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AN OVERVIEW: RESTORING PATHOGENESIS'S ROLE WITH A NEW EMPIRICAL TREATMENT MODULATION IN ULCERATIVE PATIENT

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ABSTRACT

There are few different types of ulcer have different causes such as common ulcer sickness which is erosion in the lining of the stomach or duodenum. Others pressure ulcers is a localized injury range in severity from reddening occurs to the skin to severe, deep craters with exposed muscle or bone which also called bedsores or pressure sores of the skin. The predominant reasons in the Countries are contamination with *Helicobacter pylori* and use of non-steroidal anti-inflammatory (NSAIDs) drugs; gastric ulcerate is comprehensively acid secretion with average or low while poor mucosal defense in mucus and bicarbonate secretion plays a greater role; multifactorial interactions between mucosal, neuro-humoral factors and the autonomic nervous system plays a pivotal role causes stress ulcer; rises incidence of ulcer due to more consumption of alcohol; genetic factors and other diseases like chronic obstructive pulmonary/airways disease, asymptomatic bowel syndrome, chronic pancreatitis and crohn's disease have pathogenesis associated with ulcer. Hence we explore the possibility classification of the revolutionary treatment of ulcer disease by decrease of gastric acid secretion, H+/K+ ATPase Inhibitor, muscarinic receptor antagonists, mucosal coating agents, etc. and also some herbal medicines and their constituents used in treatment or prevention of ulcer. The aim of present study was to review on various pathogenetic factors, its multifactorial treatment with proper diagnosis, herbal medicines in treating ulcer in world and modulation management of pressure ulcer by occupational therapist through pressure mapping technique under the International Standards Organization (ISO) protocol.

KEYWORDS: Pressure Ulcer, NSAIDs, Gastric Ulcer, Duodenal Ulcer.

INTRODUCTION

A digestive ulcer (DU) is a sore which figure out when digestive juices were away the ruling of the digestive system. DU is occurs in the lining of the stubbornness, duodenum or cloudiness part of the gullet. Reviewer reported aprroximtely10 percent of adults were affected by DU once in lifetime. In countries United States around 50,000 people showed a DU in a year. There are different facts and reports on DU about peptic ulcers can occurs anywhere in the tonic system, terminate bacteria with symptoms desire agonize, consciousness likely dyspepsia, qualm and indisputable represent of dosage such as Proton pump inhibitors (PPIs).[1]

A pressure ulcer is a type of ulcer which occurs due to localized injury to the skin or underlying tissue especially over a bony prominence. There are two types of predisposing factors that are classified as intrinsic (aging skin, poor mobility, poor nourishment, co-morbidities) and extrinsic (force, abrasion, shear). A European survey reported about pressure ulcers patients with 25 hospitals a prevalence rate of 18.1 % with the most frequently affected areas being the sacrum and heels.[2]

DU globally reporting along with the different rates of hospitalizations and mortality, withdraw over the ended copulate of decades, attributed in part to complicate alter in the endanger factors for diseases ailing, reductions in the *H. pylori* influence, use of anti-secretary agents, NSAIDs and a senescent arena.[3] Peptic ulcer indisposition (PUD) is characterized by discontinuance in the inner lining of the gastro enteric (GI) essays of gastric acid secretion or pepsin. It shows muscularis propriabed of the gastric epithelial tissue[3]. Pathogenesis of these diseases occurs in the stomach and proximal duodenum; also may involve in the esophagus, distal duodenum or jejunum. Epigastria disquiet reported of occurrence within 15-30 records sequential pulverize in patients with a gastric ulcer; duodenal ulcerate pain for 2-3 hours after a repast **Fig.1.**[4] A recent article reviewed on gastric ulcerate is comprehensively acid secretion with average or low while poor mucosal defense in

mucus and bicarbonate secretion plays a greater role. In duodenal ulcerate sour secretion is high in helter-skelter half of the patients but normal in the rest. There are various stages of ulceration affects the body parts such as through erosion which is the initial stage that damage mucosal lining approximately 1-2 cm across, secondarily emerge ulcer by the marked or scarred disruption of the smooth tissue in the stomach and duodenum if erosion is not treated. Finally conditions of ulcer showing life-threatening with bleeding ulcer. This pathogenic disease becomes a partial or complete hole in the stomach causing hemorrhage and showed medical emergency with significant GI complications.[5] PUD was reported inclusive problem with an ages wager can be decrease and improved.[6]

The incidences of digestive ulcer were reported as geographical variations that more than 50% of the untried peptic ulcerate conjuncture story in developing countries. Eastern Europe and Asia, Central and South America are contaminant areas and; Southern Asia, North and East Africa, North America Australia and New Zealand were in less risk area of DU respectively.[7]

PUD has common and distinguishable etiology of ulcer such as *H. pylori* infection, NSAIDs medications, zollinger-ellison syndrome, malignancy (gastric/lung cancer, lymphomas), stress (acute illness, burns, head injury), viral infection, vascular insufficiency, radiation therapy, crohn disease and chemotherapy.[8] ***H. pylorus*** is a bacillus organism in the sites of gastric epithelial cells. Reviewer was reported about these bacilli which are responsible for causing 90% of duodenal ulcers and 70% to 90% of gastric ulcers.[9] There are various virulence factors of *H. Pylori* likely secretion of urease infringes down carbamide into ammonia and preserve the animal by offset the acidic gastric surrounding; toxins associated with desire mucosal turbulence and entertainer parenchyma evil and flagella affect in the gastric epithelial tissue. NSAIDs are the second most habitual cause of PUD after *H. pylori* infections. NSAID inhibits prostaglandin in presence of COX-1 enzyme, decrease gastric mucilage and bicarbonate production and also loss in mucosal lineage flow. There are different medications apart from NSAIDs like corticosteroids; bisphosphonates, potassium chloride, steroids and fluorouracil which reported an etiologic of PUD. Smoking and alcohol can induce tartness and irritate the gastric mucous membrane.

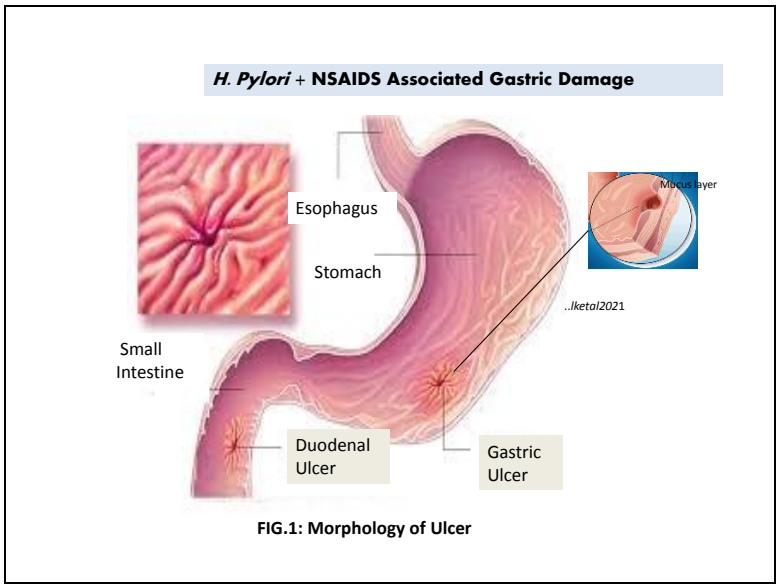

FIG.1: Morphology of Ulcer

Ulcerate disorder with or without the once enrolled through Zollinger-Ellison concurrence condition that can cause digestive ulcers **Fig**.**2**. The patients have more than tumors in the stomach sweetbread and duodenum that produce a copious amount of gastric hormone. This leads to presence of acid in the higher bowel and duodenum.[9] A researcher finds different evidence from last decades of discovery that NSAIDs such as 2-(acetyloxy) benzoic acid, ibuprofen, and naproxen sodium is another thread bare object of digestive ulcers. NSAIDs can affect the stomach's plead mechanisms in differently and produce the stubbornness vulnerable to the mischievous consequence of acid and pepsin which form pituita and bicarbonate. This natural bicarbonate was neutralizing tonic fluids and break into less hurtful agents.[10] Genetically it has been reported that 20% of digestive ulcerate disease patients also affected by duodenal ulcers. Researchers have found and implies about hereditary basis for sensibility to *H. pylori* epidemic. The hereditary exploration cases are sometimes reporting seasonably and it may show greater venture in the future.[10] Lifestyle risk can be emerge through smoking which can extend casualty of ulcerate cases, especially if affected with *H. pylori*. Smoking also contributes to ulcer recurrence. While there are not much evidence reported between alcohol and peptic ulcers, ulcers are common in those who reporting cirrhosis of the liver.[11]

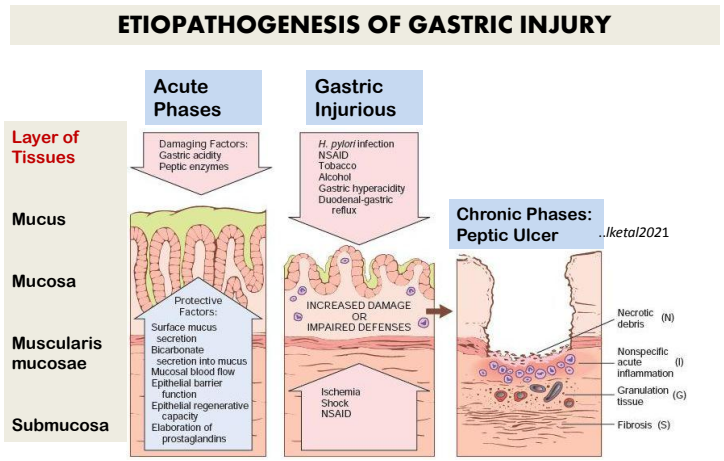

FIG.2: Pathogenesis of Ulcer

Etiopathogenesis and Predispose Factors of Ulcer

Infection of H. pylori in GIT

Researcher reviewed about *H. pylori bacillus* which can induce antral gastritis in many patients with gastric or duodenal ulcer. *It* has been reported that *H. pylori* present in the sites of antrum of more than 95 percent of duodenal ulcer patients and 75 percent of gastric ulcer patients.[12, 13] This organism is found in the layer of mucus or beneath the mucus adhering to gastric epithelium attach to the intercellular junctions. Besides its etiopathogenesis factors *H. pylori* showing a powerful formation of urease and the consequently produce ammonia which raised pH microenvironment, enabling to survive the organism. This ammonia may reflect cytotoxic action. It has been seen that destruction of gastric epithelial microvilli in acute infected by *H. pylori*, formation of gastric metaplasia, arise in the duodenal cap which may associated with changes in high gastric output reported in electron microscopic studies.[14] *H. pylori* colonization that may induces mucosal injury and ulcer.[15]

NSAIDs and other related Medications

NSAIDs are clinically prescribed medicine used in the world and showed a variety of injury of gastro-duodenal mucosa with haemorrhages, erosions and ulcers. *N*SAIDs related medications aspirin and other salicylates in high dosages induced different biochemical changes in form of denaturation of mucus glycoproteins and mucus cell proteins. These get rid of protective mucus layer and discharge mucus from epithelial cells and cell desquamation. These cells can be diminishing by acidic drug or gastric contents to a neutral pH to attenuate these conditions.[16] Lysosomes are membrane in mucosa and parietal cells that contain an array of hydrolytic enzymes which are capable for cellular autolytic reactions.[17] *N*SAIDs related medications inhibit the platelet aggregation (strengthen bleeding), causes vasoconstriction and acid secretion through inhibition of PG cyclo-oxygenase, reduced PGE and endothelial cell PGI.[18] Mast cells on degranulation formation release a histamine mediator which stimulates the acid secretion and shows vasodilatations; also affect microvasculature of the mucosa for bleeding. The cells contribute to destruction on conversion of hydroperoxy to hydroxyl fatty acids and several free radical formation prognoses to damaging tissues.[19] This mentioned pathogenesis has additive or synergistic effects of the drug, cellular autolysis, protein synthesis and regenerating zones of the mucosa in ulceration.

Ciggy Smoking: Researcher reviewed smoker's histories who mostly suffer from gastric and duodenal ulcers as compared to non-smokers. It has been found that still not much mechanism has been reported about tobacco except its pharmacological properties as causative properties of nicotine and only few mechanisms have been proposed to explain the effect of smoking on peptic ulcer like stimulation effect for secretion of acid, variation of blood flow or motility, reflux of bile and decrease in the prostaglandins.[20,21]

Diet was considered possible and Epidemiological evidence implicates in the geographical distribution of duodenal ulceration among people. Like consumption of more oil leads to peroxidation of lipid and were store in form of unsaturated fatty acids which increase the production of cytotoxic ketoaldehydes and can suppressed the ulceration.[22]

Psychological distress: Many psychologists over 50 years ago reported the researches on the "Executive Monkeys" showing significant differences in behavioural experiential manipulations can produce gastric ulceration and even may lead to death. This study caught the interest of research in the public and in the scientific world.[23] Stress ulceration in the stomach is established as one of ulcerogenic factor with clinical conditions like burns, sepsis, trauma, shock, head injury and neurological confusion.[23] It has been seen that

multifactorial interactions between mucosal, neuro-humoral factors and the autonomic nervous system plays a pivotal role causes stress ulcer.[24] The stress occurs through cerebral marginal site to hypothalamus and transmitted to medulla oblongata with spinal cord which then causes stimulation of gastric mucosa. Then stimulation is occurs from medulla oblangata to the vagus which rises secretions and motility of gastric.[25] Due to stimulation on splanchnic nerve by spinal cord causes disruption in circulation, modest constriction of gastric vessels and lowering of gastric blood flow. The stress affects the releasing of adreno-corticotropic hormone with its function which steers to raise gastric secretions and fall off gastric mucosal resistance.[26] Sometimes disturbances and deficiency of nutrition causes local tissues injury which enhances with rapid appearance in form of chronic ulcer.[27] Electrical stimulation in distinct sites of the limbic organizes important factors for occurring of stress ulcer such as in secretion and motility of gastric and mucosal blood flow. The disorders of neural and brain-gut axis producing several disruptive and protective mediators (amino acids, biogenic amines and peptides) of stress ulcer genesis.[28]

Alcohol: In the present report about the gastric mucosa were greatly affected and apparently causes cell and plasma membrane damage due to rapid penetration of 50-100 percent of ethanol, which then results in increased permeability in membrane and intracellular accumulation of water and sodium.[29] The stage of leaky membrane formation is common in the development of cell injury. Normal distribution of electrolytes unable to balance between intracellular and extracellular compartments due to increased permeability of membrane; where causes the massive intracellular accumulation of calcium electrolytes that resembles a pathogenesis steps to injurious of gastric mucosa.[30] This types of changes results in cell death and erosion or exfoliation in the superficial epithelium. Ethanol causes lipid peroxiation due to attribution of free radical damage at site of occurring lesion in gastric mucosa. Present studies were reviewed different cases on cirrhosis disease which is linked to rises incidence of ulcer due to more consumption of alchol.[31]

Other diseases and genetic factors

Genetic factors (familial amyloidosis and gastro-cutaneous syndrome) and other diseases like chronic obstructive pulmonary/airways disease, asymptomatic bowel syndrome, chronic pancreatitis and crohn's disease have pathogenesis associated with ulcer.[32]

Pressure ulcers disrupts blood supply to the capillary network, increase blood flow and depriving tissues of oxygen and nutrients which are caused by unrelieved pressure due to great force over a short period or with less force over a longer period. The common sites for pressure ulcers are greater trochanters, sacrum, ischial tuberosities, heels and lateral malleoli.[2]

Following drugs were classified and discussed of the revolutionary treatment of ulcer disease TABLE 1.[34,41]

1. Decrease of Gastric acid secretion: H2 Histamines such as cimetidine, ranitidine are acts as H2-receptor antagonists which are broadly used and novel pills over the previous decade. These antagonists are capable of reducing over 90% of food stimulated, basal and nocturnal secretion of gastric acid stimulated by cholinomimetic drugs, gastrin, histamine and vagal stimulation[33]. Histamine antagonists were prevents the occurrence of stress which induced ulcers. However, these antagonists are sometimes preferred to be use in combination with antacids. H2 Histamine was reported in the medical management of Zollinger-Ellison syndrome and gastric hypersecretory states.[34] It has been reported that on recurrence of ulcer after healing showing a complication of treatment with H2-receptor antagonists and therefore a longer therapy is needed. The other H2 antagonists such as cimetidine, famotidine, nizatidine etc. are remarkable but not used in chronic stage of ulcer and these are under investigation to remark further for better antiulcer activity.[35] Glaxo Laboratories were developed the new anti-ulcer drug Ranitidine bismuth citrate (RBC) in combination with clarithromycin to eradicate *H. pylori.*[36]

2. H+/K+ ATPase Inhibitor

Gastric proton pump inhibitors constitute a pathogenesis inhibition of acid secretion as comparison to blockade receptor by histamine and cholinergic. Omeprazole is not directly inhibits H+K+ ATPase enzyme but is reversibly transformed as sulphenamide in acidic which then reacts with thiols to form disulfides and thus producing an action through enzyme-drug complex at the site. It has been reported that omeprazole, lansoprazole and series of benzimidazoles derivatives etc. are long acting inhibitors of acid secretion and *H. pylori.*[37]

3. Muscarinic receptor antagonists

Pirenzepine is a selective muscarinic M-I receptor antagonists which reduces gastric acid secretion. It has cytoprotective effect against gastric mucosal lesions induced by ethanol, HCl and NaOH; also show an efficacy in duodenal ulcer.[38]

4. Mucosal coating agents

Sucralfate is reported as sulphated disaccharide-basic aluminium sulfate complex. It forms an adherent coating with proteinaceous material at ulcer sites in mucosal. These were accountant for extensive polymerization and cross linking of sucralfate formation at low pH. The coating provides barrier to hydrogen ion diffusion, decrease peptic efficacy and then adsorbs the bile salts. Further ulcer healing has been seen due to binding of sucralfate on epidermal growth factor and fibroblast growth factor.[38] Bismuth sub citrate (BSC) as tripotassium dicitrate bismuthate, currently is the most clinically effective in ulcer, gastric acid secretion.[39] Carbenexolone is a synthetic derivative of glycyrrhizin

acid which also reported in valuable promoting healing of peptic ulcers. The mechanism of action is not well understood but, is shows an effect on mucus, increasing its secretion and viscosity and thereby protecting mucosa from acid and pepsin.[40] Recently sucralfate and BSC were reported to suppress the associated *H. pylori* infection.

5. Miscellaneous drugs: Some calcium channel blockers such as nifedipine and diltiazem were reported as active against in ulcers diseases. Gastrin receptor antagonist and mast cell stabilizer also found to possess antiulcer activity.[41]

6. Herbal Medicines: Natural remedies from herbal medicinal plants were offer many potential efficacy to treat peptic ulcer from last many years. *Allium sativum*, family Liliaceace commonly called Garlic is a natural plant and home remedies were suggested. *A. sativum* potent bioactive constituents can be used for the prophylactic treatment in gastric ulceration patients who had tendency to develop.[42] *Aloe vera*, family Euphorbiaceae is widely distributed and common in tropical and sub-tropical India regions. The component in *A. Vera* Lectin juice inhibit acid secretion and also reported a beneficial effect in consumption and relief of digestive related problems such as irritable bowel syndrome, heartburn, reduce vasoconstriction and improves healing of ulcer healing.[43] *Azadirachta indica*, family: Meliaceae commonly named Neem which is a native tree of India and found in many Asian countries and tropical regions of the western hemisphere. *A. indica* reported a significantly inhibition of gastric ulceration induced by indomethacin and also acts through histamine H2 receptor.[44] *Curcuma longa*, family: Zingiberaceae commonly named Turmeric which showed the gastroprotective efficacy of turmeric oil and significantly decreased the gastric ulcer in rodent stomach. *Carica papaya*, family: Caricaceae commonly called Papaya fruits are reported to possess antiulcer efficacy. Papaya has peptine and due to alkaline properties, alkaline secretions pass over the burnt walls of the stomach, slowly it tends to heal and dishminshes stomach ulcer. Others individuals plants such as *Asparagus racemosus, Bauhinia variegate, Euphorbia umbellate, Emblica officinalis, Hibiscus cannabinus, Withania somnifera, Zingiber officianale, Withania somnifera, Tephrosia purpurea, Indigofera tinctoria, Mangifera indica etc.* were reported respectively as potent antiulcer activity.[44,45]

Search For Modulation Management of Ulcer Through Therapy Organizational level

Occupational therapy (OT) is a profession of allied health subject that underlying belief with engaging in occupations promotes both health and wellness. There are a greater role of the occupational therapist (OT's) in all age's patient's in a variety of fields to improve and maintain skills for daily activities and well-being.

Just from the early 1990s Pressure mapping arrays (PMA's) have evolved and become increasingly reliable with advances in technology for therapy. OT's is not only used PMA's to assist with the risk assessment of pressure ulcers, but also to educate clients, caregivers and health-care professionals in pressure ulcer prevention and management. The Braden scale were designed as an pressure ulcer risk assessment tools with an objective therapy to determine the physiological and non-physiological variables associated with the prediction of pressure ulcers. A prospective therapy was design about PMA's can be used with children or adults at risk of pressure ulceration, particularly those with lack of sensation, less mobility, lack of nutrition and acute or chronic ailments. Especially those people who are sitting mostly in a wheelchair at daytime. OT with pressure mapping systems can be uses in hospitals, clinics, community settings and patient's homes.

Therapist working with completes assessment process of pressure mapping under the International Standards Organization (ISO) protocol[47]. They adapt the most appropriate wheelchair or seat cushion and aimed to educate patients and caregivers regarding pressure ulcer prevention and management as: Patients have to initially position on a firm surface of a mat table with the pressure sensing mat placed between the buttocks and the seating surface. These recognize postural irregularity, flexion areas and thin fame. The latter should be followed by palpation like touch, eversion, feeling etc. Then patients have to pressure mapped on their own seating facet. The adaptable wedge of the wheelchair is examined and looks over such as to make certain the footplates are at the accurate height. Then have to positioned on an alternative cushions depending upon the basis of patients requirement at possibility level, posture, steadiness and restraint **Fig.3**.

FIGURE 3: Pressure Mapping Therapy: Wheel chair and alternative ROHO cushions for prevention and management of ulcer

OT's were perceptibly scores the levels from finest to best pressure issue. Top scoring pressure distribution is characterized by an even spread of pressure including good femoral loading and no areas of excessively high pressure. Those cushions which showing poor pressure distributions for an individual are not reused[48]. The results of a pressure mapping assessment were reported sitting areas of high interface pressure and postural abnormalities. Therapist were uses the pressure mapping to compare seating surfaces. These steps find out the

optimal sitting surfaces for each patient and provide immediate biofeedback to patient, caregivers and health professionals, visually demonstrating the benefit of an optimal sitting posture and cushion on lowering interface pressures and thus minimise the pressure ulcer risk in clients.[49]

There are interventions sessions reported on the clients who were educated on the optimal sitting position. Biofeedback is adapted on them through visualizing pressure maps of their usual sitting position. OT's reported the therapy benefits of shifting weight from the buttocks and the outcome of impoverished posture or incorrect placement of cushions. Therapist guide to client about the importance of adjusting other components of the seating systems such as the use or adjustment of wheelchair footplates and the use of tilt and recline functions. The pressure mapping technique also let optimal cushion position for high-risk patients such as air filled cushions or cushions with accessories.[50]

Table 1: Uses of Drugs For The Treatment of Ulcer Disease.

Sr.NO.	Classification of Antiulcer Drugs	Drugs	MOA of Antiulcer Drugs	Side Effect of Antiulcer Drugs
1	**Reduction of Gastric acid secretion H2 Histamines**	CIMETIDINE	Drugs competitively blocks histamine	Tiredness, loose motions, impotence and make bigger mammary gland in men
		RANITIDINE	This agents are reversible inhibitor on H2 histamine	Fecal impaction, gastric upset, loose motions, neuralgia
		FAMOTIDINE	This agents are competitive inhibitor on H2 receptor	Black defecation, apprehension and turn loose of the dermis
		ROXATIDINE	Drugs conquer and repress the effect of histamine on the parietal cells of the belly	Skin explosion, sickness, diarrhea
2	**Proton Pump Inhibitors**	OMEPRAZOLE	Omeprazole inhibits the action of parietal cell H+/K+ATP pump	Itching, blisters, muscle aches, back, leg stomach pain
		ESOMEPRAZOLE	Causes Irreversible action on the H+/K+ATPase in the proton pump	Blown up, fatigue, color changes in urine
		LANSOPRAZOLE	Lansoprazole inhibits the H+/K+ ATPase	Tenderness, faint, weak, constipation
		PANTOPRAZOLE	This covalently binds to the proton H+/K+ATP pump	Arthritis, vertigo
		RABEPRAZOLE	Rabeprazole inhibits H+/K+ ATPase of the gastric cell layer	Weight swift, formication of the hands and tootsy, yellow color to eyeball and skin
3	**Anti-cholinergic drugs**	PIRENZEPINE	Are Muscarinic receptor antagonist	Dryness, waterlessness and blurred vision
		PROPANTHELINE	Blocking the receptors acetylcholine on smooth muscle	Strain, ageusia
		OXYPHENONIUM	Dual action such as specific anticholinergic effect and direct efficacy upon smooth muscle	Difficulty in eat up, alimentary stoppage, vomiting
4	**Prostaglandin analogues**	MISOPROSTOL	These stimulates prostaglandin E1receptor on the parietal cell	Severe sensitivity, heart burn, flatulence
5	**Anti-H. pylori drugs**	AMOXICILLIN	Shows bactericidal action against bacterial organism	Feeling tenderness, blood in urine, distended
		CLARITHROMYCIN,	Agents are protein synthesis inhibitors	Heart pain, diarrhea, sickness
		TETRACYCLINE	This inhibits the bacterial growth by inhibiting translation	Mouth swelling, sickness, nausea

CONCLUSION

A recent review on restoring pathogenesis's role with a new empirical treatment modulation in ulcerative patient found that preventive measures of either stomach ulcer, duodenal ulcer or pressure ulcer has distinguishable etiology of ulcer such as *H. pylori* infection, NSAIDs medications, Zollinger-Ellison syndrome, malignancy (gastric/lung cancer, lymphomas), stress (acute illness, burns, head injury), viral infection, vascular insufficiency, radiation therapy, crohn disease and chemotherapy. This article reviewed the various revolutionary treatments and herbs which are used for the treatment of ulcer. It is evident stated that present mentioned medicines have significant antiulcer efficacy and plants proven a safe option due to less side effects for the diagnosis and management of ulcer. In summary, in ulcer patients pressure injuries are a common consequence and given the robust research considering both the clinical and economic implication of therapy through pressure mapping systems by a OT's which provide valuable information regarding maintenance of skin integrity and therefore assisting clinicians in the overall management and prevention of pressure ulcers, also to make a strong evidence to practice at both clinician and therapy level.

REFERENCES

1. Testerman TL, Morris J. Beyond the stomach: an updated view of Helicobacter pylori pathogenesis, diagnosis and treatment. W J Gastroenter, 2014; 20(36): 12781-12808.
2. Katrien V, Michael C, Carol D, Lena G, Tom D. Pressure ulcer prevalence in Europe: a pilot study. J Eval Clin Prac., 2007; 13(2): 227-235.
3. Epelboym I, Mazeh H. Zollinger-Ellison syndrome: classical considerations and current controversies. Oncologist., 2014; 19(1): 44-50.
4. Chey WD, Wong BC. American College of Gastroenterology guideline on the management of *Helicobacter pylori* infection. Amer J Gastroenter, 2007; 102(8): 1808-1825.
5. Javid G, Zargar SA, Saif R. Comparison of p.o. or i.v. proton pump inhibitors on 72-h intragastric pH in bleeding peptic ulcer. J Gastroenter Hepat., 2009; 24(7): 1236-1243.
6. Lai KC, Lam SK, Chu KM. Lansoprazole for the prevention of recurrences of ulcer complications from long-term low-dose aspirin use. N Eng J Med., 2002; 346(26): 2033-2038.
7. Sung JJ, Tsoi KK, Ma TK, Yung MY, Lau JY, Chiu PW. Causes of mortality in patients with peptic ulcer bleeding: a prospective cohort study of 10,428 cases. Amer J Gastroenter, 2010; 105(1): 84-89.
8. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. American Journal of Gastroenterology, 2013; 108(3): 308-328.
9. Kim JS, Park SM, Kim BW. Endoscopic management of peptic ulcer bleeding. Clin Endos 2015; 48(2): 106-111.
10. Cirocchi R, Soreide K, Di Saverio S. Meta-analysis of perioperative outcomes of acute laparoscopic versus open repair of perforated gastroduodenal ulcers. J Trauma Acute Care Surg., 2018; 85(2): 417-425.
11. Wang AY, Peura DA. The prevalence and incidence of Helicobacter pylori-associated peptic ulcer disease and upper gastrointestinal bleeding throughout the world. Gastro Endos Clinics N Amer., 2011; 21(4): 613-635.
12. Scheeres DE, Dekryger LL. Surgical treatment of peptic ulcers before and after the introduction of H2 blockers. Amer J Med., 1987; 53(7): 392-397.
13. Svanes C, Soreide J, Skarstein A, Fevang B, Bakke P, Vollset S, et al. Smoking and ulcer perforation. Gut., 1997; 41(2): 177-180.
14. Rosenstock S, Jorgensen T, Bonnevie O, Andersen L. Risk factors for peptic ulcer disease: a population based prospective cohort study comprising 2416 Danish adults. Gut., 2003; 52(2):186-193.
15. Kurata JH, Nogawa AN. Meta-analysis of risk factors for peptic ulcer. Non steroidal anti inflammatory drugs, *Helicobacter pylori* and smoking. J Clin Gastroenter, 1997; 24(1): 2-17.
16. Chikly BJ. Manual Techniques Addressing the Lymphatic System: Origins and Development. J Amer Osteo Assoc., 2005; 105(10): 457-464.
17. Horsen K, Soreidi JA, Kvaloy JT. Epidemiology of perforated peptic ulcer: Age and gender adjusted analysis of incidence and mortality. W J Gastroenter, 2013; 19(3): 347-354.
18. Suerbaum S, Michetti P. *Helicobacter pylori*. The New England Journal of medicine, 2002; 347(15): 1175-1186.
19. Eisner F, Hermann D, Bajaeifer K. Gastric Ulcer Complications after the Introduction of Proton Pump Inhibitors into Clinical Routine: 20 Year Experience. Vis Med., 2017; 33(3): 221-226.
20. Carvalho AC, Guedes MM, Souza AL, Trevisan MT, Lima AF, Santos FA. Gastroprotective effect of mangiferin, a xanthonoid from *Mangifera indica*, against gastric injury induced by ethanol and indomethacin in rodents. Planta Med., 2007; 73(2): 1372-1376.
21. Neelima N, Sudhakar M, Patil MB, Lakshmi BV. Anti-ulcer activity and HPTLC analysis of *Mangifera indica* L. leaves. Int J Pharm Phyto Res., 2017; 1(3):146-55.
22. Narayanan M, Reddy KM, Marsicano E. Peptic Ulcer Disease and *Helicobacter pylori* infection. Mis Med., 2018; 115(3): 219-224.
23. Lanas A, Carrera LP, Arguedas Y, García S, Bujanda L, Calvet X, et al. Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. Clin Gastroenter Hepat., 2015; 13(5): 906-912.

24. Huang Brady JV, Porter RW, Conrad DG, Mason JW. Avoidance behavior and the development of gastro duodenal ulcers. J Exp Anal Behav., 1958; 1: 69-72.
25. Snowden FM. Emerging and reemerging diseases: a historical perspective. Immun Rev., 2008; 225(1): 9-26.
26. Lanas A, Chan FKL. Peptic ulcer disease. Lancet., 2017; 390(10094): 613-624.
27. Banerjee S, Cash BD, Dominitz JA, Baron TH, Anderson MA, Ben-Menachem T, et al. The role of endoscopy in the management of patients with peptic ulcer disease. Gastro Endo., 2010; 71(4): 663-668.
28. Malfertheiner P, Megraud F, Morain CA, Gisbert JP, Kuipers EJ, Axon AT, et al. Management of *Helicobacter pylori* infection-the Maastricht V/Florence Consensus Report, Gut 2017; 66(1): 6-30.
29. Strand DS, Kim D, Peura DA. 25 Years of Proton Pump Inhibitors: A Comprehensive Review. Gut.,., L. 2017; 11(1): 27-37.
30. Charpignon C, Lesgourgues B, Pariente A, Nahon S, Pelaquier A, Gatineau SG, et al. Peptic ulcer disease: One in five is related to neither *Helicobacter pylori* nor aspirin/NSAID intake. Alim Pharm Ther., 2013; 38(8), 946-954.
31. Levenstein S, Rosenstock S, Jacobsen RK, Jorgensen T. Psychological stress increases risk for peptic ulcer, regardless of *Helicobacter pylori* infection or use of nonsteroidal anti-inflammatory drugs. Clin Gastroenter Hepat., 2015; 13(3): 498-506.
32. McColl KE. *Helicobacter pylori* negative nonsteroidal anti-inflammatory drug-negative ulcer. Gastroenter Clin N Amer., 2009; 38(2): 353-361.
33. Siddique O, Ovalle A, Siddique AS, Moss SF. *Helicobacter pylori* infection: An update for the internist in the age of increasing global antibiotic resistance. Amer J Med., 2018; 131(5): 473-479.
34. Hooi JKY, Lai WY, Suen MMY, Underwood FE, Tanyingoh D, Malfertheiner P, et al. Global prevalence of *Helicobacter pylori* infection: Systematic review and meta-analysis. Gastroenter, 2017; 153(2): 420-429.
35. Zaki M, Coudron PE, Mc Cuen RW, Harrington L, Chu S, Schubert ML. *H Pylori* acutely inhibits gastric secretion by activating CGRP sensory neurons coupled to stimulation of somatostatin and inhibition of histamine secretion. Amer J Phy Gast. Liver Phy., 2013; 304(8): G715-722.
36. El Omar EM, Oien K, El Nujumi A, Gillen D, Wirz , Dahill S, et al. *Helicobacter pylori* infection and chronic gastric acid hyposecretion. Gastroenter, 1997; 113(1): 15-2.
37. Moss SP, Legon S, Bishop AE, Polak JM, Calam J. Effect of *Helicobacter pylori* on gastric somatostatin in duodenal ulcer disease. Lancet., 1992; 340(8825): 930-932.
38. Bhala N, Emberson J, Merhi A, Abramson S, Arber N, Baron JA, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: Meta-analyses of individual participant data from randomised trials. Lancet., 2013; 382 (9894): 769-779.
39. Bjarnason I, Scarpignato C, Takeuchi K, Rainsford KD. Determinants of the short-term gastric damage caused by NSAIDs in man. Alim Pharm Thera 2007; 26(1): 95-106.
40. Mossner J. The indications, applications, and risks of proton pump inhibitors. Deut Arzte Intern., 2016; 113(27-28): 477-483.
41. Maes ML, Fixen DR, Linnebur SA. Adverse effects of proton-pump inhibitor use in older adults: A review of the evidence. Thera Adv Drug Safety, 2017; 8(9): 273-927.
42. Pension J, Wormsley KG. Adverse reactions and interactions with H2-receptor antagonists. J Med Toxic., 1986; 1(3): 192-116.
43. Wauthoz N, Balde A, Balde ES, Van Damme M, Duez P. Ethnopharmacology of *Mangifera indica* L. bark and pharmacological studies of its main C-glucosylxanthone, mangiferin. Intern J Biomed Pharma Sci., 2007; 1(3): 112-119.
44. Srinivas RL, Lakshmi SM, Sharma SN, Reddy GK, Prasanna KR. Medicinal plants as anti-ulcer agents. J Pharma Phyto., 2013; 2(4): 91-97.
45. Gupta M. Pharmacological properties and traditional therapeutic uses of important Indian spices: A review. Intern J Food Pro., 2010; 13(5): 1092-1116.
46. Bergstrom, Nancy, Braden, Barbara J, Laguzza, Antoinette, et al. The braden scale for predicting pressure sore risk. Nur Res 1987; 36 (4): 205-210.
47. Regan M, Teasell R, Wolfe D, Keast D, Mortenson W, Aubut J. A systematic review of therapeutic interventions for pressure ulcers following spinal cord injury. Arch Phy Med Reh., 2009; 90(2): 213-231.
48. Ji-Su Park, Sang-Heon Lee. Comparing the interface pressure redistribution of three different types of cushions: differences according to age groups and cushion preferences. J Phy Thera Sci., 2017; 29(1): 57-63.
49. Eun-Ji Go, Sang-Heon Lee. Effects on sitting pressure distribution during the application of different cushions and anterior height wedges. J Phys Thera Sci., 2017; 29(3): 390-393.
50. Mendes PVB, Gradim LCC, Silva NS, Allegretti ALC, Carrijo DCM, Cruz DMCD. Pressure distribution analysis in three wheelchairs cushions of subjects with spinal cord injury. Dis Reha Ass Techn., 2019; 14(6): 555-560.