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A REVIEW ARTICLE ON PREVALENCE OF COLORECTAL CANCER WITH RANITIDINE

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ABSTRACT

The relation between use of histamine-2-receptor (H2-receptor) antagonists and colorectal cancer risk was investigated in an exceedingly case-control study. The incidence of gastric cancer was raised for the primary few years once the beginning of treatment with H2-receptor antagonists, this could replicate misdiagnosis of some early gastric cancers. The findings square measure against long persistence of AN excess risk of gastric cancer in association with use of H2-receptor antagonists. In this review article, Includes the some of the article wised study review on prevalence of colorectal cancer with ranitidine.

KEYWORDS: Ranitidine, Colorectal cancer, Prevalence.

INTRODUCTION

Ranitidine

H2-receptor antagonist ranitidine is now well established as a potent inhibitor of gastric acid secretion, effective within the treatment and prophylaxis of gastrointestinal lesions aggravated by gastric acid secretion.

Therapeutic trials of several thousand patients with peptic ulcer disease confirm that ranitidine 300 mg daily administered orally in single or divided doses is a minimum of as effective as cimetidine 800-1,000 mg daily healing of duodenal and gastric ulcers. Similar doses of ranitidine have been shown to relieve the symptoms of reflux esophagitis and cure or prevent gastrointestinal damage caused by ulcerogenic drugs. Ranitidine 150 mg taken orally at night maintains long-term healing of ulcers. Ranitidine has also shown good results in the treatment of Zollinger-Ellison syndrome and in the prevention of aspiration pneumonia when administered before surgery and in term pregnant women. It may even have an area within the management of upper acute gastrointestinal bleeding and within the prevention of stress ulcers within the medical care setting, although these areas require further consideration. Ranitidine has been used safely in obstetric patients during labor, in children, the elderly and in patients with renal impairment when administered in appropriate doses. The drug is very well tolerated and is only rarely associated with serious adverse effects or clinically significant drug interactions.

Even at high doses, ranitidine appears to lack antiandrogenic effects.[1] Ranitidine, is a medicine that decreases the production of acid in the stomach. It is commonly used to treat peptic ulcer, gastroesophageal reflux disease and syndrome.

There is also experimental evidence of benefits to hives. It can be taken orally, by injection into the muscle or vein.

Histamine regulates the function of osteoclasts and osteoblasts, but the data regarding the influence of histamine H2 receptor antagonists on bone tissue are ambiguous. Factors that influence skeletal growth can have a significant impact on peak bone mass and the future risk of fractures. The aim of our study was to assess the influence of ranitidine in colorectal cancer.[2] Ranitidine, a selective H2 receptor antagonist, is approved for a number of gastrointestinal indications, including treatment and / or maintenance regimens for duodenal and gastric ulcers, hypersecretory conditions, roux disease gastroesophageal (GERD)and erosive esophagitis, usually ranging from 150 mg od to 150 mg q.i.d. Several studies using the usual prescription doses have also suggested the efficacy of ranitidine to improve symptoms of a variety of non-ulcerative conditions such as dyspepsia and episodic heartburn.

Acid suppressants are commonly prescribed medications. Laboratory studies suggest a mechanism by which they may increase the risk of colorectal cancer (CRC). Some epidemiological studies have studied the use of acid suppressants and the risk of CRC; none have documented a global association. We sought to determine whether acid suppressants are associated with the risk of CRC.

Ranitidine was discovered in 1976 and came into

commercial use in 1981.[3] it's on the earth Health Organization's List of Essential Medicines, the safest and best drugs needed during a system. It is available as a generic medicine. The 2015 wholesale price in the developing world was around $ 0.01 to 0.05 per pill. In the us, it's about $ 0.05 per dose. In 2016, it was the 50th most prescribed drug in the United States, with over 15 million prescriptions. In September 2019, N-nitrous dimethylamine toxin was found to occur in ranitidine from various manufacturers, resulting in distribution stops and recalls.[4,5,6,7]

Certain ranitidine preparations are available without prescription (OTC) in several countries. In the United States, 75 and 150 mg tablets are available without prescription. Larger doses and pack sizes require a prescription. For the treatment of ulcers, a nightly dose is especially important - as increased gastric / duodenal pH promotes overnight healing when the stomach and duodenum are empty. On the other hand, for the treatment of reflux, lower and more frequent doses are more effective. Ranitidine used to be given long term in the treatment of reflux, sometimes indefinitely. However, proton pump inhibitors (PPIs) have assumed this role. In addition, quite rapid tachyphylaxis may develop within six weeks of starting treatment, further limiting its potential for long-term use. People with Zollinger-Ellison syndrome received very high doses without causing harm. Ranitidine is contraindicated for patients with hypersensitivity to the drug. Some adverse effects have been reported as events in clinical trials: Rare reports have been made of malaise, dizziness, drowsiness, insomnia and dizziness.

In severely ill elderly patients, cases of reversible mental confusion, agitation, depression and hallucinations have been reported. Ranitidine causes fewer CNS adverse reactions and drug interactions compared with cimetidine. Arrhythmias such as tachycardia, bradycardia, atrioventricular block and premature ventricular beats have also been reported.[1,3]

Most of the published studies which refer to the time of onset of pharmacodynamic action have not used a precise definition of onset and have often only provided a qualitative description of the results5-12. In addition, most studies have not included a placebo treatment; therefore, the start has been defined from the initial pretreatment values, 9 or in terms of the value assigned by the investigator.[8] Thrombocytopenia is a rare but known side effect. Drug-induced thrombocytopenia usually takes weeks or months to seem, but may appear within 12 hours of ingestion of a sensitized individual. Platelet counts typically fall to 80% of normal and thrombocytopenia may be associated with neutropenia and anemia. Rashes have been observed, including rare cases of erythema multiforme and rare cases of hair loss and vasculitis. In September 2019, the US Food and Drug Administration (FDA) discovered that some ranitidine drugs, including some products sold under the Zantac brand, contained a nitrosamine impurity called N-nitroso dimethylamine (NDMA), classified as a probable human carcinogen with low levels. Health Canada announced that it was evaluating NDMA in ranitidine and requested manufacturers to stop distributing ranitidine products in Canada until NDMA levels in products were found to be safe. Health Canada announced that ranitidine drugs were being recovered by Sandoz Canada, Apotex Inc., Pro Doc Limitée, Sanis Health Inc. and Sivem Pharmaceuticals ULC. The European Medicines Agency (EMA) has initiated an EU-wide review of the drugs. ranitidine at the request of the European Commission. In September 2019, Sandoz issued a "precautionary arrest in distribution" of all ranitidine-containing medicines. days later after a recall of ranitidine hydrochloride capsules in the United States. The Italian Medicines Agency.[6]

AIFA, reminded all ranitidine that uses an active pharmaceutical ingredient (API) from Saraca Laboratories. The German Pharmacists Committee (AMK) has published a list of withdrawn products. The Therapeutic Products Administration (TGA) in Australia has published a list of withdrawn products. In September 2019, Apotex withdrew all over-the- counter ranitidine (OTC) tablets sold in the United States from Walmart, Rite Aid, and Walgreens. Walmart, Rite Aid, Walgreens, and CVS later removed Zantac and some generics from their shelves.[9]

In October 2019, the US Food and Drug Administration (FDA) noted that a third-party lab used higher temperatures in its tests to look for nitrosamine impurities. NDMA was generated by the heat added, but higher temperatures were recommended for the use of a gas chromatography - mass spectrometry (GC/MS) method to test NDMA on valsartan and angiotensin II receptor blockers (ARBs). The FDA has stated that it recommends the use of a mass spectrometry high performance liquid chromatography (LC-HRMS Chromatography-High Resolution -Liquid Mass Spectrometry) test protocol to test ranitidine samples. Its LC-HRMS test method doesn't use elevated temperatures and showed much lower levels of NDMA in ranitidine drugs than those reported by the third-party laboratory. International regulators using similar LC-MS testing methods have also shown the presence of low NDMA levels in ranitidine samples. The FDA has provided additional guidance on the use of another mass spectrometric liquid chromatography (LC-MS) method based on a triple quadrupole MS platform.[7]

In October 2019, Sanofi replaced all over-the- counter Zantac in the United States and Canada, Perrigo issued a worldwide ranitidine recall, Dr. Reddy issued a recall of all ranitidine products within the us, and Novitium Pharma. replaced all ranitidine hydrochloride capsules in the United States.[10]

In November 2019, the FDA stated that its tests found

NDMA levels in ranitidine and nizatidine similar to the levels you would expect to be exposed to if you eat ordinary foods such as grilled or smoked meats. They also stated that their simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) tests indicate that NDMA is not formed when exposed to stomach acid with a normal diet. The FDA has advised companies to recover their ranitidine if the test shows NDMA levels above the acceptable daily intake (96 nanograms per day or 0.32 parts per million ranitidine). At the same time, they indicated that some levels of NDMA found in the drugs still exceed what the FDA considers acceptable for these drugs.

In November 2019 Aurobindo Pharma, Amneal Pharmaceuticals, American Health Packaging, Golden State Medical Supply and Precision Dose recalled several batches of ranitidine tablets, capsules and syrup.[11]

In December 2019, the FDA asked ranitidine and nizatidine product manufacturers to expand their NDMA trials to include all drug batches before making them available to consumers. In December 2019 Glenmark Pharmaceutical Inc., USA, withdrew some batches of ranitidine tablets.

In January 2020, Appco Pharma LLC and Northwind Pharmaceuticals withdrew a few batches of ranitidine tablets and capsules.

Ranitidine is a competitive and reversible inhibitor of histamine action on H2 receptors found in gastric parietal cells. This results in decreased gastric acid secretion and gastric volume and reduced concentration of hydrogen ions.

Absorption: Oral: 50%
Protein Binding: 15%

Metabolism: N-oxide is the main metabolite. Elimination of half-life: With normal renal function, ranitidine administered orally has a half-life of 2.5 to 3.0 hours. If taken intravenously, the half-life is usually 2.0 to 2.5 hours in a patient with normal creatinine clearance.

In addition, it about 30% of the oral dose is collected in the urine as an unabsorbed drug within 24 hours. In the elderly population, plasma half-life of ranitidine is prolonged to 3-4 hours, secondary to decreased renal function, causing decreased clearance.[11,10]

Colorectal cancer

Colorectal cancer (CRC), also referred to as bowel cancer, carcinoma or rectal cancer, is that the development of colon or rectal cancer (parts of the massive intestine). invade or spread to other parts of the body. Signs and symptoms may include blood in the stool, changes in bowel movements, weight loss, and feeling tired all the time. Most colorectal cancers are thanks to adulthood and lifestyle factors, with only alittle number of cases thanks to underlying genetic disorders. Other risk factors include diet, obesity, smoking, and lack of physical activity. Dietary factors that increase risk include red meat, processed meat and alcohol. Another risk factor is inflammatory bowel disease, which incorporates regional enteritis and colitis. Some of the inherited genetic disorders which will cause colorectal cancer include familial adenomatous polyposis and hereditary nonpolyposis carcinoma; however, these account for fewer than 5% of cases. It usually begins as a benign tumor, usually in the form of a polyp, which eventually becomes cancerous. Bowel cancer can be diagnosed by obtaining a colon sample during a sigmoidoscopy or colonoscopy. This is followed by medical imaging to work out if the disease has spread. Screening is effective in preventing and decreasing colorectal cancer deaths. Screening by one of several methods is recommended from 50 to 75 years of age. During colonoscopy, small polyps could also be removed if found. If a large polyp or tumor is found, a biopsy may be performed to see if it is cancerous. Aspirin and other non-steroidal anti-inflammatory drugs lower the risk. Its general use is not recommended for this purpose, however, due to side effects.[12]

Most carcinoma originates from noncancerous, or benign, tumors called adenomatous polyps that form on the inner walls of the huge intestine. Cancerous cells may spread from malignant tumors to other parts of the body through the blood and lymph systems.[13] Colorectal cancer, also referred to as bowel cancer, colon cancer, or rectal cancer, is any cancer that affects the colon and therefore the rectum. The American Cancer Society estimate that about 1 in 21 men and 1 in 23 women within the us will develop colorectal cancer during their lifetime.

Each year nearly 137,000 people are diagnosed with colorectal cancer, often referred to as colon cancer,[12] in the U.S. and over 50,000 people die from it annually. The disease, however, is essentially preventable with regular screening and is treatable with early detection. Treatments used for colorectal cancer may include some combination of surgery, radiotherapy, chemotherapy, and targeted therapy.[14] Colon wall-confined cancers could even be curable with surgery, while cancer that has spread widely is generally not curable, with targeted treatment to improve quality of life and Excretion: The main route of excretion is urine. symptoms. The five-year survival rate in the United States is about 65%. The individual probability of survival depends on how advanced the cancer is, whether or not all cancer can be removed with surgery and the person's overall health. Globally, colorectal cancer is the third most common cancer, accounting for about 10% of all cases.[15]

The signs and symptoms of colorectal cancer depend on the location of the tumor in the intestine and whether it has spread to other parts of the body (metastasis). Classic

warning signs include: worsening constipation, bloody stools, decreased stool (thickness), loss of appetite, weight loss and nausea or vomiting in someone over 50 years of age. About 50% of individuals with colorectal cancer report no symptoms. Rectal bleeding or anemia are high risk symptoms in people over 50 years. Weight loss and changes in a person's bowel habits are usually of concern only if they are associated with rectal bleeding.[14] Over 75–95% of colorectal cancer occurs in people with little or no genetic risk. Risk factors include old age, male gender, high fat intake, sugar, alcohol, red meat, processed meat, obesity, smoking, and lack of exercise. Approximately 10% of cases are related to insufficient activity. The risk of alcohol seems to increase with more than one drink a day. Drinking 5 glasses of water a day is associated with a decreased risk of colorectal cancer and adenomatous polyps. Streptococcus gallolyticus is associated with colorectal cancer. Some Streptococcus bovis / Streptococcus equinus complex strains are consumed by millions of people daily and therefore can be safe. 25 to 80% of individuals with Streptococcus bovis / gallolyticus bacteremia have concomitant colorectal tumors. Seroprevalence of Streptococcus bovis / gallolyticus is considered a candidate marker for early prediction of an underlying bowel injury in a high-risk population. It has been suggested that the presence of antibodies against Streptococcus bovis / gallolyticus antigens or the antigens themselves within the bloodstream may act as markers of colon carcinogenesis.[16]

People with inflammatory bowel disease (ulcerative colitis and Crohn's disease) have a higher risk of colon cancer. The risk increases the longer a person has the disease and the worse the severity of inflammation.[17] In these high-risk groups, prevention with regular colonoscopies is recommended. Endoscopic surveillance in this high-risk population may reduce the development of colorectal cancer through early diagnosis and may also reduce the chances of death from colon cancer. People with inflammatory bowel disease account for less than 2% of colon cancer cases annually. In people with Crohn's disease, 2% have colorectal cancer after 10 years, 8% after 20 years, and 18% after 30 years. In people who have ulcerative colitis, approximately 16% develop a cancer precursor or colon cancer over 30 years.

N-nitroso dimethylamine

N-nitroso dimethylamine may be a volatile, combustible, yellow and oily liquid nitrosamine with a characteristic slight odour that decomposes on exposure to light and emits toxic oxide smoke when heated to decomposition. N-nitroso dimethylamine is mainly used in laboratory research to induce tumours in experimental animals. This substance can be formed while cooking foods, especially cured meats and fish, which contain sodium nitrite as a preservative, but is also found in many vegetables, cheeses, alcoholic beverages and fruits, and as a contaminant in rubber products. Exposure to N-Nitroso dimethylamine irritates the skin and eyes and damages the liver. This substance is reasonably expected to be human carcinogenic.

NDMA is assessed as a probable human carcinogen (a substance that might cause cancer) supported results from laboratory tests. NDMA could also be a known environmental contaminant and located in water and foods, including meats, dairy products, and vegetables.[18]

The health effects of overexposure to NDMA include jaundice, nausea, fever, vomiting, abdominal cramps and dizziness. High levels of exposure can cause reduced function of the kidneys and lungs.

Ranitidine is contraindicated for patients known to possess hypersensitivity to the drug.

Unless directed by your doctor, you should not take OTC Zantac for extended than fortnight. If you're taking Zantac for stomach ulcers, it'd take up to eight weeks before an ulcer heals. You should keep using the medication as your doctor prescribes and tell your doctor if your symptoms don't improve after six weeks. They lower the quantity of acid in your stomach, but studies have shown that taking them for an extended time can raise your chances of great kidney problems and possibly lead to kidney failure. Other heartburn medicines called H2 blockers (Pepcid, Tagamet, Zantac) are less likely to cause these issues.

The primary sources of human exposure to NDMA are tobacco smoke, chewing tobacco, diet [cured meats (particularly bacon), beer, fish, cheese, and other food items], toiletry and cosmetic products (for example, shampoos and cleansers), interior air of cars, and various other household goods, like detergents. N-nitroso dimethylamine causes liver cancer, whereas some of tobacco specific nitrosamines causes lung cancer. Volatile N-nitrosamines induce tumours in a variety of human organs, including the tongue, oesophagus, lung, pancreas, liver, kidney and bladder. NDMA is assessed as a probable human carcinogen (a substance that would cause cancer) supported results from laboratory tests. NDMA may be a known environmental contaminant and located in water and foods, including meats, dairy products, and vegetables. NDMA isn't currently produced in pure form or commercially utilized in the us, apart from research purposes. It was formerly utilized in production of liquid rocket propellant, antioxidants, additives for lubricants and softeners for copolymers. NDMA is assessed as a probable human carcinogen (a substance that would cause cancer) supported results from laboratory tests. NDMA may be a known environmental contaminant and located in water and foods, including meats, dairy products, and vegetables. Some Heartburn Drugs May Increase Heart Attack Risk The results also found that folks who were taking H2 receptor blockers — another sort of prescription medication used for acid reflux, like Zantac, Tagamet

and Pepcid — did not face an increased risk for heart attack.

Prevalence studies

Number (proportion) of people with the disease at a particular point in time Under certain assumptions: P/(1-P) =ID POR=I 1 D 1/I 0 D 0. Therefore, differences in prevalence may be due to differences in incidence, differences in duration, or both.[19]

Prevalence gives a figure for an element (disease, injury, health status etc) at one point in time (point prevalence) or period of time (period prevalence). Period prevalence provides the higher measure of the factor since it includes all cases between two dates, whereas point prevalence only counts cases on a specific date. It is a measure of disease that permits us to work out an individual's likelihood of getting a disease. It is most meaningfully reported because the number of cases as a fraction of the entire population in danger and may be further categorised consistent with different subsets of the population.[20]

Prevalence may be a statistical concept pertaining to the amount of cases of a disease that are present during a particular population at a given time, whereas incidence refers to the number of new cases that develop in a given period of time.[21]

Point prevalence usually refers to the quantity of individuals who have a specific disease at a particular point in time. It's determined by taking the total of the people with the disease over the total of people in the population.[23]

Prevalence may be a measure of disease that permits us to work out an individual's likelihood of getting a disease. Therefore, the number of prevalent cases is the total number of cases of disease existing in a population.[24] There are two types of prevalence.

Point prevalence Period prevalence Point prevalence is that the number of persons with disease during an interval (e.g., one year) divided by number of persons within the population; that’s, prevalence at the start of an interval plus any incident cases.

Period prevalence is that the proportion of a population that has the condition at a while during a given period (e.g., 12-month prevalence), and includes people that have already got the condition at the start of the study period as well as those who acquire it during that period.[26]

The distinction between point prevalence and period prevalence is usually not made because most prevalence estimates that you simply will encounter within the medical literature are point prevalence.[27]

Incidence

Incidence is that the number of instances of an element (disease, injury, health status etc) during a given period (day, month, year, decade) during a specified population (age group, community, country etc). Incidence can tell us how many cases of a particular factor have been suffered by a specified population in a given period of time. It is a measure of disease that allows us to determine a person's probability of being diagnosed with a disease during a given period of time or it might tell us how patterns of a condition within a population change over time. Incidence is usually expressed as a rate, something that is measured within a set number of people and in a time period.[28]

Incidence versus Prevalence

Incidence is often confused with prevalence. The easy way to remember the difference is that prevalence is the proportion of cases in the population at a given time rather than rate of occurrence of new cases. Thus, incidence conveys information about the danger of contracting the disease, whereas prevalence indicates how widespread the disease is.

Prevalence refers to proportion of persons who have a condition at or during a specific period of time, whereas incidence refers to the proportion or rate of persons who develop a condition during a particular time period.[29,30]

CONCLUSION

Colorectal cancer (CRC), additionally illustrious as bowel cancer and colon cancer, is that the development of cancer from the colon or rectum (parts of the large intestine). Ranitidine belongs to a bunch of medicine referred to as histamine-2 blockers.

The relation between use of histamine-2- receptor (H2-receptor) antagonists and colorectal cancer risk was investigated in an exceedingly case-control study. The incidence of gastric cancer was raised for the primary few years once the beginning of treatment with H2- receptor antagonists, this could replicate misdiagnosis of some early gastric cancers. The findings measure against long persistence of an excess risk of gastric cancer in association with use of H2-receptor antagonists.

FDA has advised companies to recall their ranitidine if testing shows levels of NDMA above the suitable daily intake (96 nanograms per day or 0.32 parts per million for ranitidine).

Patients taking prescription ranitidine who wish to prevent should ask their health care professional about other treatment options. Multiple drugs are approved for an equivalent or similar use as ranitidine.

In this review article, Includes the some of the article wised study review on prevalence of colorectal cancer with ranitidine. The presence of NDMA in ranitidine brands may cause colorectal cancer.

Drug Administration (FDA). 28 October 2019. Archived from the original on 29 October 2019. Retrieved 28 October 2019. FDA observed the testing method used by a third-party laboratory uses higher temperatures. The higher temperatures generated very high levels of NDMA from ranitidine products because of the test procedure. FDA published the method for testing angiotensin II receptor blockers (ARBs) for nitrosamine impurities. That method is not suitable for testing ranitidine because heating the sample generates NDMA.FDA recommends using an LC-HRMS testing protocol to test samples of ranitidine. FDA's LC-HRMS testing method does not use elevated temperatures and has shown the presence of much lower levels of NDMA in ranitidine medicines than reported by the third- party laboratory. International regulators using similar LC-MS testing methods have also shown the presence of low levels of NDMA in ranitidine samples. This article incorporates text from this source, which is in the public domain.

This is the first cross- country study in North America to describe the presentation and incidence of restrictive eating disorders among children. Cases were identified through the Canadian Paediatric Surveillance system. The eating disturbances seen in young children can result in serious medical consequences, which can occur in the absence of weight loss or other restrictive eating disorder symptoms.

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