

Stress and Other Factors Involved in the Pathophysiology of Irritable Bowel Syndrome. Review

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Abstract

Stress is associated with gastrointestinal diseases. Irritable bowel syndrome (IBS) is a common multifactorial functional gastrointestinal disorder with a point prevalence of 11% in the adult western population. However, it can reach 35% depending on the country. It has observed a higher prevalence of functional digestive disorders in certain families which has established the possibility of a genetic predisposition the variability in prevalence can be due to different symptom-based diagnostic criteria, sample selection, access to health care, and/or cultural factors. Authors have demonstrated the role of negative affects, including depression, anxiety, and anger, on pathogenesis and clinical manifestations of IBS. In inpatients with psychological stress have been demonstrated increased rates of IBS and dyspepsia.

The etiopathogenesis of IBS not yet completely understood. This pathology is characterized by: abnormal colonic motility with alterations in bowel habits (constipation and/or diarrhea), altered stool passage (urgency or feeling of incomplete evacuation), visceral hypersensitivity, perception of pain incremented and feelings of abdominal distension, alimentary intolerance, participation of mast cells and inflammation, alteration of the intestinal microbiota, affectation of the autonomic nervous system, and by the influence of the stress in its development and evolution.

The autonomic nervous system, stress-hormone system, and immune system have an important role in the pathophysiology of IBS. It is know that stressors that affect and alter the hypothalamic-pituitary-adrenal and the intestine-brain axis induce the secretion of hormones, cytokines or regulating proteins and other mediators. These make up a complex network of interactions with an important dysregulation, affectation of the gastrointestinal tract, recurrent clinic manifestations, and propensity to the chronicity and to the deterioration of the quality of life. However, there are substantial differences in the response each individual to acute or chronic stress. Therefore, is obvious to evaluate the organic and psychological consequences of individuals under stress with IBS, for the prescription of timely therapy.

Keywords: *Stress; Eustress; Distress; Irritable Bowel Syndrome; Hypothalamic-Pituitary-Adrenal Axis; The Intestine-Brain Axis; Cytokines; Psychological Therapy*

Introduction

The affectation of the stress worldwide is very important due its psychosocial and work repercussion. Stress-related diseases have determined the increase of long-term sick leave during the last decade in many European countries (Ec) [1-3]. 80% of the general population in Ec will have an increase of work related stress in the next five years. Factors connected to stress have been evaluated [1]. According to Statistics Sweden about 66% of the Swedish working population perceives their work situation as stressful and 42.5% that work was

too psychologically demanding [4]. Fifty percent of workers in industrialized countries consider their work as “mentally demanding”. In Latin America, work stress is recognized as one of the great epidemics of modern working life [5].

The existence of benefits to patients with cancer [6], arthritis [7], fibromyalgia [8] and chronic pain [9] with the utilization of psychology therapy in its various modalities, reveal the influence that have the stress on pathological entities. Many are the causes that can provoker stress, in addition, to the work and the diseases. Authors appoint that the prenatal exposure to severe life events increases the possibility of hospitalization for asthma in the offspring [10]. Also, the stress can affect all the organic systems, such as: gastrointestinal, SNC, respiratory, endocrine, cardiovascular and immune among others and make it through the stimuli and network of mediators or regulating proteins as part of various mechanisms. One consequence of chronic stress is burnout [11] which is a condition called Exhaustion Disorder (ED). The diagnostic criteria include exhaustion, cognitive dysfunction, sleep problems and somatic symptoms. A dominant feature is the lack of energy [12]. The prevalence of moderate to high burnout in midwives varies from 20 to 59% in countries such as Sweden [13]; Norway [14], United Kingdom (UK) [15-18]; and Australia [19-21].

It is necessary to define stress and its types for greater understanding. Stress is a set of physiological and psychological events experienced by the body when is subjected to strong demands. When the stress is excessive due to too stimulation, we are in the presence of Distress, with loss of the harmony between the body and the mind, what prevents respond appropriately to situations everyday life. On the other hand, the term Eustress, is used to define the situation in which good physical and mental health facilitates the body as a whole acquire and develop its full potential. The state of eustress is clearly associated optimize mental and physical conditions. The most important is to achieve a moderate level of stress that allows solving adequately the situations of the daily life [22].

Risk factors that can cause stress are many, such as: the degree of responsibility, work overload, the suffering “by diverse causes”, inability to file complaints and problems of group interrelationship. The above is raised in the work area but is extensive in many aspects to the family environment especially if it is consider the human being as a biopsychosocial entity with goals, dreams and achievements [23]. WHO revels: “Health is not only the absence of disease but a positive state of physical, mental and social well-being” [5].

Therefore, based in the importance of this theme, it is present in this review the evaluation of all the relevant aspects relate with the stress and its influence in the pathophysiology of a chronic clinic entity as is irritable bowel syndrome that affect the quality of life of the ill patients.

Stress and Hypothalamic-pituitary-adrenal (HPA) axis

HPA axis plays a key role in adaptation to environmental stresses. Regulation of glucocorticoid secretion through adrenocorticotrophic hormone (ACTH) is critical to life and essential to maintain the mammalian response to stressor [24]. The nucleus paraventricularis hypothalami (NPH) of the HPA axis, secretes corticotrophin releasing hormone (CRH) and arginine vasopressin (AV); the pituitary gland that is sensitive to CRH and AV, secretes ACTH which act on the adrenal gland cortex and secretes glucocorticoids, mainly cortisol and dehydroepiandrosterone (DHEA) in humans and non-human primates [25,26].

Stress: participation of regulating proteins and hormones

Researchers have shown the importance of stress hormones such as glucocorticoids and catecholamines which inhibit the production of the following proinflammatory regulating proteins: Interferon-gamma (IFN- γ), interleukin-12 (IL-12) and tumor necrosis factor alpha (TNF- α). IFN- γ inhibit Th2 cells with diminish of the production of anti-inflammatory cytokines, such as Interleukin-4 (IL-4) Interleukin-10 (IL-10). IL-12 stimulates Th1 cells which secrete interleukin-2 that favor the production by regulatory T cells of inhibitory cytokines, such as: transforming growth factor- β (TGF-beta) and IL-10. TGF-beta inhibits the Th1 and Th17 cells both producer of proinflammatory regulating proteins. IL-10 breaks macrophages. Therefore, an excessive immune response stimulates an important negative feedback mechanism, which protects to the organism of excesses of proinflammatory cytokines and other products of activated macrophages which results in tissue damage [27].

Stress and irritable bowel syndrome (IBS)

Stress is associated with gastrointestinal diseases [28,29]. IBS is a common multifactorial functional gastrointestinal disorder with a point prevalence of 11% in the adult western population. However, it can reach 35% in some country. The variability in prevalence can be due to different symptom-based diagnostic criteria, sample selection, access to health care, and/or cultural factors [30-33].

The observation of a higher prevalence of functional digestive disorders in certain families [34] has led to the possibility of a genetic predisposition. A study in twins concluded that the possibility of suffering functional digestive disorders can be attributed in 56.9% to genetic factors and in 43.1% to environmental factors [35].

Authors have demonstrated the role of negative affects, including depression, anxiety, and anger, on pathogenesis and clinical manifestations of IBS. The autonomic nervous system, stress-hormone system, and immune system have an important role in the pathophysiology of the negative affects on IBS [36]. It is has observed the stress impact on the developing brain-gut-microbiota axis [37]. In inpatients with psychological stress have been demonstrated increased rates of irritable bowel syndrome (IBS) and dyspepsia [38].

Researches have suggested a relevant role for mucosal immune activation in IBS. In the majority of cases the routine histologic examination reveals no mucosal abnormality. However, in quantitative histological, immune-histochemical and ultrastructural analyses reveal the presence of subtle morphologic changes in mast and enterochromaffin cells, as well as, in lymphocytes and enteric nerves. These changes are very important as have led linking central and enteric nervous systems to immune processes [39].

The etiopathogenesis of IBS not yet completely understood. Complex interactions of abnormal colonic motility with alterations in bowel habits (constipation and/or diarrhea), altered stool passage (urgency or feeling of incomplete evacuation), visceral hypersensitivity, perception of pain incremented and feelings of abdominal distension [40,41], participation of mast cells and inflammation [42], Alimentary intolerance [43], participation of the intestinal microbial community and alteration of microbiota [44,45], affectation of the autonomic nervous system [46,47], and, acute and chronic stress [48,49] are determinate factors in the development and evolution of IBS.

With respect to behaviors and psychology aspects, many investigations have provided very valuable information. Researches appoint the existence of high positive (PA) and negative affects (NA) individuals. PA involves happiness, interest, motivation, and mental alertness [50]. In de case of High NA individuals usually present significant levels of distress, even in the "absence of objective stressors". They are also more introspective, suffer from poor self-esteem, and tend to focus on the negative side with hyper-reactive in front of stressful events [51]. The right hemisphere of brain (frontal lobes) have been implicated in NA and behavioral inhibition (withdrawal tendencies), whereas the left hemisphere have been implicated in PA and approach behaviors. It is recognized the existence of separate cerebral circuits and anatomical systems mediating positive and negative affectivity. Neurobiological differences determine the propensity towards one or the other type [52]. All the expressed, establish the importance of the psychological contention mechanisms and the family education when the unpleasant circumstances of life are present. In this form can avoid or control problems of health before the presence of chronic state of discomfort. However, the genetic condition, early maternal care, environmental factors and life experiences of each of the individual among others are relevant factors that should always be considered for the evaluation of the results of the both medical and psychological therapies used.

Authors appoint that the "Neuroticism" is defined as the tendency to negative experiences and distressing emotions [53] and it is characterized by emotional instability. "Neuroticism" has been related with a broad range of diseases such as IBS [54,55], even when depression and other risk factors are controlled. "Type D personality" a concept derived from empirical and theoretical research, is characterize by: NA, and social inhibition (SI) [56,57]. This type of personality is vulnerable to chronic stress, and it has been associated with medical comorbidity as well as unfavorable medical and psychological clinical courses [58]. In IBS is has studied the serotonin (5-HT) neurotransmission system, and it is has hypothesized that the co-occurrence of NA and IBS may be related to serotonergic hypofunction both in the emotional motor system and Central Nervous System [59].

Cytokines and other mediators in irritable bowel syndrome (IBS)

Studies have shown increased levels of the proinflammatory cytokines such as interleukin-6(IL-6) and interleukin-8 (IL-8) in IBS patients, whereas the comorbidity, including depressive states, is associated with increased levels of interleukin-1 beta (IL-1 β) and tumor necrosis factor- α (TNF-alpha) [60]. Researchers have found higher levels of IL-6 and C-reactive protein (CRP) among individuals with high anger and lower levels among those with high anger control [61]. Nowadays, it is marked the hypothesis of the “cytokines of depression”. It is consider that psychosocial and internal stressors can trigger depression by inflammatory processes induced by cytokines, and by alterations in the neuroendocrine system [62]. However, the regulating proteins form a network so extensive that it needs to be discussed later.

The gut-brain (or brain-gut) axis [63-65] is a set of channels of communication between these organs. In a bidirectional type connection, the central nervous system sends information to the intestine anatomic pathways, such as hormones, neurotransmitters and cytokines [66-68]. This axis is stimulated by stress to start all the mechanisms of connection and feedback. Authors appoint that in IBS there is hyper function of the sympathetic activity along with hypofunction of the parasympathetic activity which has been described in anxiety disorders [69].

Similarities and differences between IBS and IBD

IBS shares some similarities in symptoms with intestinal inflammatory disease (IBD) but are distinct medical conditions. IBS is a functional disorder with abdominal pain and alterations in defecation. The clinical value of IBS diagnostic criteria is determined by its ability to discriminate between functional and organic pathology [70].

IBD represents a range of organic, immune-mediated inflammatory disorders (e.g., Crohn's disease and ulcerative colitis), characterized by abdominal pain, urgent diarrhea, rectal bleeding, weight loss and fatigue among other clinic manifestations. In Crohn's disease (CD), but not in ulcerative colitis (UC), the intestinal injury is discontinuous with granulomatous inflammation. Although IBS and IBD are disorders different, both are associated with low quality of life and the possibility of that psychological intervention can be helpful to decrease symptoms and improved the conditions mental and organic of patients [71,72].

Psychology therapy in IBS

Cognitive-behavioral therapy (CBT) for IBS “emphasizes cognitive, emotional, and behavioral strategies to better cope with physiological and psychological stressors”. Authors have demonstrated the effectiveness of the therapy for IBS in terms of improved gastrointestinal symptoms, quality of life, and the role of stress management as key mechanisms to regulate IBS pathophysiology. The treatment showed promising results in individual affected by IBS [73-79]. CBT was developed initially as a treatment for depression. In the CBT model, the relationship between situations, thoughts, behaviors, physical reactions, and emotions is the primary center of treatment [80].

In 1984 was appoint the utility and effect of the hypnotherapy(HT) in IBS and it is found that is more effective than control treatment to improve gastrointestinal disorders and quality of life [81]. HT has been effective in 83% of the cases with long-term therapeutic benefits, for 1 - 5 years after the course of treatment [82]. HT is as effective as dietary treatment (FODMAPS) for IBS [83]. Further research in this area is warranted. However, the HT has been beneficous to other diseases or chronic symptomatology, such as: cancer [6], arthritis [7], fibromyalgia [8], and chronic pain [9]. The mechanism of action for HT in IBS is not fully understood. Hypothetically the HT has direct effects on gut function [84,85], visceral sensitivity [86] and psychological factors (e.g., cognitive patterns, anxiety, and depression) [87,88]. Studies of imaging have suggested that HT may normalize pain processing in the anterior cingulate cortex, a region of the brain with collar shape surrounding the corpus callosum, which has been shown to be over-active in some IBS patients [89,90].

There are other methods that could help to the patients with IBS, such as: Mindfulness-based therapy (MBT) with exercises of breathing, eating, listening and observation. Although there are many variations of MBTs, most are based on Jon Kabat-Zinn's Mindfulness Based Stress Reduction (MBSR) program for coping with chronic illness [91]. A short program in mindfulness meditation produces demonstrable effects on brain and immune function. These findings suggest that meditation may change brain and immune function in positive ways. It is required additional research [92].

Physiological, affective, cognitive, and behavioral factors have been postulated and evaluated in IBS. It is necessary to take conscience of the quality of life that we deserve. From our site of daily activity and subjected to constant stress we could all learn the psychological tools that allow a better life. Forgetting this, affect us and influences directly and indirectly to others. The people who inhabitants in the world need to change, in a congruent way, to achieve a better coexistence and happiness. The contention of the family is very important but in case of cannot obtain this; the help psychology, the resilience and sharing with positive people are key factors.

Conclusions

Irritable bowel syndrome (IBS) is a common multifactorial functional gastrointestinal disorder with an etiopathogenesis not yet completely understood. Authors have demonstrated the role of negative affects, including depression, anxiety, and anger, on pathogenesis and clinical manifestations of IBS. In inpatients with psychological stress have been demonstrated increased rates of IBS and dyspepsia.

Genetic condition, pleasant or not familiar situations, selective or general insight of educational elements, lived experiences, perception of the environment positively or negatively and the resilience establishes differences between the individuals. Stressors that affect and alter the hypothalamic-pituitary-adrenal and the intestine-brain axis induce the secretion of hormones, cytokines and other mediators. These make up a complex network of interactions with an important dysregulation, affectation of the gastrointestinal tract, recurrent clinic manifestations, and predisposition to the chronicity and to the deterioration of the quality of life. However, there are substantial differences in the response each individual to acute or chronic stress. Therefore, is obvious to evaluate the organic and psychological consequences of individuals under stress with IBS and implement the relevant measures.

Conflict of Interest

I have no conflict of interest.

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