

Gastrointestinal symptoms from theoretical knowledge to pharmaceutical approach during COVID-19 pandemic

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ABSTRACT

Usually gastrointestinal discomfort is a very common complaint and most of the time it's easy to manage in daily pharmaceutical practice. But some conditions can lead to further complications or become worse over time, so it's really important that patients can access advice and support when they need it. Pharmacists are in the position to guide the selection of the best treatment by confirming the diagnosis, sending patients with alarm symptoms to physicians and educating patients on the proper use of their OTC medication. Gastrointestinal symptoms such as diarrhea and nausea/vomiting are often recognized among the patients with COVID-19. The impact of pharmacist intervention is needed in order to ensure reliable information for preventing, detecting, treating and managing coronavirus infection.

Keywords: gastrointestinal symptoms, pharmacist, COVID-19

INTRODUCTION

Gastrointestinal (GI) disorders are among the diseases with the highest incidence globally. Annually in Europe over 1 million deaths are caused by gastrointestinal pathologies in patients of all ages, and the management of these diseases is a challenge for the entire health system.

A study conducted by United European Gastroenterology in 2013 across Europa emphasizes the need for understanding the real burden of GI disease and their impact on the patients' lives. Many of these diseases are still poorly documented and

receive little attention from medical systems despite of their association with huge healthcare costs, high morbidity and an important percent of reduces productivity on daily base activities. People who live in Eastern European countries are more affected by GI disorders than the population from western countries. Romania and Italy register the highest incidence of hepatitis B and C, and 21% of the patients had complained of discrimination at workplace because of their illness [1]. More than 40% of population worldwide is affected of functional GI disease and the prevalence of GI disease seems to increase in the last 30 years as a result of global ageing and unhealthy eating habits [2, 3].

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THE ROLE OF THE PHARMACIST IN THE MANAGEMENT OF GI DISORDERS

According to the law 95/2006 stipulations, the pharmacist in Romania is employed as a health specialist (professional health) and enters in his attributions the information and counseling of patients regarding the prescribed medicines, as well as the appropriate mode of drug administration. Also, article 568, paragraph 2 of the law specifies that it is the pharmacist's responsibility to collaborate with the doctor to establish and monitor the patient's therapy [4].

Mostly, the pharmacist is in the last position in the doctor-patient-pharmacist triad, dealing with the issuance of medical prescriptions and advising patients on how to administer the medication received. However, it often happens that patients with minor or moderate symptoms for various conditions arrive at the pharmacy before reaching the doctor [5]. Thus, the pharmacist finds himself in the position where it is necessary to perform a careful and rigorous anamnesis of the patient to determine if he can issue over-the-counter (OTC) medication for the symptoms presented or it is necessary to direct the patient to a specialized medical consultation.

GI disorders are the most common conditions for which the patient first addresses to pharmacist and only later to doctor. In this case, the anamnesis of patients requires increased attention because gastrointestinal symptoms may be present in some pathologies or in physiological conditions (heartburn in pregnancy, accelerated intestinal transit under stress, constipation in the case of a sedentary lifestyle/ unhealthy eating habits and other). Also, it is very important the pharmacist's skills in helping the patient to cooperate in achieving a more objective anamnesis.

The data obtained from the patient's questionnaire must provide sufficient information so that the pharmacist can decide the next step in the patient's treatment. The patient's age, onset of symptoms, pre-existing conditions, detailed description of symptoms (location, intensity, features) and pre-existing treatments are required to complete the anamnesis [6].

Although the most frequent gastrointestinal symptoms reported by patients may seem common and the first tendency would be an easiness approach, it happens that a simple flatulence can announce a serious condition (Table 1) and pharmacist intervention may be a key factor for early diagnosis and a favorable evolution of the patient's condition [7].

TABLE 1. Pathologies associated with gastrointestinal symptoms

SYMPTOM - NAUSEA	
Digestive disorders	food poisoning, hepatitis, liver cirrhosis, intestinal obstruction
Neurological disorders	motion sickness, brain trauma, migraines, meningitis, hydrocephalus, multiple sclerosis, birth defects, Guillain-Barre syndrome, stroke, bleeding, intracranial convulsions
Metabolic disorders	renal failure, adrenal insufficiency, hypercalcemia, hyponatremia, uremia, hyperthyroidism, diabetes
Infections	bacterial infections: otitis media, pneumonia, urinary tract infections adenovirus or rotavirus infections
Psycho-emotional disorders	alcoholism, anxiety, depression, anorexia, bulimia
Heart diseases	heart attack
Drug administration	antibiotics, anticonvulsants, chemotherapeutic agents, radiation exposure, hormones, nonsteroidal anti-inflammatory drugs, cardiovascular therapy
SYMPTOM - VOMITING	
Digestive disorders	gastritis, ulcer, food poisoning, gastroenteritis, peritonitis, appendicitis, cholecystitis, pancreatitis, hepatitis, pyloric stenosis, acute abdomen
Neurological disorders	migraines, allergies, stroke, motion sickness, Meniere's syndrome, hydrocephalus, intracranial hypertension
Metabolic disorders	hypercalcemia, uremia, adrenal insufficiency, hypoglycemia, hyperglycemia
Infections	swine flu, norovirus infection
Psycho-emotional disorders	alcoholism, anorexia, bulimia
Drug administration	chemotherapeutic agents, opioids, emetics
SYMPTOM - DIARRHEA	
Digestive disorders	food intolerances, enterocolitis, irritable bowel syndrome, diverticulosis, Crohn's disease, celiac disease, malabsorption syndrome, colon cancer, ulcerative colitis, intestinal dysbiosis

Metabolic disorders	vitamin deficiency (niacin), enzyme deficiency
Infections	bacterial: Salmonella typhi, Campylobacter, Escherichia coli, Shigella, Vibrio cholerae, Clostridium perfringens, Klebsiella oxytoca, Yersinia enterocolitica, Bacillus cereus viral: rotavirus, hepatitis virus, herpes simplex virus, cytomegalovirus, SARS-CoV-2 parasitic: Giardia lamblia, Cryptosporidium, Entamoeba histolytica fungal: Candida albicans
Psycho-emotional disorders	anxiety, depression, psychosis, panic attacks, manic depressive syndrome
Drug administration	magnesium sulfate, antibiotics, colchicine, anthraquinones, castor oil anti-hypertensives drugs, chemotherapeutic agents, radiotherapy
SYMPTOM - CONSTIPATION	
Gastrointestinal disorders	anal fissures, hemorrhoids, irritable bowel, intestinal stenosis
Neurological disorders	Parkinson disease, dementia
Metabolic disorders	hormonal imbalances, hypothyroidism, parathyroidism, hypercalcemia, diabetes
Psycho-emotional disorders	depression, bulimia, obsessive-compulsive disorders
Drug administration	antacids, calcium salts, anti-inflammatory drugs, antiparkinsonian drugs, iron, opioids, muscle relaxant drugs
SYMPTOM - ABDOMINAL PAIN	
Digestive disorders	indigestion, food poisoning, gastroenteritis, biliary colic, gastroesophageal reflux disease, constipation, irritable bowel syndrome, Crohn's disease, hiatal hernia, celiac disease, neoplasms, ulcers, gastritis, peritonitis, biliary lithiasis, pancreatitis, diverticulitis, ruptured spleen, appendicitis, meteorism
Gynecological disorders	ovarian cysts, endometriosis, pelvic inflammatory disease, premenstrual syndrome, ectopic pregnancy
Metabolic disorders	ketoacidosis, Sickle cell disease, porphyria
Infections	Escherichia coli, Campylobacter, rotavirus, Salmonella, Shigella, Human papilloma virus, Neisseria gonorrhoeae, Chlamydia
Psycho-emotional disorders	headache, panic attack
Cardiac disorders	heart attack, aortic dissection, enteromezenteric infarction
Drug administration	nonsteroidal anti-inflammatory drugs, laxatives
SYMPTOM - FLATULENCE	
Digestive disorders	gastritis, ulcer, irritable bowel syndrome, constipation, biliary dyskinesia, short bowel syndrome, intestinal dysbiosis, gastroparesis, dyspepsia, gastroesophageal reflux disease, ascites, Crohn's disease
Metabolic disorders	lactase deficiency
Infections	Giardia intestinalis
Psycho-emotional disorders	stress, anxiety
SYMPTOM - PYROSIS	
Digestive disorders	gastroesophageal reflux disease, gastritis, ulcers, hiatal hernia
Metabolic disorders	obesity, diabetes
Cardiac disorders	ischemic heart disease
Drug administration	bisphosphonates, theophylline
SYMPTOM - RETRO-STERNAL PAIN	
Digestive disorders	gastroesophageal reflux disease, gastritis, ulcers
Cardiac disorders	heart attack, angina pectoris, aortic dissection

If the patient's condition allows, the pharmacist can advise him on OTC medication treatment options, on required hygienic-dietary regime as well as on the signs and symptoms that patient should follow along with the urge to consult a doctor if the symptoms persist for several days and do not improve under treatment [8].

The pharmacist has a wide range of OTC drugs and dietary supplements that he can recommend in the GI pathology, such as [9]: substitutes for gastric secretion

(digestive enzymes), substitutes for pancreatic secretion (enzymatic complexes of trypsin, chymotrypsin, amylases), cholergics/cholecystokinetics (salts of bile acids, magnesium sulfate, Cynara scolymus extract), antacids, gastric mucosa protectors and regeneration stimulants, antidiarrheal drugs (diosmectitis, pectins, rehydration salts, probiotics, loperamide), laxatives (mucilages, vegetable fibers, lactulose, sodium docusate, bisacodil), antiflatulents (medicinal charcoal, dimethicone), antispastic (drotaverine).

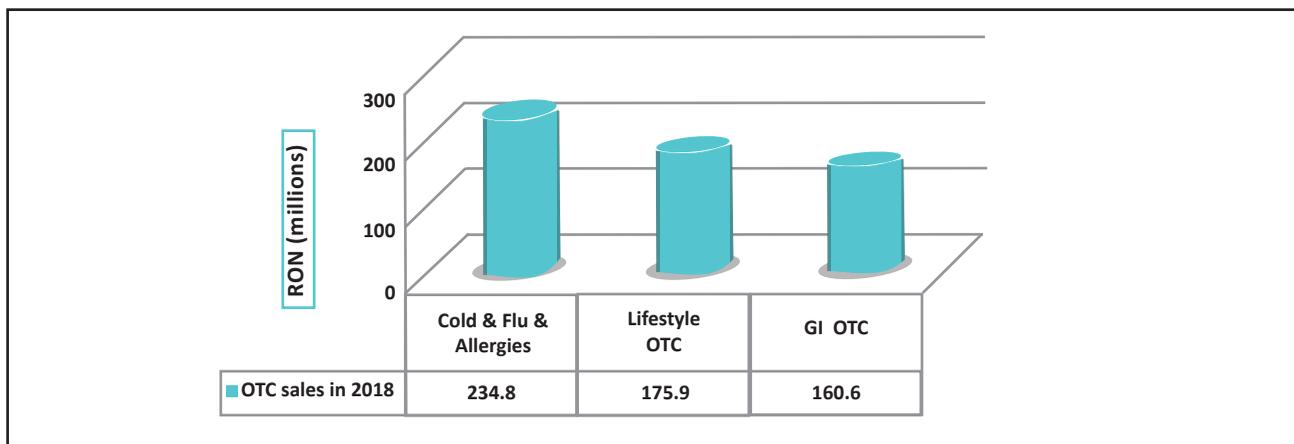


FIGURE 1. Top sales of OTC products in Romania in 2018

The variety of OTC options could lead to identify and recommend the optimal treatment for each patient an ongoing challenge for pharmaceutical practice. A study conducted by the company Cegedim highlights the fact that in Romania, in 2018, the sale of OTC products addressed to GI tract diseases is on the 3rd place after those for colds, flu and allergy and those from Lifestyle OTC category (Figure 1) [10].

Another task that belongs to the pharmacist is the release of the medication prescribed by the gastroenterologist. The role of the pharmacist is in this case crucial to ensure the effectiveness of the therapeutic scheme by complying with the patient's treatment. The pharmacist explains the dosage and route of administration to the patient, specifies the most known drug-food interactions and the possible side effects, in an adapted language so that the patient could understand all the recommendations made [11].

GI SYMPTOMS IN COVID-19

Although SARS-CoV-2 infection is mainly characterized by respiratory symptoms, according to a cohort study conducted in 9 hospitals in Massachusetts, on 318 patients aged 18 years and over, 2/3 of COVID-19 positive patients had at least one gastrointestinal symptom [12]. Another study was performed on 95 patients in Zhuhai, China, with a prevalence of GI symptoms greater than 60%. A significant percentage of them had the onset of GI symptoms after hospitalization, while only 11 patients had them since the beginning of the disease. All patients experienced an exacerbation of the symptoms during hospitalization, probably as a result of the cumulated of virucidal action with adverse reactions to the administered treatment [13]. The analysis revealed the presence of viral RNA in stool and in all digestive tract compo-

nents: esophagus, epithelial cells of the stomach mucosa, duodenum or rectum thus leading to the hypothesis of orofecal transmission of viral infection [14].

The mechanisms of GI symptoms in COVID-19 are not fully understood at this time (apparently the expression of ACE2 receptors in the digestive tract plays the most important role), but patients with only GI symptoms have performed a better evolution compared to patients with respiratory symptoms. Patients with associated GI and respiratory symptoms had the worst prognosis.

The main digestive symptoms presented by positive tested patients for SARS-CoV-2 are: diarrhea, vomiting, abdominal pain, anorexia, nausea or secondary bacterial infections (*Clostridium difficile*) [15, 16].

THE PHARMACIST IN COMMUNITY PHARMACY DURING COVID-19 PANDEMIC

Since the beginning of the pandemic, pharmacists around the world have combined the efforts with doctors and other medical specialists to strengthen the first line of defense against COVID-19. Although under the threat of becoming ill themselves and/or being a vector for the virus to their families, pharmacists have remained in position because the appearance and spread of SARS-CoV-2 in the world not canceled the presence of chronic diseases or the incidence of others pathogens infections [17, 18]. Due to the activity characteristics, pharmacists in Romania could not choose for teleworking or reducing the program in order to reduce the risk of contamination as was in the case of family doctors or other specialists which based on the government decision were able to perform remote consultations

TABLE 2. Pharmacists extra-tasks and their impact on pandemic

TASKS	IMPACT
Counseling and educating the public: (i) disease prevention, (ii) infection control	All patients have access to qualified and verified medical information about COVID-19 and receive appropriate medical advices on their particular situation related to pandemic
Ensuring appropriate stocks of pharmaceutical products	Pharmacies are able to provide specific pharmaceuticals products required in the pandemic (antiseptics, medicinal gloves and masks). All chronic patients have access to the basic medication in order to minimize the need for medical controls and interventions.

and release online medical prescriptions during the period of decree of the emergency state [19].

During the pandemic, in addition to the basic responsibilities, according to the recommendations of the International Pharmaceutical Federation, other tasks designed to reduce the spread of the virus were assigned to community pharmacists (Table 2) [20].

CONCLUSIONS

In the context of the current global situation, the joint effort is the one that contributes to obtaining positive results in the fight against a virus whose behavior is

still a challenge for the medical world. Pharmacists alongside other medical professionals are working hard support the affected population and stop the spread of the virus. The non-specific symptoms of COVID-19, in particular that of the gastrointestinal tract, make it difficult the early diagnosis and the therapeutic approach, requiring a close doctor-patient-pharmacist collaboration to establish an effective treatment scheme that takes into account both clinical aspects, as well as pharmacological implications. The pharmaceutical approach to GI diseases involves a pharmacist's meticulous evaluation of the patient's condition and all treatment options for a favorable evolution of the patient's health.

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