the following, which are linked to the specific drug record:
(Sharkey *et al*., 2018)

•Aminosalicyclic Acid (5-ASA) Derivatives:
o Balsalazide, Mesalamine, Olsalazine, Sulfasalazine.

•Immunosuppressive Agents:
o Azathioprine, Mercaptopurine, Methotrexate.

•Tumor Necrosis Factor Antagonists:
o Adalimumab, Certolizumab, Golimumab, Infliximab.

•Miscellaneous
o Metronidazole, Natalizumab, Vedolizumab .

Irritable bowel syndrome or functional bowel disease is a common, but not well understood syndrome or collection of symptoms marked by variable degrees of diarrhea and constipation with abdominal bloating and pain. Symptomatic therapies with antidiarrheal agents, drugs for constipation, analgesics, prokinetic agents or antispasmotics are often applied. Medications developed specifically for irritable bowel syndrome include agents that affect specific gastrointestinal receptors or hormones and include tegaserod, alosetron, linaclotide, plecanatide, prucalopride, and lubiprostone. None of these agents, however, is particularly hepatotoxic. Eluxadoline is a unique agent that is used to treat diarrhea-predominant irritable bowel syndrome. It is a mixed opioid receptor agonist (mu) and antagonist (delta) and can cause spasm of the sphincter of Oddi and pancreatitis accompanied by marked serum aminotransferase elevations. Linaclotide and plecanatide are guanylate cyclase C receptor agonists and are used to treat chronic idiopathic constipation or "constipation predominant" irritable bowel syndrome. Similarly, cisapride, prucalopride and tegaserod are serotonin type 4 receptor agonists that are used for chronic idiopathic constipation. Agents discussed in LiverTox. (Sharkey *et al*.,2018).

include the following:
which are linked to the specific drug record:
•Antimuscarinics/Antispasmodics:
o Dicyclomine, Glycopyrrolate, Hyoscyamine, Methscopolamine.

•Prokinetic Agents:
o Alosetron, Cisapride, Domperidone, Linaclotide, Lubiprostone, Metoclopramide, Plecanatide, Prucalopride, Tegaserod.

•Opioid receptor mixed agonist/antagonist o Eluxadoline.

CHAPTER THREE

Omeprazole:

Omeprazole is a drug that is used to prevent ulcers that occur in the gastrointestinal tract caused by bacterial infection, and it is used to treat stomach ulcers and also treat acidity, as well as to get rid of visual reflux, and it is one of the most internationally recognized drugs for treating acidity.
The drug was approved by the Food and Drug Administration in 1989 AD, and the United States of America marketed it under different names in the same year of approval (Johnson, 2013) .

Omeprazole is known to be an antacid for the stomach, which is prescribed to patients who suffer from increased acid secretion in the stomach. Where omeprazole modifies the activity of the enzymatic system responsible for the secretion of acid, and thus reduces the secretions of enzymes present in the stomach cells, and the acid decreases as a result of this in the stomach. (Mastroianni, 2009)

Omeprazole is also used to treat heartburn, heartburn, acute gastritis, duodenitis, and esophagitis, all of which are cases in which the level of acidity in the stomach increases. It is also used with a number of other medicines to treat Helicobacter pylori (stomach germ).(Rodrigues, 2019).

The effect of Omeprazole on the body:

Some studies have confirmed that treatment with any type of selective or non-selective anti-inflammatory that contains inhibitors of stomach acids may have a small chance of harming the upper gastrointestinal tract, but it may harm the entire gastrointestinal tract. Therefore, it is recommended to use drugs that contain single antibiotics to limit the damage to the gastrointestinal tract.
(Menegassi ,2010) .

Increasing the use of omeprazole for a long period of more than two weeks may cause many problems, including a continuous decrease in the acidity of the intestines, which causes the growth of some types of microbes, which may not have tolerated the natural acidity of the intestines in the past and may cause large cases of diarrhea. It may reach severe pneumonia, and the patient may suffer from severe indigestion, and it may also cause a problem in the body absorbing some vitamins, such as vitamin B12, and some minerals, such as calcium.
(Härmark ,2007).

And it leads later to osteoporosis, and the patient may also be exposed to fractures easily, so it is never preferable to take drugs without a doctor's order, and therefore you should be careful not to use the drug excessively. The patient should refrain from consuming coffee and tea to reduce caffeine, and the doctor should be informed of the existence of pregnancy or even planning to become pregnant.

Also, in the case of breastfeeding, comprehensive examinations must be done before starting to take the drug so that all symptoms that require taking the drug are known.Caution should be exercised by patients with liver disease, and the doctor should be informed before taking the dose, and it should not be used except under medical supervision, and the medicine should be stored away from high temperatures, light and moisture as well.(Myers *et al*.,2001).

The effect of omeprazole on the kidneys :

It was pointed out that man dealt with the problems of stomach acidity in various ways, both reliable and unreliable.
But no drugs appeared to treat this condition until the mid-seventies of the last century with the introduction of the drug cimetidine, which was targeting the production of stomach acid in particular. This treatment has achieved tremendous popularity, then it was followed by drugs of the same class known as H2 blockers or histamine receptor blockers (H2 blockers), including famotidine and ranitidine.(Harding *et al*., 1996)

Currently, other leading drugs have advanced on H2 blockers, which are in the category of Proton Pump Inhibitors (PPI), which have become the most prescribed drugs by doctors for stomach and esophageal problems that can be treated - or at least mitigated - by reducing acid levels in the stomach. stomach.
Here, esomeprazole is a drug that belongs to the family of proton-pump inhibitors, which, as I mentioned, are drugs that reduce acid secretion from the stomach lining.

Proton pump inhibitors are used to treat several conditions such as: heartburn, gastroesophageal reflux, gastro-intestinal ulcers, and damage to the lower part of the esophagus caused by stomach acid reflux
(Stevens *et al*., 2011).

Esomeprazole has other uses that also include - according to the National Library of Health in the United States - reducing the possibility of ulcers in those who take non-steroidal anti-inflammatory drugs continuously such as aspirin and Voltaren, and treating conditions in which the stomach produces a large amount of acid such as Zollinger-Ellison syndrome.

As for the long-term risks, according to the US National Library, those who take proton pump inhibitors may be at increased risk of hip, vertebrae and wrist fractures, and this is related to those who take high doses or take treatment for a year or more continuously.

This is because PPIs affect calcium absorption, which explains the increased risk of fractures. According to Harvard University, proton pump inhibitors may also increase the risk of pneumonia and the risk of infection with bacteria (Clostridium difficile) in hospitals, which may lead to severe complications such as diarrhea and colitis.(Linsky *et al*,. 2010).

As for the negative effects of these drugs on the kidneys, which is the main subject of this issue of the Riyadh Clinic, previous studies have indicated the possibility of temporary tissue inflammation in the kidneys that may lead to acute kidney failure when using such drugs. On the other hand, a study conducted (Johns Hopkins, 2016) .

with an increased risk of chronic kidney disease. The study, which included the follow-up of more than 10,000 people without previous kidney disease, indicated that people who were constantly using such drugs were 1.5 times more likely to develop chronic kidney failure compared to people who did not use these drugs. The results of this study were confirmed by two other studies, the latest of which was from St. Louis University and published in February of this year.
(Cadle *et al*.,2007) .

The first study indicated the need for further studies to find out whether proton pump inhibitors themselves are the cause of kidney problems and then recommend their use, or that the results were due to other comorbidites that coincided with the use of this treatment .
That is, it did not say that proton pump inhibitors lead to kidney failure by itself, as the messages circulated on the communication sites claimProesmans
(Boeck,2003) .

In the same context, the Saudi Gastroenterology Society indicated in the recommendations of the 15th conference of the society, which was held recently in Jeddah, the necessity of dispensing proton inhibitor drugs to treat gastro esophageal reflux under medical supervision.
(Fraser *et al*., 2013) .

In conclusion, the medical data approved so far do not say that proton pump inhibitors cause kidney failure, and until this moment there are no medical warnings from official scientific bodies about stopping the use of such drugs.
However, it should be noted that the leaflet attached to the drug esomeprazole indicates that the drug may have effects on the kidneys, but they are very rare (may affect one out of every ten thousand), and the leaflet also stresses the need to consult a doctor before taking the treatment in several cases, including if The person has severe kidney problems (Cea Soriano *et al* .,2014) .

Therefore, it is logical that taking "proton pump inhibitors" is reasonable when there is a chronic stomach acid problem, or when it is expected to arise. However, transient cases of mild heartburn do not need to be treated with these drugs, but rather with old drugs or with drugs of the "H2 blockers" class.
Finally, the advice that we can give to the followers of this clinic is that if you are taking proton pump inhibitors without a prescription،

you should see a doctor, as the proton pump inhibitors to which this drug belongs and in the long run may increase the risk of other disease conditions. Such as osteoporosis, kidney and liver diseases. Also, if it is used for a long time,We should discuss with your attending physician about its side effects on your health and ways to prevent it ،
medications you use that may increase its side effects. (Carvajal *et al*., 2007) .

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