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Gastroesophageal reflux disease

Heartburn from a psychological view

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Although gastroesophageal reflux disease (GERD) can be traced back to disorders of the gastroesophageal junction, stress and other relevant psychological factors can play an important role in the process of GERD. It would seem that, primarily, altered symptom perception based on threshold reduction exists in some patients. In an effort to describe the sensitisation for reflux symptoms, both central and peripheral factors can be discussed. The following is conceivable: that well defined personality factors moderate the effect of stress on the gastroesophageal junction, just as they can influence the perception and assessment of symptoms. Additionally, psychiatric disorders as comorbidities can also accompany GERD. For this reason, it is necessary to consider if an extension of hitherto psychological interventions could be helpful in patients with a subjective link between reflux and stress on an emotional personality related level, or in patients with attendant psychiatric disorders. This broadening relates both to the conservative use of antireflux medication and to surgical therapy, since a postoperative shift in symptoms can occur. The effectiveness of psychological interventions in several gastrointestinal patient groups could already be shown in the past, whereas evidence for their effectiveness in patients suffering with GERD is partly still outstanding and should be investigated in the future especially as several individual promising starts have been made.

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The world-wide variation in the significance of gastroesophageal reflux disease (GERD) can be clearly described by its strongly divergent incidence. In the western world, GERD represents the most common disease of the upper gastrointestinal tract. Approximately 40% of the adult Western population suffers from GERD-related symptoms monthly, but in contrast, the incidence in Senegal is close to 0.5%. Parallel to this, significant racial differences, but also differences relating to age, the intensity of symptoms and the kind of complications of the disease are known.[1, 2]

The spectrum of typical symptoms ranges from heartburn, epigastric and chest pain, regurgitation, belching, sometimes accompanied by sensations of taste and dysphagia, to respiratory symptoms. However, more accurate anamnesis raises an additional spectrum of untypical symptoms which can be linked to GERD.[3, 4] Nevertheless, a symptom is how a person perceives and interprets a stimulus. Therefore, GERD symptoms and the perceived severity are more than a simple pathological reflux of gastric contents back into the esophagus. The purpose of this

review is to analyse the relationship between GERD and possible psychological aspects.

A psychological view

Since the end of the 1970's, an increased number of studies have been performed in order to establish potential relations between the symptoms and causal factors of GERD on the one hand, and psycho-physiological, as well as other psychologically relevant factors on the other. Recent studies have shown, that up to 60% of patients with GERD-related symptoms noticed an increase in complaints under conditions of stress.[5, 6] On the basis of pH monitoring of reflux patients, it could be established that less than 20% of the objective reflux episodes accompany subjective reflux symptoms, as seen from the patients point of view.[7] Contrary to this, complaints without objective results are perceived [8] whereby a slight correlation between acid exposure in the esophagus and symptom perception is acknowledge.[9]

In recent years, numerous studies in this context have been performed in order to link possible psychophysiological factors such as psychological stress or personality aspects with reflux-associated processes. It must be noted that most studies proceeded under laboratory conditions and therefore did not take into consideration everyday stress situations, or were conducted with healthy individuals. Some of the physiological stressors performed (*e.g.* cold pressor task) produced highly individual threshold values with respect to their perception, despite defined physical properties and well standardised research practices in relation to the sampling. Furthermore, the intensity of mental stressors from motivation as well as the intellectual potential and pre-experiences or expectational attitude are sample dependent. As a consequence of this, the results are under controversial discussion.

Psychological stress and esophageal manometry

In 1925 and 1927 [10, 11] the first tests with respect to changes in motility of the distal esophagus and laboratory induced stress had already been conducted by Jacobson. Rubin *et al.*[12] conclude that non-propulsive contractions in the distal esophagus can be induced in 5 healthy individuals through burdensome questioning. Young *et al.*[13] investigated the effects of the "cold-pressor-task", noise disturbance of 100 dB and cognitive problem solving exercises on esophagal manometric values in 25 healthy individuals. A short-lived rise in pressure at the lower esophageal sphincter, followed by relaxation and changes in esophageal motility occurred under both physiological and cognitive stress conditions. Additionally, Ayres *et al.*[14] found comparable results in patients with irritable colon, as did Anderson *et al.*[15] in 19 patients with non-cardiac chest pain. A significant rise in amplitude of esophagus contraction occurred under a variety of stress conditions, whereby cognitive problem solving exercises proved to be more burdensome that noise disturbance. Other studies [16, 17] proved that stress is accompanied by a postprandial slowing of sphincter relaxation or gives rise to intensified contraction of the hiatal crura whereby, in principle, a rise in sphincter pressure and reduced reflux occurs. From these results it is possible to infer, that different stress conditions lead to changes in esophagus motility and changes to the lower sphincter, and can thus be partly linked to reflux events. However, changes as a result of long-term stress on the function of the gastroesophageal junction have not been shown.

Psychological stress and pH-monitoring

Investigations into possible relations between laboratory stress and pH monitoring produced negative results. Bradley *et al.*[6] found no relation between distinct experimental stressors and objective parameters such as the number of reflux episodes, duration of the longest reflux phase or the total acid value of the test phase in 17 reflux patients. Whereas, other physiological parameters such as heart rate and blood pressure rose significantly, providing evidence as to the

stressful nature of the test phase. In contrast to the above, patients with subjective links between stress and their reflux symptoms, a significant rise in exclusively subjectively perceived complaints experienced under test conditions. Cook and Collins [18] achieved partly comparable results in healthy subjects, during the course of their investigations into postprandial reflux. Likewise, Sonnenberg *et al.*[19] found no association of any sort between noise disturbance and acid secretion in the stomach, blood supply to the mucosa in healthy subjects.

Nevertheless, Holtman *et al.*[20] reported interesting findings: the authors investigated the effect of mental stress on the gastric acid secretion with respect to personality traits. The trait "impulsiveness" was found to be a relevant one in healthy subjects. People with highly pronounced "impulsiveness" exhibited a significant rise in acid, whilst the acid values fell in people with less pronounced "impulsiveness". These results lead to the conclusion that stress evokes only limited changes in acid secretion. A change would most likely take place in the subgroup of GERD patients with a subjective interaction between stress and perceived symptoms and within the confines of emotion and a defined personality structure. A further moderating variable could be "fear".[21, 22] This increases in times of stress and leads *via* the neuronal level, centrally, to a sensitising of physiological processes and thereby to increased symptom and pain perception. That such an event could form the basis for sensitive esophagus or NERD (non-esophagitis reflux disease) in patients, is at the very least, under debate [23-25] and the subject of current studies. Fundamentally, it is known that patients suffering from endoscopic negative reflux disease display a comparable symptom spectrum and with corresponding intensity, as well as identical disease profile to patients with an erosive disease.[26]

NERD and "functional heartburn"

On the basis of current research, it has to be assumed, however, that NERD is fundamentally not the question of a pure psychological phenomenon. Galmiche and de Varannes [27] offer a detailed overview of non erosive reflux disease. Cohen and Snape [28] present a plausible hypothetical model of potential psycho-physiological and cognitive interactions between excitatory and inhibitory neurohumeral substances with stress and their effect on the distal sphincter. Few neuro-physiological studies of the gastroesophageal junction [29, 30] describe nervous reflux and stimulation processes which are responsible for the perception of pain, vomiting or false sensations and which can at least, be indirectly linked to reflux events. Kellow *et al.*[31] and Drossman *et al.*[32] present reviews about fundamental principles of neuro-gastroenterology with respect to physiology and symptom perception.

In approximately 40% of NERD patients no evidence for a pathological acid burden on the distal esophagus has been found using pH monitoring. Despite existing parallels to GERD or NERD, the disease profile is described as "functional heartburn" and according to the "Rome II Consensus Report" is categorised under functional esophagus disorders.[33]

As per definition, the diagnosis "functional heartburn" is given when primary symptoms (heartburn or chest pain) appear for a period of 12 weeks (within the previous 12 months) and without any pathological explanation such as GERD, achalasia or esophageal motility disorders. Contrary to patients with GERD, there is a significantly stronger link between acid exposure (whether low or normal) in the distal esophagus and the timely perception of symptoms in patients diagnosed with "functional heartburn".[34] The real cause in unclear, however, hypersensitivity of the receptors in the esophagus to intraluminal stimuli is primarily suspected [34, 35] (hypersensitive esophagus). Shi *et al.*[36] experimentally showed (intra-esophageal balloon distention test) that mechanical stimuli lead to symptoms significantly earlier in these patients than in other individuals. Mixed reflux, as a further factor is also discussed.[37] Principally, psychological factors are also discussed alongside the various possible physiological explanations. In contrast to other

functional gastrointestinal disorders very few studies exist [22, 38, 39] which concentrate exclusively on possible links between psychological factors and "functional heartburn", rather, it is more than likely the case that partly highly controversial results exist. The most probable potential factors are stress or fear. Treatment is *per se* identical with all GERD.[40] Furthermore, the prescribing of antidepressive medication in low doses is also under discussion.

Personality and symptom perception

As mentioned above, beside impulsiveness and fear, it seems that other characteristics such as social withdrawal, depression or somatisation can also be associated with changes in motility and gastric acid secretion.[21-23, 41, 42]

Own results [33] on 100 reflux patients support the view that besides partly significant differences in personality, differences in the stress management strategies of routine daily life exist between stress sensitive and unspecified stress reflux patients. Stress sensitive patients favour an intensely active stress management; frequently show aggressive tendencies and are more likely to forego social support respectively display less tendency of flight when under stress. As far as their personality structure is concerned, they perceive themselves as highly achievement orientated, experience at the same time a greater number of physical complaints and tend toward psychosomatic misperceptions. Moreover, apart from more numerous and more stressful reflux symptoms, stress specific reflux patients report further gastrointestinal symptoms. These, despite successful surgical therapy performed in the light of intensifies or displaced symptoms, nevertheless come to the forefront. Significant differences with respect to the time of day (upright *versus* supine refluxers) at which events occur could also be confirmed. Over 90% stress sensitive GERD patients can be described as daytime refluxers. Differences in objective parameters (DeMeester Score, esophageal manometry) have not been found. Velanovich *et al.*[25] came to similar conclusions. The authors found no or only slight correlation between the pressure on the lower esophageal sphincter, results from pH monitoring, the degree of GERD and quality of life. Significant links were only found between the number of perceived complaints and quality of life.

On the basis of these reports, it does not seem to be a question of a "psycho-physiological" disease, as was previously thought, even if GERD-related symptoms are significantly more present in patients with psychiatric comorbidities.[41, 43] However, it is certain that GERD, that is, the perception of GERD symptoms perception as a result of stress, emotional stress, a particular type of personality structure can be influenced in some of the patients. This knowledge should therefore be incorporated in the process of medical diagnosis and therapy of at least this element of patients.

Medical treatment and affecting psychological aspects

From the medical point of view, there are 2 fundamentally different treatment concepts, which can each be followed when indications are clearly defined. In the present review, the potential option of endoscopic treatment procedures has been excluded. Generally, the aim of any therapy, besides the achievement of a disease free state, and thereby an improvement in patients quality of life as seen from the patients point of view, is the healing of esophagitis, the prevention of the development of progressive disease and also prevention with respect to the development of a potential Barretts' esophagus. This fundamental aim of therapy can be achieved with the use of antazida, prokinetics, H2 antagonists and/or proton pump inhibitors. The signal to discuss surgical therapy is only given if suffering is particularly high and quality of life is severely impaired; if complications of GERD have arisen; if a causal functional defect is evident and lastly, if general health of the patient is good enough to withstand an operation.[2]

Accompanying medical therapy, patients

are in most cases obliged to initiate particular behavioral changes in order to achieve a further improvement in the disease profile.[44] However, no prospective randomized studies exist, which unequivocally and wholly support the efficacy of these theoretical improvement measures. Here, it is primarily a question of behavior related measures of everyday habits, and a consequence of this is the emergence of the first possible psychologically oriented interventions. It is common known that it is not always easy, despite medical advice, to effect behavioral change or the abandonement of daily rituals (*e.g.* weight reduction, eating behavor, stress management). This is often only achievable through appropriate psychological intervention.

Nevertheless, GERD is a chronic condition and the majority of the patients' need a lifelong medication to treat their symptoms. In this relation it has to be stated that a long-term use of drug therapy is always a question of patients compliance, even if a "on demand" therapy is under debate. Own data [45] have shown that approximately 25% of GERD patients referred to presurgical examination are not compliant in relation to medical prescriptions, and about 40% are just partly compliant. The reasons for being non-compliant are, in general, a rejection of any kind of medication use, less information about GERD, low severity of GERD, but also an aspect of patients' personality which also affect quality of surgical outcome.

Interventions from a psychological view

Several studies have been conducted from a psychological point of view. These investigated the effect of biofeedback on the lower esophageal sphincter pressure and on reflux symptoms.[46-48] Due to the high technological cost involved, most of these were single case studies. Gordon *et al.*[48] used biofeedback to alter the resting pressure of the lower esophageal sphincter from 2.7 mmHg to 8.7 mmHg in only 10 sittings in a patient who had been suffering from GERD-related symptoms for 8 years. At the same time, reflux symptoms and also the number of single reflux events were significantly reduced. The effect of hypnosis induced deep relaxation on gastric acid secretion was investigated and a reduction in the latter was evident.[49] This relaxation technique is nevertheless concerned with a selective method which presupposes a special choice of patient and is therefore of only limited application.

Only one systematically applied investigation was concerned with the effect of progressive muscle relaxation (Jacobson) on reflux events. This relaxation technique is easy to learn, efficient and is successfully practised in phobia therapy, stress management or on patients with gastrointestinal disorders. McDonald-Haile *et al.*[50] were able to show that progressive muscle relaxation, leads to a reduction in subjective symptoms, as well as to an objectively lower acid exposition in the esophagus. Additionally, an anxiolytic effect was also achieved. Unclear, however, is the exact mode of operation of this relaxation on reflux events. According to the authors, in the context of perceptional changes, not only is it possible to directly influence the gastroesophageal junction and the hiatal crura, it is also possible to influence these areas *via* an anxiolytic change in the form of a moderation process.

In contrast to medical therapy, surgical intervention studies substantiate the effect of psychological factors on the subjective quality of the results.[51, 52] Personality traits seem to play an essential role in the subjective assessment of stress of postoperatively essential adaptation processes (*e.g.* eating behavior) as well as in the subjective assessment of dysphagia.[52] Also in respect to patients' personality, the initial degree of compliance with former antireflux medication seems to be a good predictor of surgical outcome. Own data [53] have shown that surgically treated patients with former non-compliance with medication are eventually limited good candidates for surgery. In contrast to compliant patients, these group of patients significantly suffered from higher a degree of dysphagia and other so-called surgical side-effects

(*e.g.* gas-related problems), needed postoperatively more additional medical intervention including redo-surgery, and quality of life improvement or patients' satisfaction was comparable negatively affected. In relation to these findings, initial results of an existing intervention study substantiate with respect to this the positive effect of an additional, psychological intervention on surgical patients.[54]

Finally, an essential aspect should be pointed out. It is certain that a not inconsiderable number of psychiatric disorders can appear as comorbidity to gastrointestinal diseases.[55, 56] In this respect, prevalence between 5% and 20% are put forward according to disorder profile. Depression and panic disorders are in the forefront.[57] The literature alludes to possible associations with the emergence of panic disorder where there are existing functional esophageal disorders, just as there can be with GERD. Behavioral techniques exist in the treatment of panic disorders with GERD symptoms. Own results, also, surprisingly substantiate a positive effect of laparoscopic antireflux surgery in GERD patients with comorbidity of a panic disorder. In this way, the elimination of anxiety disorders in 1/3 of these patients was achieved within the first few postoperative months.[58] In contrast, other psychiatric comorbidities in GERD patients are able to affect surgical outcome negatively.[59, 60] As previously published,[60] GERD patients with major depression as comorbidity, when treated with laparoscopic Nissen fundoplication, show a significant lower quality of life improvement and a higher degree of swallowing problems or postoperative adaptation problems in comparison to patients who underwent a Toupet fundoplication. The authors concluded that eventually a Toupet fundoplication, independently from manometric findings, could be beneficial in such a group of patients with psychiatric comorbidities to improve subjective surgical outcome. However, further investigations in this field are needed and could be helpful for all, gastroenterologists as well as surgeons, to find an optimal procedure resulting in a high level of patients satisfaction and quality of life improvement.

Riassunto

Malattia da reflusso gastroesofageo. Il bruciore di stomaco da un punto di vista psicologico

Sebbene la malattia da reflusso gastroesofageo (MRGE) possa essere fatta risalire a dei disturbi della giunzione gastroesofagea, lo stress e altri rilevanti fattori psicologici possono svolgere un ruolo importante nel processo della MRGE. Sembrerebbe che, inizialmente, esista in alcuni pazienti un'alterata percezione dei sintomi, basata su una riduzione della soglia. Nel tentativo di descrivere la sensazione dei sintomi da reflusso, possono essere discussi sia fattori di tipo centrale sia periferico. È ipotizzabile quanto segue: che ben definiti fattori della personalità moderino l'effetto dello stress sulla giunzione gastroesofagea, così come possono influenzare la percezione e la valutazione dei sintomi.

Inoltre, la MRGE può anche essere accompagnata da disturbi psichiatrici, come comorbidità. Per questo motivo, è necessario considerare se un ampiamento degli interventi psicologici finora eseguiti possa essere utile nei pazienti con un legame soggettivo tra il reflusso e lo stress, su un livello relativo di personalità emotiva, o in pazienti con associati disturbi psichiatrici. Questo allargamento ha attinenza sia con l'uso cauto di una cura antireflusso che con una terapia chirurgica, dal momento che può verificarsi un cambiamento dei sintomi. Nel passato si è anche potuta dimostrare l'efficacia degli interventi psicologici in diversi gruppi di pazienti con problemi gastrointestinali, mentre le prove della loro efficacia nei pazienti affetti da MRGE sono ancora in parte in via di valutazione, nel futuro dovrebbero essere ancora verificate dal momento che sono già stati compiuti dei notevoli progressi.

Parole chiave: Malattia da reflusso gastroesofageo, psicopatologia - Psicologia - Stress.

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