Hormonal Regulation in Peptic Ulcer Disease: A Comprehensive Review

Bharath K M Pharm, Pradeep VN M pharm, Madhumathi K M pharm, Alameen S M. Pharm, Maalavika S M pharm, Arvind S M.pharm, Dr.Sengottuvelu S M.pharm.,Ph.D, K.Gladys Kalpana M Pharm,Dr.T. Sivakumar M.pharm.,Ph.D.

1st Author: Department of Pharmacology, Nandha College of Pharmacy, The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu.

2nd Author: Department of Pharmaceutics, Vellalar College of pharmacy, The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu.

3rd, 4th, 5th, 6th, 7th, 8th, Author: Department of Pharmacology, Nandha College of Pharmacy, The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu.

9th Author: Department of Pharmaceutical Chemistry, Nandha College of Pharmacy, The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu.

*Corresponding author:

Mr. Bharath K, M Pharm.

Department of Pharmacology,

Nandha College of Pharmacy,

The Tamil Nadu Dr. M.G.R. Medical University,

Chennai, Tamil Nadu.

Abstract:

Peptic ulcers are localized erosions in the gastric or duodenal mucosa caused by an imbalance between mucosal defense mechanisms and aggressive factors, such as gastric acid and pepsin. Hormones play a pivotal role in regulating gastric physiology, including acid secretion, mucosal protection, and motility, all of which influence the pathogenesis of peptic ulcers. Gastrin, secreted by G cells, stimulates acid secretion and promotes mucosal proliferation but may contribute to hyperacidity in Zollinger-Ellison syndrome and other hypergastrinemic states. Conversely, somatostatin, produced by D cells, inhibits gastrin release and acid secretion, serving as a protective mechanism against ulcer formation.

Histamine, released by enterochromaffin-like (ECL) cells, is another key mediator, acting on H2 receptors to potentiate acid secretion. Glucocorticoids, while important for stress response, impair mucosal repair and defense, increasing the risk of ulcers, particularly in chronic stress conditions. Prostaglandins, derived from arachidonic acid, enhance mucosal defense by stimulating mucus and bicarbonate secretion and maintaining mucosal blood flow; their inhibition by nonsteroidal anti-inflammatory drugs (NSAIDs) is a common ulcerogenic mechanism. Additionally, ghrelin, leptin, and motilin modulate gastric motility and repair processes, indirectly influencing ulcerogenesis.

Emerging evidence highlights the role of neuroendocrine hormones, such as corticotropin-releasing factor (CRF), in stress-related ulcer development. Understanding the interplay of these hormones provides insight into the pathophysiology of peptic ulcers and offers avenues for targeted therapeutic strategies, such as hormone modulation, to enhance mucosal protection and reduce disease burden.

Keyword: Peptic ulcer, Hormones, Gastrin, Histamin, Helicobacter pylori, Zollinger-Ellison syndrome

Introduction:

The condition known as "peptic ulcer" refers to acid reflux illness, which harms the digestive system and results in a mucosal breach that extends to the submucosa. Peptic ulcers usually develop in the stomach or proximal duodenum, although they can also arise in the esophagus or Meckel's diverticulum. In this lecture, peptic ulcer disease is used to describe peptic ulcers in the stomach or duodenum.
The majority of peptic ulcer diseases were thought to be brought on by stress, dietary factors, or a hypersecretory acidic environment before the discovery of Helicobacter pylori infection and the widespread use of non-steroidal anti-inflammatory drugs (NSAIDs) in the second half of the 20th century. [1–3]

Epidemiology:

With an annual incidence of 0.1–0.3%, the lifetime prevalence of peptic ulcer disease in the general population is estimated to be between 5 and 10%. However, given that

epidemiological studies have shown a notable decrease in the condition's incidence, hospitalization rates, and mortality over the past 20 to 30 years, the prevalence and incidence of peptic ulcer disease are probably lower than these global estimates, especially in high-income countries. These decreasing numbers might be the consequence of new therapies or a cohort trend that cannot be fully explained by known causes (e.g., NSAID use and H pylori infection).

The prevalence of many gastrointestinal illnesses varies, suggesting that peptic ulcer disease may have an underlying birth-cohort pattern.

All ulcer types (H pylori-associated, NSAID-associated, and idiopathic) have seen a decrease, and the overall pattern is consistent with the population's lowering prevalence of H pylori infection, with a birth-cohort effect also evident in areas with low infection rates. These results demonstrate the important part that H pylori infection plays in the onset of peptic ulcer disease as well as its observed temporal variations.

From 1921 through 2004, the risk of death from stomach ulcers was 10–30 years higher than that from duodenal ulcers in a number of European countries with different healthcare systems and socioeconomic circumstances. There has been a documented decline in gastric and duodenal ulcer mortality in Central America, South America, and Asia, with a birth-cohort effect similar to that in Europe, where high rates were observed in late 19th-century individuals, and a 10–20 year postponed peak mortality for duodenal ulcer patients.

Over the past 20 years, peptic ulcer disease has steadily declined throughout Asia among a number of ethnic groups, including Malay, Chinese, and Indian people. This decrease was accompanied by a decrease in H pylori-associated peptic ulcer disease. Additional research has shown a decline in hospital admissions for peptic ulcer disease complications in the 21st century, with an incidence of 79 cases per 100,000 individuals annually and fewer than 30 cases of complications from peptic ulcer disease per 100,000 individuals annually. However, the introduction of anti-secretary drugs and increased use of NSAIDs do not seem to explain the ulcer-related mortality trends observed by Sonnenberg. The decrease in complications from peptic ulcer disease could be linked to the global prevalence of antisecretory medications and a more judicious use of NSAIDs compared to earlier practices. [8,9,10]

Various Hormones in Peptic Ulcer:

Gastrin:

Gastrin is a peptide hormone produced by G(gastrin)-Cells in the antroduodenal lining. Gastrin is a powerful enhancer of gastric acid secretion and also has trophic effects on the parietal, chief, and enterochromaffin-like (ECL) cells located in the oxyntic mucosa. The primary physiological trigger for gastrin secretion is food ingestion, while gastric acid generated by parietal cells in the oxyntic mucosa serves as the key inhibitor of antral gastrin secretion (Walsh & Lam 1980).

Therefore, the stimulating effect of gastrin on acid production and the suppressive influence of acid on gastrin release indicate a feedback loop between gastrin and gastric acid secretion.

It has been proposed that this feedback mechanism is facilitated by the stimulation of acid on the inhibitory paracrine effect of somatostatin regarding the antral G-cell. [16,17]

Hypergastrinaemic Peptic Ulcer Disease:

There are three comparatively uncommon disorders that result in peptic ulcer due to hypergastrinaemic hyperchlorhydria: Zollinger-Ellison syndrome (gastrinoma), hyperfunction of antral G-cells, and retained antrum after gastrectomy with a Billroth II anastomosis. The Zollinger-Ellison syndrome is defined by the excessive secretion of gastrin from malignant endocrine tumors (gastrinomas) primarily situated in the pancreas. Antral G-cell hyperfunction is defined by an excessive gastrin secretion from the antrum after eating, even with gastric acid hypersecretion occurring.

This condition may or may not occur alongside antral G-cell hyperplasia. Excluded retained antrum occurs due to gastric surgery, during which isolated antral tissue remains at the duodenal stump. In the excluded antrum, the secretion of gastrin is not suppressed by acid, leading to hypergastrinaemia and excessive gastric acid production in the gastric remnant. The three disorders linked to hypergastrinaemic hyperchlorhydria can be distinguished from one another through provocation tests using secretin and food.

Bolus injections of secretin promote gastrin release from tumors but do not affect antral tissue, while feeding significantly enhances gastrin secretion in cases of antral G-cell hyperfunction, unlike in Zollinger-Ellison syndrome or the excluded retained antrum post-gastrectomy. [18,19]

Normolgastrinaemic Peptic Ulcer Disease:

Since approximately half of all patients with duodenal ulcers have elevated stomach acid secretion, a decrease in these levels would be expected even though regular duodenal ulcer disease does not result in reduced basal serum gastrin levels. A disturbed feedback mechanism between the generation of antral gastrin and stomach acid is shown by the absence of decreased baseline serum gastrin levels and increased gastric acid output.

The finding that patients with duodenal ulcers have increased gastrin secretion after meal provides more evidence of this feedback system's malfunction. Even when duodenal ulcer disease patients are divided into groups with normal and high stomach acid secretion, this peculiar self-regulation of gastrin secretion in response to meals is still visible. This means that people who produce normal amounts of stomach acid have a higher serum gastrin response after eating, while people who secrete too much gastric acid have post-meal serum gastrin levels that are within normal ranges. The finding that people with duodenal ulcers show less reduction of postprandial gastrin secretion after meal acidification than healthy persons suggests a malfunction in the feedback mechanism between gastric acid and postprandial gastrin release. Although the precise mechanism underlying the aberrant autoregulation of gastrin secretion in duodenal ulcer disease is still unknown, reported decreases in somatostatin levels and an elevated gastrin/somatostatin ratio in the antral

mucosa have suggested that impaired suppression of gastrin secretion by antral somatostatin may be the cause.

However, a number of further research have not been able to confirm these findings. Since gastric acid output in patients with duodenal ulcer disease is more reactive to both internal and external gastrin, the raised serum gastrin levels after meals may have a pathogenic function. The increased parietal cell mass in duodenal ulcer patients is probably the cause of this.

Prospective studies with patients genetically predisposed to duodenal ulcers are necessary to investigate whether the increased parietal cell mass is due to the trophic effects of gastrin on the oxyntic mucosa. Because they produce less stomach acid, people with gastric ulcers have normal or slightly elevated serum gastrin levels.

Secretin:

Secretin's main job is to cause the pancreas to produce bicarbonate. It is released from the duodenum and jejunum in response to acid in the proximal gut lumen (pH threshold 4.0). However, secretin also slows down gastric emptying, suppresses the generation of stomach acid, and decreases the serum gastrin response to protein-rich meals. These effects of secretin are seen in both humans and laboratory animals; however, no research has compared the effects of secretin in healthy individuals with those who have duodenal ulcers, and the pattern and dose-response relationships in humans remain unclear. Since the contents of the jejunum and duodenum are never acidified, endogenous secretin is probably not secreted.

This allowed for the evaluation of the effects of specific external secretin dosages on stomach emptying, food-induced acid secretion, and serum gastrin levels. Secretin was administered intravenously at fixed rates of 0, 0.25, 0.5, 1.5, and 3.0 µg per kg per hour. Results from healthy individuals and those with duodenal ulcers were analyzed and compared. [21,22,23,24,25]

Histamine:

It might be pushing the boundaries to classify histamine among gastrointestinal hormones or humoral agents, since it is widely recognized that this substance is distributed throughout the body just like the mast cells from which it is thought to originate.

Nonetheless, the strong influence histamine exerts on gastric acid secretion and its relatively high concentration in the intestine hopefully justify its inclusion in this discussion. Among the different methods for inducing peptic ulceration in experimental animals, histamine injections in beeswax, as detailed by G.F. Code and R.L. Vareo, have proved to be one of the most reliable and efficient. In humans, histamine may also contribute to the development of peptic ulcers, especially in those with portal hypertension.

It is commonly acknowledged that in instances of liver cirrhosis, the prevalence of peptic ulcers can reach as high as 25%. Bleeding after a properly executed portacaval shunt may result from a gastric or duodenal ulcer just as much as from ongoing varices. The reasons for the heightened vulnerability to gastric and duodenal ulcers in cirrhotic patients, whether they

have portacaval shunts or not, are thought to be linked to certain intestinal secretagogues that are either not metabolized by the liver or are circumventing that organ. Eiseman's experiments suggest that histamine is probably the secretogogue.[16-20]

Insulin:

The gastric secretory reaction to hypoglycemia after insulin administration is biphasic in nature. The initial reaction that occurs within 30 to 45 minutes post-insulin injection relies on intact vagal innervations to the stomach and is probably caused by direct vagal influence on the parietal cell, along with gastrin release induced by the vagus.

The second phase, occurring several hours post-insulin administration, is believed to result from the stimulation of gastric secretion via the pituitary-adrenal axis. Recent studies by Sircus et al. have critically and thoroughly examined the second phase of gastric secretion. The findings from the Edinburgh group cast doubt on insulin's capability to affect gastric secretion through the pituitary and adrenal glands.

A more plausible explanation seems to be that the second phase is facilitated by the antrum, as antrectomy eliminates it. This connection highlights the respective impacts of direct vagal influence on parietal cells and indirect vagal effects on gastrin secretion from the antrum. According to Sircus and colleagues, the immediate effect on the vagus lasted between 2 to 2.5 hours, while the indirect effect was noticeable for 5 to 6 hours.

In humans, the occurrence of insulin-secreting tumors in the pancreas along with peptic ulcers is rare. Reports of cases have been made by H. O. Janowitz and B. B. Crohn, K. H. MacGregor, and B. Pender. In Pender's case report, a hereditary factor seemed evident as both a father and daughter had pancreatic tumors that produced insulin.

Serotonin:

Clinical observations have indicated a connection between serotonin (5-hydroxytryptamine) and peptic ulceration, as evidenced by the high incidence of peptic ulcers (38%) found in patients with metastatic carcinoid tumors. Establishing a possible causal relationship based on serotonin's effect on gastric secretion is challenging.

In dogs, serotonin seems to suppress gastric secretion, while in humans, it functions by reducing gastric acid production. A recent study by Campbell and colleagues on a carcinoid tumor leading to multiple peptic ulcers and elevated gastric acid secretion is especially noteworthy, as the tumor was discovered to have 5-hydroxytryptophan instead of 5-hydroxytryptamine. Moreover, the tumor had significant amounts of histamine.

It is uncertain if 5-hydroxytryptophan acts as a stimulant for gastric acid secretion, but histamine may indeed explain the frequent occurrence of ulcers in patients with metastatic carcinoid tumors. Few, if any, histamine tests have been conducted in these patients—an oversight that may soon be addressed.[17,18]

Chalones:

This term describes gastrointestinal tract-produced hormones that have the ability to suppress gastric secretion. Enterogasterone was the first chalone found, and it was probably released because of the fat in the upper jejunum and duodenum.

Enterogasterone's exact mode of action is still unknown, but according to Gregory 12, it suppresses the antral phase of gastric secretion physiologically, most likely by preventing the antrum from releasing gastrin. The possibility that an inhibitory hormone could emerge from the stomach antrum in the event of severe acidity of the antral contents has received a lot of attention lately. This significant reaction to inhibition has been extensively studied, with the findings for or against the existence of such a chalone being hotly contested. Dragstedt and his colleagues think that the inhibition of antral acid is caused by disruption in the synthesis or secretion of gastrin, whereas Duval and Thompson believe that acid exposure to the antral mucosa leads to the creation of an inhibitory hormone.

This discussion holds significance beyond academic curiosity, as the isolation and purification of such a chalone could potentially yield a powerful antiulcer treatment agent. [18,19]

Thyrotropin-Releasing Hormone:

Studies in physiology and pathophysiology have shown that the gastrointestinal and central nervous systems interact significantly. The physiological regulation of gastric secretory and motor processes has been shown to be considerably influenced by the vagus nerve and different neuropeptides. Acute gastric mucosal lesions are also known to result from severe head trauma and neurosurgical procedures.

However, none of the many studies that tried to connect these stress-related changes in the central nervous system to effects on the stomach were able to identify a common mediator or pathway. Experiments have successfully connected the formation of stomach ulcers to the stimulation and destruction of different hypothalamic regions, suggesting a major role for hypothalamic mediation. The ways in which the hypothalamus might contribute to the development of stress ulcers are primarily unclear. Multiple recent studies have demonstrated that hypothalamic peptides have various important impacts on the gastrointestinal system. Specifically, thyrotropin-releasing hormone (TRH), which has undergone the most thorough investigation, has been noted to promote gastric acid secretion when given intracerebroventricularly in rats.

Indirect evidence indicates that stress enhances the release of TRH and corticotrophin-releasing factor (CRF), yet it remains unclear if these peptides play a role in the development of stress ulcers. [26-30]

Adrenal gland:

An increase in gastric acid and pepsin secretion during adrenal stimulation has demonstrated a link between the stomach and the adrenal gland. By causing or reactivating peptic ulcers when ACTH or adrenal steroids are administered, the adrenal gland has been linked to the development of peptic ulcer disease.

On the other hand, those with Addison's disease, or adrenal insufficiency, usually exhibit a decrease in stomach acidity as well as an unusually low incidence of chronic peptic ulcers. Regardless of neurogenic transmission, it has been proposed that emotional stress and other distress signals may cause both acute and chronic peptic ulcers in humans by traveling through the hypothalamus, pituitary, and adrenal glands to the stomach.

According to contemporary views put out by Selye and Ingle, the link between the stomach and the adrenal glands might be seen as a "permissive" conditioned phenomenon. With regard to the adrenal cortex, the stomach typically functions in a semi-autonomous manner, relying on appropriate adrenocortical function for acid-peptic activity. Adrenocortical activity more closely regulates the stomach in stressful conditions.

Through decreased peptic activity in patients with adrenal insufficiency and increased gastric secretion in patients with pituitary and adrenal overactivity (Cushing's disease), this paper will demonstrate the similarities between gastric and adrenal activities. This presentation emphasizes the role of the adrenal gland in peptic ulcer disease, pointing out that individuals with Addison's disease receiving glucocorticoid replacement medication may develop gastric or duodenal ulcers in addition to increased gastric output.

Chronic peptic ulcers are uncommon in people with Addison's illness, according to several experts. Maranon claims three clinical cases of peptic ulcers among 160 individuals, but he found no peptic ulcers in 25 postmortem examinations of Addisonian patients.

Only 24 of the 120 patients in Jarvis et al.'s research of Addison's illness had roentgenologic examinations because of digestive problems. Two patients, both of whom had a history of ulcers prior to the beginning of adrenal insufficiency, showed duodenal bulb deformity without a visible crater. The rarity of chronic peptic ulcers in Addison's disease seems to be linked to a reduced production of hydrochloric acid. Grawitz was the first to observe achylia in this illness, a finding that has been consistently validated by numerous researchers. Rowntree and Snell noted achlorhydria in 53% of the patients examined, with a significant decrease in free acid in nearly all other cases except for two.

Several studies have recently reported that approximately 50% of people with Addison's illness had achlorhydria, namely Soffer in 1948 and Sorkin in 1949. Feyrter and Klima found that their group of Addison's illness patients, the majority of whom had histamine anacidity, had a similar drop in free acid. In more than half of the instances, Maranon saw a decrease or inhibition of hydrochloric acid secretion.

A instance of untreated Addison's illness with a markedly diminished acid response following histamine stimulation was recently described by Stempien. Additional evidence of the adrenal

cortex's critical role in controlling appropriate gastric secretory activity comes from investigations conducted on animals. Rats who had bilateral adrenalectomy showed a considerable decrease in stomach output, but rats that had only the adrenal medulla removed showed no change, according to Tuerkischer and Wertheimer.

The decrease in secretion could return to normal through the use of adrenocortical extract, but not with desoxycorticosterone acetate or regular saline. Madden and Ramsburg showed that adrenalectomy led to a decrease in gastric secretion volume in rats with pylorus ligation. The administration of saline and desoxycorticosterone acetate partially recovered the volume of gastric secretion. Recently, Welbourn and Code reported that adrenalectomy in pylorus-ligated rats led to a notable reduction in acid secretion, which returned to normal levels with cortisone administration.

Likewise, Haroutunian and Segal observed a decrease in gastric volume in adrenalectomized Shay rats, which exhibited protection against ulcer formation in these test subjects. Porter et al. discovered that the delayed acid response elicited by electrical stimulation of the posterior hypothalamus in monkeys could be eliminated by performing a bilateral adrenalectomy. The histologic analysis of most stomachs in patients with Addison's disease experiencing achylia showed atrophy, interstitial inflammation, and substitution of fundic glandular cells with mucoid cells, nearly leading to the total loss of parietal cells.

In rats that underwent adrenalectomy, Baker and Bridgman observed a decrease in the size of the cellular components lining the gastric tubules and pits over a span of three weeks, with the mucoid chief cells and zymogenic cells exhibiting the greatest reduction. In the studies to be detailed, urinary pepsinogen excretion (uropepsin) served as a quantitative measure of gastric secretory function.

Earlier research suggests that it reliably indicates gastric pepsin output and constitutes a stable percentage of total pepsinogen production by the peptic chief cells, roughly 1%. [6-10]

Estrogen:

Estrogen has been demonstrated to avert peptic ulcers in animals, yet the underlying mechanisms are still not well understood. Recently, we noted that basal and acid-stimulated DBS levels were greater in young female mice compared to age-matched males; the use of estrogen receptor (ER) antagonists in mice completely eliminated acid-stimulated DBS; estradiol increased DBS in a dose-dependent manner in vitro and in vivo in mice; and both ER and ER were present in the duodenal epithelium of male and female mice.

Since DBS is crucial for safeguarding the duodenum from acid-related damage, variations in DBS linked to sex might account for the reduced incidence of duodenal ulcers in women. Consequently, we investigated whether human DBS is influenced by estrogen and if this regulatory mechanism correlates with a reduced occurrence of duodenal ulcers in premenopausal women. Our results support the innovative idea that estrogen influences human DBS, potentially explaining the sex differences seen in the incidence of duodenal ulcers.[31]

Somatostatin:

In patients with duodenal ulcers, GH-RIH significantly suppresses both the basal and meal-stimulated gastric responses by reducing the acid and pepsin response to pentagastrin in a dose-dependent manner. As far as we are aware, no human studies have been done to examine how GH-RIH affects the stomach stimulation brought on by food. We found that GH-RIH was highly effective at inhibiting both basal and meal-triggered gastric secretion. This inhibitory effect was linked to a significant decrease in serum levels of insulin, HGH, and gastrin. [11,12]

It's common knowledge that eating increases the production of acid by directly influencing the parietal cells and by causing the mucosal lining of the colon and antrum to produce hormones. The barostat approach was used in both the control and GH-RIH infusion trials to maintain the stomach's distention pressure at constant levels and to maintain the gastric pH at 5.5 regardless of the acid secretion rate.

Given that variations in gastric pH and distention are known to affect gastric output, this is an important consideration. GH-RIH significantly decreased the serum gastrin response following a meal in these experimental settings with stable pH and distention, indicating that a reduction in gastrin release represents a partial mechanism for inhibiting acid secretion triggered by meals. Serum gastrin levels and acid outputs in response to a meal have been found to positively correlate both before and during GH-RIH infusion.

However, the same amount of GH-RIH had similar effects on the stomach acid production triggered by equipotent meals and pentagastrin in the same subjects, suggesting that GH-RIH probably directly affects the parietal cells. Our current research indicates that acid secretion triggered by histamine is not affected by inhibition from GH-RIH. Attributing a slight decrease in acid output, noticed after discontinuing GH-RIH infusion, to the influence of this hormone on gastric secretion is challenging. It is worth noting that unlike acid secretion, the production of pepsin in response to histamine was notably diminished by GH-RIH, suggesting that this hormone is a stronger suppressor of pepsin compared to acid secretion.

Linked to the inhibition of gastric secretion caused by GH-RIH was a reduction in serum HGH and insulin levels. Recent studies have shown a substantial correlation between growth hormone and gastrin, suggesting that growth hormone may regulate the synthesis and/or production of gastrin and that gastrin may affect growth hormone's effects on the gastrointestinal tract. Although it seems unlikely, the effects of GH-RIH on serum gastrin levels shown in our investigation might be related to growth hormone release inhibition, albeit this hypothesis has not been ruled out.

It is challenging to assess the importance of gastric suppression by GH-RIH in patients with duodenal ulcers since the mechanism of release and the quantity of hormone produced in the digestive tract are yet unknown. Since the method of release and the amount of hormone released in the digestive system are yet unclear, it is difficult to evaluate the significance of gastric inhibition by GH-RIH in patients with duodenal ulcers. GH-RIH has not yet been

discovered in the peripheral blood circulation, and it is still unknown if the dosages employed to demonstrate the effects are pharmacological or physiological.

A possible physiological role for this hormone in controlling gastric secretion and gastrin release is suggested by the finding that some argyrophilic cells inside the gastric mucosa adjacent both oxyntic cells and gastrin-secreting cells exhibited GH-RIH-like immune reactivity. The influence of GH-RIH may be partly attributed to the local "paracrine" action of this peptide on the oxyntic glands, as the GH-RIH positive cells are extensively distributed throughout the secretory cells in the stomach mucosa.

GH-RIH is a potentially helpful therapeutic supplement in the treatment of peptic ulcers, particularly in Zollinger-Ellison syndrome, due to its ability to suppress gastric secretion and serum gastrin levels. However, long-term GH-RIH medication has been shown to impair platelet aggregation and induce severe thrombocytopenia in experimental animals, but not in people. Before this interesting and maybe helpful hormone is used clinically to treat peptic ulcer disease, more study on how GH-RIH affects homeostasis is necessary. [11-15]

Pituitary:

Pituitary adenoma and peptic ulcer are only accidentally related when the adenoma is a separate endocrine tumor; however, this is frequently the case when the pituitary tumors are a component of the polyglandular endocrine adenomatosis syndrome. Most of the individuals who have been carefully investigated have shown symptoms of hypopituitarism, and the pituitary adenomas in this disease are usually eosinophilic or chromophobe.

Consequently, merely 1 percent of those with acromegaly also experience peptic ulcers, and hypophysectomy in test animals significantly decreases both parietal cell volume and gastric output. It has been observed that Pitressin administered parenterally can experimentally cause acute peptic ulcers that typically heal quickly, potentially by inducing gastric mucosal ischemia subsequently followed by localized hemorrhages.

Parathyroid:

Parathyroid dysfunction has also been linked to a modified occurrence of peptic ulcers. Parathormone has been shown to affect gastric secretions by regulating serum calcium levels. Hypoparathyroidism is linked to diminished gastric production of acid and pepsin. It is claimed that peptic ulcers rarely occur alongside hypoparathyroidism, though there is scant evidence suggesting that this connection has ever been investigated.

The main cell, oxyphil cell, and water-clear cell are the three cell types that make up the parathyroid gland. Whereas original hyperplasia often affects the water-clear cells, instances of subsequent hyperparathyroidism due to renal illness are associated with principal cell hyperplasia. There is evidence that parathyroid hyperfunction is associated with a greater incidence of duodenal ulcers, with rates ranging from 13 to 25 percent. Compared to normal duodenal ulcers, where blood calcium levels stay normal, these ulcers may also be less amenable to medical therapy. Occasionally, parathyroidectomy can be used to treat these

ulcers. Since only the chronic kind of peptic ulceration has been discussed, it is important to recognize the difference between acute and chronic forms of hyperkalemia.

Serum calcium levels usually stay below 16 mg. percent in situations of acute hypercalcemia, but they normally range between 18 and 19 mg. percent in cases of chronic hyperparathyroidism, which is characterized by a progressive rise in hyperkalemia.

Animals suffering from acute exogenous hyperparathyroidism develop metastatic calcification in areas of relative alkalinity, or places where acid is released. The stomach, kidneys, and lungs are the most often affected areas. These calcifications form around the chief and parietal cells in the interstitial spaces of the stomach. This may cause hemorrhagic gastritis, which might lead to achlorhydria, and necrosis of the bottom part of the stomach glands.

Acute hypercalcemia is a risk factor for chronic hypercalcemia because individuals with this disease frequently develop peptic ulcers, which can be treated with a high milk intake. Even if a patient has achlorhydria that is not responsive to histamine stimulation, exams may demonstrate duodenal abnormalities and the resulting gastritis may manifest as epigastric discomfort and frequent vomiting. In the stomachs of people with acute hypercalcemia and decreased gastric secretion, microscopic calcification has been seen; however, it has not been found in the stomachs of people with chronic hypercalcemia who also have hypersecretion of gastric acid and pepsin.

Gonad:

It has been observed that peptic ulcers often heal or exhibit fewer symptoms during pregnancy, although no positive outcome was noticed with the ulceration linked to Zollinger-Ellison syndrome. On the other hand, menstruation and menopause are reported to negatively impact peptic ulceration.

It has been observed that estrogen may help inhibit experimental ulcers caused by Cinchophen. Nonetheless, individuals with cirrhosis experience both a rise in circulating estrogens and a higher occurrence of peptic ulcers. In research involving dogs subjected to long-term histamine stimulation along with androgens or estrogens, there was no observed alteration in gastric secretion, or the occurrence or site of peptic ulcers. Likewise, there is no clear reason for the higher occurrence of duodenal ulcers in men despite an equal incidence of gastric ulcers between sexes.

Conclusion:

Peptic ulcer disease (PUD) is a multifactorial condition significantly influenced by hormonal regulation and its interplay with other physiological processes. Hormones such as gastrin, somatostatin, and ghrelin play pivotal roles in maintaining the balance between aggressive and protective factors within the gastrointestinal tract. Dysregulation of these hormones contributes to mucosal damage, impaired healing, and ulcer progression. Additionally, stress-related hormones, like cortisol, exacerbate the condition by promoting acid secretion and reducing mucosal defenses.

Understanding the hormonal mechanisms underlying PUD provides valuable insights for targeted therapeutic interventions. Emerging research on hormonal modulators and their integration into existing treatment paradigms shows promise in addressing the limitations of conventional therapies. Continued advancements in this field could lead to more effective strategies for prevention and management, ultimately improving patient outcomes. A holistic approach encompassing hormonal regulation, lifestyle modifications, and pharmacological treatments remains essential in mitigating the global burden of peptic ulcer disease.

Acknowledgements:

The authors express their sincere gratitude to Nandha college of Pharmacy for providing the necessary resources and support for this review. We extend our appreciation to our colleagues and mentors for their insightful discussions and valuable suggestions, which helped enhance the quality of this work.

We also acknowledge the contributions of researchers whose studies have been referenced in this review, as their work has significantly contributed to our understanding of Hormonal Regulation in Peptic Ulcer Disease: A Comprehensive Review

Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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