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Review Article

A Review on Various Gastro-Intestinal Effects of Mental Stress and Management

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Abstract:

Stress is caused by the situation, person cannot capable to cope with that unfavourable event and person's judgment not capable to suit the demand of that event. Symptoms of stress includes Depression, anxiety. Anger, irritability, restlessness. Feeling overwhelmed, unmotivated, or unfocused, Trouble sleeping or sleeping too much, Racing thoughts or constant worry, Problems with your memory or concentration, Making bad decisions etc. The physiological actions in gut are controlled by the Enteric nervous system [part of central nervous system]. ENS carry millions of nerve cells as sensory motor and interneurons. They have sympathetic and para-sympathetic links. After the stress stimulus is delayed and reach Hypothalamic- pituitary – adrenal axis [HPA axis] is producing Corticotrophin Releasing Factor (CRF). It directly produces some effects on gut like Changes in permeability of gut, Hypersensitivity to pain in visceral portion of gut, Increase chance of inflammation, Changes in gut motility, Gut microbiota transformation etc. The gastro-intestinal diseases like peptic ulcer, GERD, Inflammatory bowel disease, Irritable-bowel syndrome are produced. Techniques likes Yoga, meditation, physical exercises produce prevention and reduction of stress. In case of gastro- intestinal disorders some anxiolytics, ulcer- protectives, food changes can manage complications.

Keywords: Psychological stress, gastro-intestinal effects, Cortisol, Management techniques.

Introduction:

Stress is defined as process in which environmental demands strain on organism's adaptive capacity resulting in both psychological demands as well as biological changes that could place risk of illness. Stress can be considered as normal process when warning signal comes from brain after a unpleasant incident. And the body starting 'Fight or Flight' responses.

Stress is caused by the situation, person cannot capable to cope with that unfavourable event and person's judgment not capable to suit the demand of that event. Stress is a survival technique of body after get a threat stimulus as physical or physiological. [1] There are three main types of stress. These are acute, episodic acute, and chronic stress.

Some of the main sources of stress include work, finances, relationships, parenting, and day-to-day inconveniences. Stress can trigger the body's response to a perceived threat or danger, known as the fight-or-flight response. During this reaction, certain hormones like adrenaline and cortisol are released. Chronic stress, or a constant stress experienced over a prolonged period of time, can contribute to long-term problems for heart and blood vessels. The consistent and ongoing increase in heart rate, and the elevated levels of stress hormones and of blood pressure, can take a toll on the body.[2]

Symptoms of stress includes Depression, anxiety. Anger, irritability, restlessness. Feeling overwhelmed, unmotivated, or unfocused, Trouble sleeping or sleeping too much, Racing thoughts or constant worry,

Problems with your memory or concentration, Making bad decisions etc.

Stress affects all systems of the body including the musculoskeletal, respiratory, cardiovascular, endocrine, gastrointestinal, nervous, and reproductive systems.[3]

Stress management can be complicated and confusing because there are different types of stress — acute stress, episodic acute stress, and chronic stress each with its own characteristics, symptoms, duration and treatment approaches.[4]

Stress can be managed by find a balance, be kind to yourself, learn on the people you trust, eat well-balanced, regular meals, exercise regularly, get plenty of rest, practice relaxation and exercises. Stressed situation can be cope with re-balance work and home, eat well and limit alcohol and stimulants, connect with supportive people, carve out hobby time, practice meditation, stress reduction or yoga, sleep enough, make a bond with your pet.[5]

The most prominent of anti-anxiety drugs for the purpose of immediate relief are those known as benzodiazepines; among them are alprazolam, clonazepam, chlordiazepoxide, diazepam, and lorazepam.[6]

GENERAL EFFECTS ON GASTRO-INTESTINAL SYSTEM

Stress can affect digestion and what nutrients the intestines absorb. Gas production related to nutrient absorption may increase. The intestines have a tight barrier to protect the body from (most) food related bacteria. Stress can make the intestinal barrier weaker and allow gut bacteria to enter the body.[7]

Stress increases the intestinal permeability to large antigenic molecules. It can lead to mast cell activation, degranulation and colonic mucin depletion. A reversal of small bowel water and electrolyte absorption occurs in response to stress and is mediated by cholinergic system.[8]

Stress directly linked to gastro-intestinal dysfunction. One common symptom in stress includes 'flying butterflies' in the abdomen area. This feeling caused by stress induced changes in neurons of gut area. So, we understand a constant traffic signals through neurons from gut to brain. Thus gastro-intestinal system highly prone to stress induced discomfort. Pain, bloating, diarrhoea, appetite changes, vomiting, irritable bowel syndrome, ulcer, inhabitant bacterial changes, gastric PH changes are produced by influence of stress.[9]

In Oesophagus

Stress primarily changes appetite of a person. So, chance for increase or decrease intake of food by stressed individual. And also, to reduce intake of alcohol or tobacco also change the G.I function. Because of these changes heart burn and burping up of food from stomach to oesophagus takes place. Also, acid reflux, bloating and flatulence caused by these changes.[10]

In Stomach

The chronic stressed individuals have chance to develop increase of gastric acid production and stress ulcer.

In acute stress cases nausea, vomiting, bloating, loss of appetite are common gastrointestinal symptoms.[11]

In Bowel

Stress can cause either diarrhoea or constipation. Gut muscle movements are increased by stress cause rapid emptying of intestine. That leads to decrease nutrient and water absorption rate there by diarrhoea will produce. The rapid muscle movements cause G.I cramps. Diarrhoea is the major sign of irritable bowel syndrome.

Stress can also change the intestinal bacteria Content. That leads to immunity changes and more prone to get intestinal infections like inflammatory bowel disease.[12]

PATHOPHYSIOLOGY OF STRESS INDUCED G.I PROBLEMS

The stress effects on G.I tract mainly by changes in brain-gut axis responses. Thus, various abnormalities like Gastro-oesophageal reflux disease [GERD], Irritable -bowel syndrome, stress ulcer and inflammatory bowel disease etc.

The physiological actions in gut are controlled by the Enteric nervous system [part of central nervous system]. ENS carry millions of nerve cells as sensory

motor and interneurons. They have sympathetic and para-sympathetic links. After the stress stimulus is delayed and reach Hypothalamic- pituitary – adrenal axis [HPA axis] is producing Corticotrophin Releasing Factor (CRF). It directly produces some effects on gut like

1. Changes in permeability of gut.
2. Hypersensitivity to pain in visceral portion of gut.
3. Increase chance of inflammation
4. Changes in gut motility.
5. Gut microbiota transformation.

Persistent stress leads to the high amount of CRF production and sensitivity of non-adrenergic drive increased. And also decrease the response of glucocorticoid receptor. These changes indirectly lead to deviation on ENS actions.[13]

Role of CRF in G. I problems

In the stress event occurs the hypersecretion of adrenaline by the influence of Corticotrophin releasing hormone (hypothalamic peptide). It has great role in stress related gastro-intestinal problems. Apart from that cardiovascular, immune, metabolic reaction are produced by stress. CRF bind to peripheral CRF receptors and produce changes in gastric motility and mucosal function.[14]

In case of gastric motility decrease of intestinal propulsive movements resulting delaying of gastric emptying. Parentally administered CRF studies on humans, rodents etc shown that evidence. By the effect of gastric emptying delay change in gut transit also occurs. Peripheral mechanisms of central nervous system are the major reason in alteration in gut motility. The pressure waves on pyloric and duodenal region are increased by CRF. These increased propulsive movements in G. I tract leads to watery diarrhoea especially high CRF induced motility index found in patients having irritable bowel syndrome. The increase in water depletion by diarrhoea cause electrolyte (Sodium and chloride) imbalance.[15]

CRF receptors have subtypes as CRF 1 & 2. There are G- protein coupled receptors. Endogenous agonists of CRF receptors bind and Camp production increases. Urocortin 2&3 considered as endogenous agonists of CRF-2. The Urocortin 1 have effect on CRF 1&2. CP154 526 & NBI-27914 is considered as antagonists. The injection of CRF antagonists produce increase in gut motility.

Some G.I disorders characterized by mucosal barrier dysfunction. The gastric mucosa is large immune barrier against foreign pathogen. Most of immune cells found in tightly sequenced gastric mucosa. The permeability of substance through this cell junctions are very low. Mucosa composed of epithelial cells, endocrine cells and mucin producing Goblet cells.[16]

Different kind of stressors produce alteration in barrier function and increase in ion secretion. Transcellular and paracellular transport are activated by stress. So, horseradish peroxidase (HRP) like giant molecules are permeable through that function. Also, the mucin secretion, mast cell activation on mucosa also by the action of CRF.[17]

The patient with history of mental trauma is more susceptible for CRF induced gastric changes. Chronic stress produces apoptosis of epithelial cells. The defence mechanisms also reduced by persistent stress. Pathogen penetration is increased and also alteration in mucin production.[18]

EFFECT OF STRESS ON PATHOPHYSIOLOGY OF DIFFERENT DISEASES

Gastro-oesophageal reflux disease

GERD is the consequence of Brain- Gut Axis dysfunction. GERD develop by the lower oesophageal sphincter dysfunction. So, burping up of acid from stomach to oesophagus takes place. Thus, the feeling of heart burn develops. Stress has major role in development of GERD.

The chances of stress related heart burn and acid reflux is very low compared to stress ulcer. The reason for stress related GERD is unknown. Stress changes the breathing pattern and alteration in diaphragm pinch. Besides oesophageal sensitivity also increased in stressed individuals. But there is no evidence for gastric PH change by stress. Anxiolytics are found to be unable to be manage stress induced GERD.

Even though researchers don't yet fully understand the connection between GERD and anxiety, it's known that anxiety and stress can trigger or worsen symptoms

related to GERD. You may be able to relieve many of your symptoms of both conditions using at-home remedies, but both conditions do warrant a visit to a doctor

A burning sensation in your chest (heartburn), usually after eating, which might be worse at night. chest pain, difficulty in swallowing, regurgitation of food or sour liquid, sensation of a lump in your throat.[19]

MANAGEMENT

- **Antacids that neutralize stomach acid.** Antacids, such as Mylanta, Rolaids and Tums, may provide quick relief. But antacids alone won't heal an inflamed oesophagus damaged by stomach acid. Overuse of some antacids can cause side effects, such as diarrhoea or sometimes kidney problems.
- **Medications to reduce acid production.** These medications — known as H-2-receptor blockers.
- **Medications that block acid production and heal the oesophagus.** These medications — known as proton pump inhibitors — are stronger acid blockers than H-2-receptor blockers

Prescription-strength treatments for GERD include:

- **Prescription-strength H-2-receptor blockers.** These include prescription-strength famotidine (Pepcid) and nizatidine. These medications are generally well-tolerated but long-term use may be associated with a slight increase in risk of vitamin B-12 deficiency and bone fractures.
- **Prescription-strength proton pump inhibitors.** These include esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole and Dex-lansoprazole. Although generally well-tolerated, these medications might cause diarrhoea, headache, nausea and vitamin B-12 deficiency. Chronic use might increase the risk of hip fracture.
- **Medication to strengthen the lower oesophageal sphincter.** Baclofen may ease GERD by decreasing the frequency of relaxations of the lower oesophageal sphincter. Side effects might include fatigue or nausea.

Surgery and other procedures

- **Fundoplication**
- **LINX device.**
- **Transoral incisionless fundoplication (TIF).** [20]

Peptic ulcer

Most prevalent stress induced gastric abnormality is peptic ulcer. Like H. Pylori and NSAID derived peptic ulcer there is a strong background of develop peptic ulcer by psychological stress. And the mucosal damage of gut by pepsin and gastric attack.

The stress develops by,

1. Significant reduction in mucosal perfusion
2. Increase in gastric acid secretion
3. Decrease in bicarbonate release
4. Acid reflux
5. Decrease the speed of healing process in mucosa
6. Gastric propulsive movement changes.
7. Irritation on gut viscera
8. Mucosal permeability alteration
9. Increase bacterial count

High chance of peptic ulceration is found in patients admitted in intensive care unit. Stress affect Brain -Gut Axis and decrease the number of neuropeptides that have role in protection of mucosa.

Symptoms are dull pain in the stomach, weight loss,] not wanting to eat because of pain, nausea or vomiting, Bloating, feeling easily full, burping or acid reflux, heartburn, which is a burning sensation in the chest.

In one study the prisoners of Vietnam War have ulcer by stress. The chronic and persistent stress are the major threat for duodenal and peptic ulcer. In world war-2 reports of stress induced peptic ulcers also found. In the time of Hashin- Awajh earthquake in Japan a study on stress induced ulcer is conducted and found to be chance of bleeding ulcers in the time of stress. From these evidences the psychological and physical stress can produce gastric ulcer and further complications.

Stress ulcer- Even without treatment, **some ulcers will heal by themselves**. And even with treatment, ulcers sometimes come back. Certain factors such as cigarette smoking and continued use of nonsteroidal anti-

inflammatory drugs (NSAIDs) increase the risk of ulcers coming back-stopping the NSAIDs.

1. proton pump inhibitors, which cause your stomach to create less natural acid and help speed healing.
2. H2-receptor antagonists, which work much like proton pump inhibitors.[21]

Inflammatory bowel disease

Stress can evoke the ulcerative colitis and Chron's disease. In numerous studies, evidence of development of colitis by stress. Animal studies also available. In case of stress pathogenic microflora adhesion, transport and permeability to mucosal cells are increased. That give chance of exacerbation of colitis.

Some medical professionals found that chance of colitis can be increased by emotional problems. Some animal studies also stress induced ulcerative colitis was found. Another study with 10 subjects with persistent stress event on life found to be high chance of Chron's disease. Thus, the major stress events are like bereavement, marriage problem, major health issues have role in inflammatory bowel disease.

Crohn's disease is a type of inflammatory bowel disease (IBD). It causes inflammation of your digestive tract, which can lead to abdominal pain, severe diarrhoea, fatigue, weight loss and malnutrition. Inflammation caused by Crohn's disease can involve different areas of the digestive tract in different people.

MANAGEMENT

Anti-inflammatory drugs

Anti-inflammatory drugs are often the first step in the treatment of inflammatory bowel disease. Anti-inflammatories include corticosteroids and Amino-salicylates, such as mesalamine.

Immune system suppressors

These drugs work in a variety of ways to suppress the immune response that releases inflammation-inducing chemicals into the body. When released, these chemicals can damage the lining of the digestive tract. Some, examples of immunosuppressant drugs include azathioprine, mercaptopurine and methotrexate.

Biologics

Biologics are a newer category of therapy in which therapy is directed toward neutralizing proteins in the body that are causing inflammation. Examples include infliximab, adalimumab, golimumab, certolizumab, vedolizumab etc.

Antibiotics

Antibiotics may be used in addition to other medications or when infection is a concern — in cases of perianal Crohn's disease, for example. Frequently prescribed antibiotics include ciprofloxacin (Cipro) and metronidazole (Flagyl).

Other medications and supplements

In addition to controlling inflammation, some medications may help relieve your signs and symptoms, but always talk to your doctor before taking any over-the-counter medications. Depending on the severity of your IBD, your doctor may recommend one or more of the following:

- **Anti-diarrheal medications.** A fibre supplement — such as psyllium powder or methylcellulose — can help relieve mild to moderate diarrhoea by adding bulk to your stool. For more-severe diarrhoea, loperamide may be effective.
- **Pain relievers.** For mild pain, your doctor may recommend acetaminophen. However, ibuprofen, naproxen sodium and diclofenac sodium likely will make your symptoms worse and can make your disease worse as well.
- **Vitamins and supplements.** If you're not absorbing enough nutrients, your doctor may recommend vitamins and nutritional supplements.

Nutritional support

When weight loss is severe, your doctor may recommend a special diet given via a feeding tube (enteral nutrition) or nutrients injected into a vein (parenteral nutrition) to treat your IBD.[22]

Irritable bowel syndrome

Irritable bowel syndrome considered as a functional disease not an organic disease. It involves abdominal cramps, loose stools, constipation, bloating etc. Symptoms are not exist continuously remission occur frequently.

In this case psychological stress induced Brain-Gut Axis dysfunction and microflora changes have great role. Reduction in protective neuropeptides, immune system mediated hypersensitivity, motility changes on gut, microbiota changes also have a role. In the time of psychological stress evenly exacerbation is takes place.

Patients having history of sexual abuse have more prone to irritable disease. 66% of irritable bowel syndrome patients have psychological disease.

Irritable bowel syndrome (IBS) is a common disorder that affects the large intestine. Signs and symptoms include cramping, abdominal pain, bloating, gas, and diarrhoea or constipation, or both. IBS is a chronic condition that you'll need to manage long term. Onset of signs and symptoms after age 50

Weight loss, Rectal bleeding, Fever, Nausea or recurrent vomiting, Abdominal pain, especially if it's not related to a bowel movement, or occurs at night, diarrhoea that is persistent or awakens you from sleep, anaemia related to low iron

Irritable bowel syndrome can be manageable by,

- **Fibre supplements.** Taking a supplement such as psyllium with fluids may help control constipation.
- **Laxatives.** If fibre doesn't help constipation, your doctor may recommend over-the-counter laxatives, such as magnesium hydroxide oral or polyethylene glycol.
- **Anti-diarrheal medications.** Over-the-counter medications, such as loperamide, can help control diarrhoea. Your doctor might also prescribe a bile acid binder, such as cholestyramine, colestipol or cole-sevelam. Bile acid binders can cause bloating.
- **Anticholinergic medications.** Medications such as dicyclomine can help relieve painful bowel spasms. They are sometimes prescribed for people who have bouts of diarrhoea. These medications are generally safe but can cause constipation, dry mouth and blurred vision.
- **Tricyclic antidepressants.** This type of medication can help relieve depression as well as inhibit the activity of neurons that control the intestines to help reduce pain. If you have diarrhoea and abdominal pain without depression, your doctor may suggest a lower-than-normal dose of imipramine, desipramine or nortriptyline (Pamelor). Side effects — which might be reduced if you take the medication at bedtime — can include drowsiness, blurred vision, dizziness and dry mouth.
- **SSRI antidepressants.** Selective serotonin reuptake inhibitor (SSRI) antidepressants, such as fluoxetine or paroxetine, may help if you are depressed and have pain and constipation.
- **Pain medications.** Pregabalin or gabapentin might ease severe pain or bloating.[23]

Effect on intestinal barrier function

The intestinal barrier on gut made up of tightly connected cells. But there is permeability on these tight -cell junction found in case of stress. For example, mannitol and EDTA permeability on intestinal barrier on stressed rats.

In Bardy and Turnberg study found that electrolytes and water permeability on jejunal intestinal cells in stressed individuals. The reason for increasing permeability is action of elevated CRF levels. Dexamethasone can cause stress like events on intestinal barrier.

In case of highly stressed rats have elevation of mast cell number and permeability of intestinal barrier. Mast cells have CNS innervation and activated by CRF and Acetyl choline. Mast cell degranulation also increased in time of stress that produce secretory activities and spasms. And it leads to pain and loose stools called Irritable-bowel syndrome.[24]

Effect on Functional dyspepsia

The patients having dyspepsia are found under vagal tone and elevated sympathetic tone. Fear, pain and other stress responses cause delaying of gastric emptying and high intestinal contractility. These dysfunctions found to be chance of indigestion during stressed individuals. The CRF having receptor CRF-2 on vagal nucleus have role in reduction of vagal tone.

Effect on Gut microbiota modulation

By the action of Corticotrophin Releasing Factor (CRF) adrenaline release takes place and increases some bacterial virulence. For example E.coli and Jejune. Some of probiotic species reduce sensation to

the stimulus. So, the hypersensitivity reduces. But in case of stress sensitivity increases against to capsaicin like stimulus. Thus, excessive sensitivity to pain perception and hypersensitivity produces.[25]

MANAGEMENT OF STRESS

Try herbal remedies, avoid caffeine, especially coffee, practice deep breathing, mindfulness, and meditation, try calming diffuser oils or incenses, find space for yourself to relax are simple technique to manage stress.

Physical activity relieves tension and stimulates the release of chemicals in your brain called endorphins, which act as natural painkillers. Endorphins improve sleep, which can help relieve stress.

relationship between aerobic exercise and attentional focus during exercise on 33 patients with post-traumatic stress disorder (PTSD) and found that 89 percent of patients reported improvements in PTSD and anxiety sensitivity.

Cognitive- behaviour therapy (CBT) is a technique that has been proven to help reduce anxiety and stress by helping you learn to replace negative, distorted thoughts with positive ones. In one study looked at the effectiveness of CBT on quality of life, anxiety, and depression in those with IBD. Patients with IBD who reported low quality of life were randomly assigned a CBT intervention along with standard medical care for three and a half months. When compared with a control group, people with IBD who received CBT reported higher quality of life and lower levels of depression and anxiety.

Eating disorders and obesity can be associated with psychological stress. Cortisol, a hormone released by the adrenal glands, also increases appetite. Stress can affect food preferences, too. Studies have shown that "physical or emotional distress increases the intake of food high in fat, sugar, or both.

But there are certain foods that have been shown to reduce anxiety. Salmon contains omega-3 fatty acids, which are natural mood boosters. Almonds are chock full of magnesium, a mineral that helps manage cortisol levels. And oranges and other citrus fruits contain vitamin C, which can lower blood pressure

This mind-body practice combines physical poses with breathing techniques and meditation

women who engaged in hour-long Hatha yoga classes three times a week for 12 sessions achieved significant reductions in stress, anxiety, and depression. Research also shows that yoga can lower blood pressure and heart rate.

There are many meditation techniques that can help you focus your mind on an object, activity, or through to help you achieve calmness. Although the goal of meditation is not stress reduction, that is a side effect of this ancient practice.

An important part of stress reduction is self-care. For many, this involves managing your time as effectively as possible looked at the relationships between time management, anxiety, and academic motivation in 441 nursing school students using self-reported questionnaires and scales. Students who did a poor job managing their time had higher levels of anxiety and less academic motivation than individuals who were better time managers

A common side effect of stress is that you may struggle to fall asleep. If this happens three times a week for at least 3 months, you may have insomnia, an inability to fall and stay asleep. Lack of sleep can also add to your stress level and cause a cycle of stress and sleeplessness.

Better sleep habits can help management of stress.

Biofeedback- Sensors are placed on your body that call out changes in everything from your brain-wave pattern to your muscle tone. Working with a biofeedback therapist, you can start to take control of the signals by changing how your body reacts to the sensor.[26]

CONCLUSION

Stress broadly affects our body systems especially Cardio-vascular system, endocrine system, reproductive system, gastro-intestinal system, immune system etc. Gastro- intestinal system highly affected by psychological stress. Stress ulcer, irritable bowel syndrome, inflammatory bowel disorder and GERD caused by different type of stresses. Stressed induced hyper secretion of Cortisol is the major reason for the most of stress related disorders. Techniques likes Yoga, meditation, physical exercises produce

prevention and reduction of stress. In case of gastro-intestinal disorders some anxiolytics, ulcer-protectives, food changes can manage complications.

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