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

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### 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 - CONSTITUTION

### Gastrointestinal disorders
- Anal fissures, hemorrhoids, irritable bowel, intestinal stenosis

### Neurological disorders
- Parkinson disease, dementia

### Metabolic disorders
- Hormonal imbalances, hypothyroidism, paratiroidism, 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
- Gastritis, ulcer, irritable bowel syndrome, constipation, biliary dyskinesia, short bowel syndrome, intestinal dysbiosis, gastroparesis, dyspepsia, gastroesophageal reflux disease, ascites, Crohn's disease

### Metabolic disorders
- Obesity, diabetes

### Cardiac disorders
- Ischemic heart disease

### Drug administration
- Bisphosphonates, theophylline

### SYMPTOM - RETRO-STERNAL PAIN

### Digestive disorders
- Gastritis, ulcer, irritable bowel syndrome, constipation, biliary dyskinesia, short bowel syndrome, intestinal dysbiosis, gastroparesis, dyspepsia, gastroesophageal reflux disease, ascites, Crohn's disease

### Cardiac disorders
- Heart attack, angina pectoris, aortic dissection
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 Massachussets, 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 components: 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.
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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REFERENCES

1. *** The Survey of Digestive Health across Europe, Highlighting changing trends and healthcare inequalities in GI and liver disease
2. https://ueg.eu/files/662/be3159ad04564bf6b9db9e132851ebf9c.pdf.
3. Sperber AD, Bangdiwala SI, Drossman DA et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global Study. Gastroenterology 2020;S0016-5085.
4. Dirac M, Saeid S, Tsoi D. The global, regional, and national burden of gastro-oesophageal reflux disease in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. Gastroenterology & Hepatology 2020;5(6):561-587.
5. ***Law 95/2006. Practicing the profession of pharmacist.
6. Milosavljevic A, Aspden T, Harriso J. Community pharmacist-led interventions and their impact on patients’ medication adherence and other health outcomes: a systematic review. IJPP. 2018;26(5):387-397.
7. MacFarlane B. Management of gastroesophageal reflux disease in adults: a pharmacist’s perspective. IntegPharmResPract. 2018;7:41-52.
8. Gottfried J. Overview of gastrointestinal symptoms, Merck Manual. Professional Edition, 2020.
9. Boardman HF, Heely G. The role of the pharmacist in the selection and use of over-the-counter proton-pump inhibitors. Int J Clin Pharm. 2015;37(5):709-716.
10. ***https://mediateely.co/ro/atcs/A/tractul-digestiv-si-metabolism
11. ***https://www.wall-street.ro/articol/Companii/231275/primul-trimestru-al-anului-pentru-segmentul-de-piata-otc-vanzari-de-883-3-milioane-de-lei-in-crestere-cu-13-2.html.
12. Sabater-Galindo M, Ruiz de Maya S, Benrimoj S et al. Patients’ expectations of the role of the community pharmacist: Development and testing of a conceptual model. RSAP. 2017;13(2):313-320.
13. Redd WD, Zhou JC, Hathorn KE et al. Prevalence and characteristics of gastrointestinal symptoms in patients with severe acute respiratory syndrome coronavirus 2 infection in the United States: A multicenter cohort study. Gastroenterology 2020;159:765-767.
14. Lin L, Jiang X, Zhang Z et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. Gut. 2020;69:997-1001.
15. Villapol S. Gastrointestinal symptoms associated with COVID-19: impact on the gut microbiome. Transl Res. 2020;226:57-69.
16. Perisetti A, Goyal H, Gajendran M et al. Prevalence, mechanisms, and implications of gastrointestinal symptoms in COVID-19. Front Med. 2020;7:741.
17. Ma, Chunxiang, Cong, Yingzi, Zhang, Hu. COVID-19 and the digestive system. AJG. 2020;115(7):1003-1006.
18. Nguy J, Hitchen SA, Hort AL et al. The role of a Coronavirus disease 2019 pharmacist: an Australian perspective. Int J Clin Pharm. 2020;42(5):1379-1384.
19. Hayden JC, Parkin R. The challenges of COVID-19 for community pharmacists and opportunities for the future. Ir J Psychol Med. 2020;37(3):198-203.
20. ***Government Order 539/31/03/2020
21. ***Pharmacists: on the front lines of GI care, International Pharmaceutical Federation. https://www.fip.org/files/fip/news/FIP%20GI%20Care.pdf.