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Gastroesophageal reflux disease associated symptoms management in patients with chronic conditions

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ABSTRACT

Gastroesophageal reflux disease is a worldwide prevalent medical condition. It not only impacts the life quality of patients, but also plays a role in the socio-economic aspect in terms of management of symptoms and therapy. Attentive diagnosis is made after a physical examination that excludes other possible conditions such as cardiac or systemic diseases. Medication must be chosen in agreement with other underlying conditions (diabetes, autoimmune or rheumatic diseases etc.) as many interactions may occur otherwise. The role of a pharmacist plays a key role in this step. In the current situation of the pandemic, increased attention is necessary from the specialists´ point of view to fully benefit the patient.

Keywords: GERD, SARS-CoV-2, COVID-19, diabetes mellitus, autoimmune diseases, rheumatic diseases

INTRODUCTION

According to the National Health System (UK), gastro-esophageal reflux disease (GERD) is a condition that occurs when there is constant backflow of stomach acid/contents travelling upwards the cardia (acid reflux). In this case, the patient experiences heartburn and a sour taste caused by the acid [1]. Other symptoms include cough, halitosis or bloating. These symptoms are usually worsened after eating or lying down. Patients are commonly advised to first make lifestyle changes such as: eating smaller meals more frequently, losing extra-weight or adjusting their sleeping manner (for example raising one end of the bed so as to position their chest and head above the waist level, thus not permitting the acid to return). Simple yet important pieces of advice must be given by community pharmacists: advising patients to avoid smoking, alcohol, foods and beverages which may trigger the symptoms, not eating three to four hours before going to sleep, and not to interrupt

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TABLE 1. GERD classification, physiopathology and therapy

GERD classification	GERD physiopathology	Medicine
1. Reflux esophagitis	Increased esophageal sensitivity	1.Lifestyle changes
2. Barret esophagitis	Impaired antireflux barrier	2. PPIs*/H2-receptor antagonists
3.Non-erosive reflux disease	Poor motor function of the esophageal body	3.Surgical intervention

*PPIs= Proton Pump Inhibitors where; *preffered prescribed medicine*

any prescribed medicine prior to consulting a doctor (Table 1, Figure 1).

Even though the main symptoms of the new severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection consist of: fever, fatigue, dry cough and shortness of breath, gastrointestinal (GI) manifestations may occur during the clinical scenario of this viral infection [2].

After performing biopsies of the esophagus, stomach, duodenum and rectum, it was suggested that the virus could be docked in the digestive tract. This might explain the ulcers and the herpetic-type erosions in the esophagus [3].

GERD MANAGEMENT IN DIABETES MELLITUS PATIENTS

Diabetes mellitus (DM) is a metabolic, chronic condition defined by hyperglycemia, which can lead, in time, to different damage on the cardiovascular or nervous systems. According to WHO fact sheet [4], over 400 million people worldwide are diabetic, the majority of which live in low to middle-income countries. Taking into consideration the current status of imposed lockdown in many countries, proper glycemic control is imperative to counteract possible negative outcomes. Moreover, hypovitaminosis D increases the risk for insulin resistance, therefore linking the impairment of the glucose profile in the case of patients afterwards infected with coronavirus disease COVID-19 [4]. A summarized approach of the pathology and drugs present in current protocols is presented in Table 2. Prevalence

TABLE 2. DM and the therapeutic approach of COVID-19 response

Existing condition	DM Physiopathological Mechanism	Exposure to COVID-19	Negative outcome
DM is a pro-inflammatory state	Exagerated cytokine response, Pro-thrombotic hypercoagulable state	Shock, Over-activation of hemostatic system	Rapid deteriorati-on,

Therapeutical approach in the management of COVID-19

Drugs	Outcomes in the context of DM pathology
Corticosteroids Lopinavir-Ritonavir* Interferon-β1 Azithromicin** and Hydroxychloroquine Tocilizumab	Hyperglycemia Lipodistrophy, insulin resistance; *potent enzime inhibitor, should not be associated with corticoids β-cell damage ** macrolide antibiotic which can lead to dysglycemia Improves glucose profile

*where *is ritonavir and **is azithromicin*

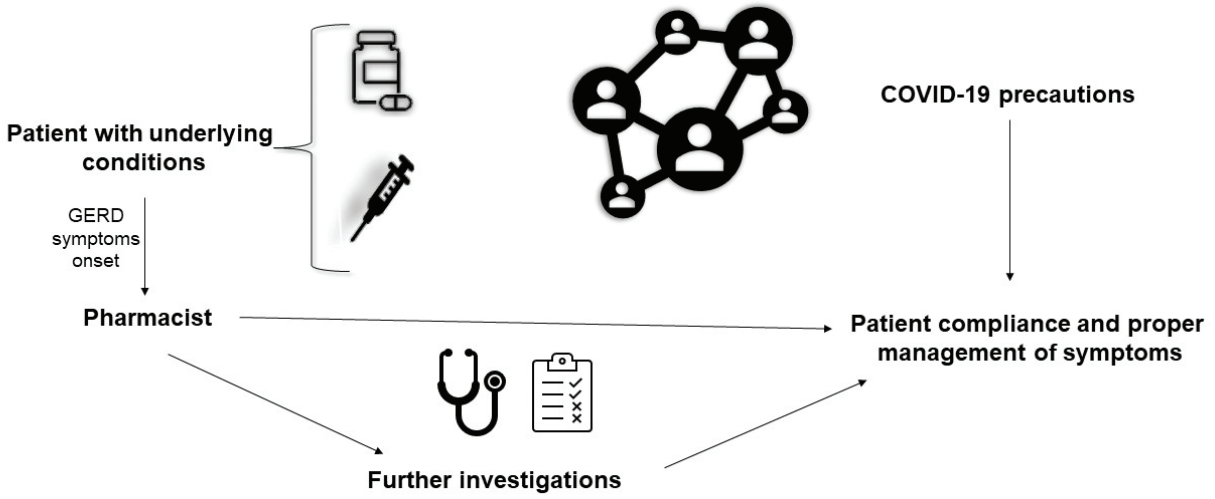

FIGURE 1. Top sales of OTC products in Romania in 2018

of GERD in DM patients is higher than in those without DM [5].

Hyperglycemia can lead to neuropathy and this in turn lead to esophageal dysmotility and GERD. As a first step, one interesting finding might be useful as a lifestyle change while in lockdown, to prevent the increase in GERD. Late-night dinners can affect gastric conditions due to a build-up of acidity from late afternoon to early evening. Stomach distension together with supine position result in the relaxation of the cardia sphincter.

When selecting GERD therapeutical agents, it should be noted that DM patients develop PPI resistance. Not only is the DM pathophysiology responsible for this effect, but also DM drugs (metformin, GLP-1 receptor agonists), which can lead to complex drug interactions and failure of PPI treatment [6]. Therefore, treatment of GERD in diabetic patients must include firstly good glycemic control, because euglycemia may reduce GERD symptoms and improve gastric motility. If necessary, histamine H2 antagonists or PPIs may be selected to suppress acid, only after careful evaluation.

Patients with DM must be extra cautious and care for strict social distancing, hand hygiene and glycemic control throughout the ongoing pandemic.

Frequently associated with DM are cardiovascular (CV) diseases. In this case, particular precautions must be taken into consideration. PPIs have been associated with an increased risk of complications (myocardial infarction or stroke) and mortality. On the other hand, H2-antagonists are not associated with such CV risk and may therefore be used as an option in this category of patients [7].

GERD MANAGEMENT IN PATIENTS WITH RHEUMATIC AND AUTOIMMUNE DISEASES

Rheumatic diseases include a wide range of pathological entities, such as: connective tissue diseases (systemic lupus erythematosus, rheumatoid arthritis, scleroderma, dermatomyositis/polymyositis, Sjögren syndrome, spondylo-arthropathies (e.g., ankylosing spondylitis, reactive arthritis, psoriatic arthritis), degenerative arthritis, metabolic disorders (gout, pseudogout), septic arthritis, and other diseases which affect the joints, bone, cartilage, tendons, and ligaments. The main tissues and organs affected by these diseases are the muscles, bones, joints, and soft tissues [8].

Antirheumatic drugs can be classified into three groups: (i) nonsteroidal antiinflammatory drugs (NSAIDs), (ii) glucocorticoids, and (iii) nonbiological and biological immunosuppressive/immunomodulating agents. The efficacy of NSAIDs is mostly limited to the control of signs and symptoms, except for a subset of patients with axial spondyloarthritis, in which case continuous use of NSAIDS may inhibit radiographic spinal progression. The efficacy of the other two groups extends beyond the control of symptoms. Their targetis to suppress inflammation and halt the progression of disease-specific organ damage. The lack of efficacy of NSAIDs in altering the course of rheumatic disease justifies their on-demand/short-term use. Glucocorticoids are potent antiinflammatory agents, but their prescription should carefully justified due to a high probability of side effects. On the other hand, biological agents have changed the treatment of rheumatic diseases, improving the outcomes and treatment goals. The main concerns in the perioperative setting are the maintenance of disease remission and minimizing the risk of wound healing delay and infection [9].

Esophageal symptoms are common for patients with rheumatic diseases and vary in forms of nature and severity from functional myopathic or neuropathic esophageal dysmotility to extrinsic lumenal compression and esophageal mucosal damage either from gastroesophageal acid reflux or opportunistic infection. The primary symptoms of heartburn, dysphagia, odynophagia, chest pain, and bleeding may be directly related to the underlying rheumatic disease or may be the unwanted effects of therapy with NSAIDs, immunosuppressants or disease-modifying agents. Easily over-looked in the context of a multisystemic disease, these esophageal symptoms may be amenable to simple treatments, but frequently require a thorough assessment by modern diagnostic tools. In many instances, functional and structural involvement of the esophagus in patients with rheumatic disorders requires a high index of suspicion for an early diagnosis, correct assessment, intensive surveillance, and aggressive therapy to avoid end-organ damage and decline in quality of life. Significant recent advances in the understanding of esophageal pathophysiology, the development of diagnostic techniques, progress in diagnostic and therapeutic endoscopy, and minimally invasive surgery allow early detection and effective long-term therapy for esopha-

geal dysfunction associated with rheumatic diseases [10].

Since the outbreak of the pandemic, concerns have been raised on the risk of SARS-CoV-2 infection and related complications among patients affected by systemic autoimmune diseases. On the one hand, these patients carry a higher risk of infections due to immunosuppression. On the other hand, immunosuppression itself may weaken the abnormal immune response that seems to be responsible for the most severe disease complications such as interstitial pneumonia. Two immune-modulating drugs largely used for immune-mediated disorders, hydroxychloroquine (HCQ) and chloroquine, have demonstrated some antiviral activity against SARS–CoV-2 *in vitro* and in small clinical studies. Similarly, tocilizumab, an anti-interleukin (IL)-6 receptor antibody approved for different rheumatic diseases, proved effective in severe SARS-CoV-2 cases, although these data warrant confirmation by controlled trials. Research up to this point suggests that patients with systemic autoimmune diseases do not carry an increased risk of SARS-CoV-2 infection. Additionally, as most patients are receiving treatment, it can be speculated that immunosuppressive treatments should not be discontinued in such cases. These results are not surprising, as a prominent immune response seems to mediate the most severe complications of COVID-19. A high percentage of patients with symptoms compatible with COVID-19 have an active disease, further suggesting that active immune response might be associated with a higher susceptibility to the infection, which however could not be confirmed in most symptomatic patients [11].

The recent outbreak of SARS-CoV-2 has also raised concerns about patients affected with autoimmune rheumatic diseases (ARD). Indeed, patients with ARD are considered at higher risk of bacterial, viral and opportunistic infections compared to the general population, owing to the underlying condition and the use of immunosuppressive drugs [12]. However, the use of some of these agents, such anti-malaria agents, janus kinase (JAK) inhibitors, tocilizumab and colchicine, is being included in the protocols of clinical trials in various research centres, as part of the management of patients with COVID-19. According to recommendations from SIR (Italian Society for Rheumatology), the maintenance of immunomodulatory and immunosuppressive therapies was suggested during the COVID-19 pandemic. This suggestion aims at avoiding disease relapses, which could occur with abrupt therapy withdrawal [13]. Pending the results of further investigations coming from an ongoing international alliance of SARS-CoV-2 cases with rheumatic diseases, research up to this point suggests that patients with chronic systemic autoimmune diseases do not seem to be at increased risk of SARS-CoV-2 infection or complications compared with the general population.

CONCLUSIONS

In conclusion, the ongoing pandemic has made it difficult for practitioners and prescribers to help patients as they normally would, and also for patients to seek the help they need, as the emotional ground cannot be disconsidered. Given the symptomatic importance GERD has, it firstly comes to the community pharmacists´ attention to address this issue and help the patient to fully understand his condition. Moreover, since currently available GERD medication do not provide a cure for the long term, constant care is essential. It is rarely the case that other pathologies are not associated with GERD, therefore managing the underlying condition must be considered as a fundamental point in therapy.

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