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CHRONIC COUGH ASSOCIATED WITH GASTROINTESTINAL DYSFUNCTION

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რეზიუმე

ქრონიკული, მუდმივი ხველა არის საერთო კლინიკური პრობლემა, რომლის მიზეზი ზოგჯერ ამოუცნობი რჩება. გასტროეზოფაგური რეფლუქსი (GERD), როგორც კუჭ-ნაწლავის დისფუნქციის ერთ-ერთი გამოვლინება, ქრონიკული ხველის ყველაზე გავრცელებული მიზეზია. ასევე, ზოგიერთმა კვლევამ აჩვენა, რომ ჰელმინთები იწვევს ან ზრდის ხველის სიმძიმეს. ზემოაღნიშნულიდან გამომდინარე, წარმოდგენილი კვლევა მიზნად ისახავს კუჭ-ნაწლავის დისფუნქციის სკრინინგს და გამომწვევი მიზეზების იდენტიფიცირებას, ქრონიკული ხველის მქონე დასავლეთ საქართველოს მოსახლეობაში. კვლევაში ჩართული იყო 46 პაციენტი (18-დან 75 წლამდე, 24 ქალი და 22 მამაკაცი), რომლებმაც მიმართეს საქართველოს მეცნიერებათა აკადემიის ალერგოლოგიის, ასთმის და კლინიკური იმუნოლოგიის ეროვნულ ინსტიტუტს (წყალტუბო, საქართველო) დიაგნოსტიკისთვის. კვლევის დიზაინი მოიცავდა: 1) ანამნეზის შეგროვებას - სპეციალურად შემუშავებული კითხვარის მეშვეობით; 2) Helicobacter pylori-ზე საერთო IgM, IgG ტიტრების განსაზღვრას; 3) ასევე შეფასდა საერთო IgA, IgM, IgG ტიტრები ჰელმინთებზე: Giardia, Ascaris, Toxocara. სამედიცინო ისტორიისა და სპეციფიკური ინსტრუმენტულ-ლაბორატორიული მარკერების ანალიზის საფუძველზე 46 პაციენტიდან 17 პაციენტში ქრონიკული ხველით გამოვლინდა კუჭ-ნაწლავის დისფუნქცია. Helicobacter pylori-ის კვლევამ აჩვენა ამ მარკერის დონის მატება 17-დან 6 (35%) პაციენტში. ლაბორატორიულმა გამოკვლევებმა გამოავლინა მთლიანი IgM-ის დონის მატება 1 (5,8%) შემთხვევაში, ხოლო IgG მაღალი ტიტრი Helicobacter pylori-ზე დაფიქსირდა 5 (29%) პაციენტში. გარდა ამისა, გამოვლინდა ანტისხეულები სამივე ანალიზატორის წინააღმდეგ ჰელმინთებზე: Giardia, Ascaris, Toxocara. ხველის სახელმწიფო პროტოკოლით/გაიდლაინებით მკურნალობის პარალელურად პაციენტებს უტარდებოდათ ანტიჰელმინთური თერაპია, რამაც გამოიწვია საიმედო გამოსავალი - გამოჯანმრთელება. საბოლოო ჯამში, გასტროენტეროლოგს შეუძლია გადამწყვეტი როლი ითამაშოს რეფრაქტერული ხველისადმი სისტემატური, მრავალდისციპლინური მიდგომის მხარდაჭერაში და ასევე გონივრულად გამოიყენოს დიაგნოსტიკური ტესტირებისა და მკურნალობის სტრატეგიები.

INTRODUCTION. Chronic cough is a burdensome symptom affecting a large number of patients and contributes significant cost to the healthcare system. Chronic, persistent cough is a common clinical problem, the cause of which sometimes remains unidentifiable. Many patients with chronic cough will have seen multiple physicians, including primary care, allergy, otolaryngology, and pulmonary specialists before referral to gastroenterology [1].

Gastroesophageal reflux disease (GERD) is one of the most common causes of chronic cough. Experts associate GERD cough with a protective cough reflex from the vagus nerve, which is responsible for digestion and breathing, when stomach contents rise into the esophagus a regurgitation or

microaspiration (inhalation of very small amounts) of acid and other stomach contents that reach the throat. In some cases, chronic cough may co-occur with GERD but have other causes, like asthma, postnasal drip or bronchitis.

Before a cough can be attributed to GERD, other cardiopulmonary, infectious, and allergic causes should be ruled out. Patients should undergo spirometry, a bronchial provocation test, imaging, and bronchoscopy prior to referral to gastroenterology. If there are seasonal or other suspected allergic triggers, treatment with anti-histamines and/or nasal steroids may be appropriate in concert with an allergy evaluation. If these measures do not help, the gastroenterologist is faced with the choice of empirical treatment with acid suppressive therapy or further diagnostic testing for GERD.

Gastroesophageal reflux disease (GERD), such as common manifestation of gastrointestinal dysfunction, is due to the chronic exposure of the esophageal mucosa to acid secretion from the stomach. The relationship between GERD and H.pylori infection is still subject of debate. Pylori infection may be a factor associated with chronic cough and it may be associated with a decline in pulmonary function and reduced incidence of allergic conditions. Some studies have suggested that helminth infections induce or increase the severity of cough. The relationships between cough and Helminthes infections are not inconsistent [2,4].

Based on the above, the presented study is aimed at screening and identifying Gastrointestinal dysfunction such as extrapulmonary conditions, which are reasons for chronic, persistent cough in the West Georgian population.

MATERIAL AND METHODS. 46 patients (18 to 75 years of age, 24 women and 22 men) who applied to the National Institute of Allergology, Asthma and Clinical Immunology of the Georgian Academy of Sciences (Tskaltubo, Georgia) for diagnostic were involved in the study. Upon admission to the hospital, patients had coughs of unknown origin. To clarify gastrointestinal dysfunctions, such as the cause of cough the research design included: 1) collection of anamnesis - via a specially designed questionnaire for collecting the medical history; 2) To clarify the common etiologic factor of gastrointestinal dysfunction, conduction of laboratory examinations including detection of total IgM, IgG titers on Helicobacter pylori; also total IgA, IgM, IgG titers on helminths: Giardia, Ascaris, Toxocara, was scheduled.

RESULTS. Based on the analysis of medical history and specific instrumental-laboratory markers in 17 (37%) patients out of 46 with cough, gastrointestinal dysfunction was revealed. They had clinical manifestation of GERD associated cough: coughing mostly at night or shortly after a meal; increased coughing when lie down; persistent coughing in the absence of other common causes, such as tobacco use, respiratory infections, or medications (including ACE inhibitors) in which coughing is a side effect; coughing without asthma or postnasal drip; clear chest X-rays, normal spirometry.

Detection of Helicobacter pylori showed an increase in the level of this marker in 6 (35%) patients from 17, established the antibodies in blood on Helicobacter pylori. The laboratory examinations detected increased levels of total IgM in 1 (5,8%) case, and IgG titers were increased in 5 (29%) patients on Helicobacter pylori.

In addition, the antibodies against all three analyzers on helminths showed: Giardia, Ascaris, and Toxocara were revealed. 3 (17%) showed elevated immunoglobulin titer only to Toxocara, 1 (5,8%) only Giardia, and 2 (11%) only Ascaris, respectively. Giardia-specific Immunoglobulin antibody titers in the blood were on average 0,446 (norm <0.2); Ascaris - 0,922 (norm <0.3); Toxocara - 0,556 (norm <0.2), respectively. In parallel to the treatment under the Cough State Protocol/Guidelines, the patients were administered antihelminth therapy, resulted in a reliable solution – recovery (Table N1).

Table N1. *Analyzing the Laboratory Markers in Patients with Chronic Cough Condition*

Indicators	* I Study Group n =17			II Control Group n= 29			P value (Confidence Interval)
	Abs.	%	(M±m)	Abs.	%	(M±m)	
Helicobacter pylory	8	47	1,5±0.76	4	13	0,7±0,16	>0,05
Toxocara	3	17	0,556±0.02	2	6	0,236±0.012	>0,05
Ascaris	2	`11	0,922±0.15	1	4	0,456±0.05	>0,05
Giardia	1	5	0,446±0.06	1	4	0,235±0.06	>0,05

* I Study Group – Patients with chronic cough and gastrointestinal dysfunction; II Control Group - Patients with chronic cough, without gastrointestinal dysfunction.

Cough monitoring tools have been useful in evaluating the efficacy of cough medicines. Owing to differences in the pathology, the organs involved, and individual patient factors, treatment of chronic cough is progressing towards a personalized approach, and, in the future, novel ways to endotype patients with cough may prove valuable in management [3].

An occasional or persistent cough may be a sign of acid reflux and gastroesophageal reflux disease (GERD). Managing acid reflux often improves chronic cough and provides relief unless there are other underlying causes.

In parallel to the treatment under the Cough State Protocol/Guidelines, the patients were administered antihelminth therapy, resulting in a reliable solution – recovery. Consequently, the fact that the current study evidenced the etiologic role of helminths in the genesis of cough with unknown origin is undoubtedly actual in terms of providing target treatment and getting the desired clinical effect.

CONCLUSION. Screening for chronic cough is not carried out in clinical practice. How screening could be done and whether it would lead to clinical benefit is unclear. Screening patients with chronic respiratory disease may be beneficial as cough is often overlooked during clinical evaluation. Moreover, early identification may improve the quality of life (QOL) of patients and possibly avoid overtreatment by specifically targeting cough.

Chronic cough remains a burdensome symptom both at the patient and healthcare system level. Ultimately, the gastroenterologist can play a key role in supporting a systematic, multi-disciplinary approach to refractory cough that judiciously utilizes diagnostic testing and treatment strategies.

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SUMMARY

Chronic, persistent cough is a common clinical problem, the cause of which sometimes remains unidentifiable. Gastroesophageal reflux disease (GERD), such as manifestation of gastrointestinal dysfunction, is one of the most common causes of chronic cough. Some studies have suggested that helminth infections induce or increase the severity of cough. Based on the above, the presented study is aimed at screening and identifying gastrointestinal dysfunction such as extrapulmonary conditions, which are reasons for chronic, persistent cough in the West Georgian population. 46 patients (18 to 75 years of age, 24 women and 22 men) who applied to the National Institute of Allergology, Asthma and Clinical Immunology of the Georgian Academy of Sciences (Tskaltubo, Georgia) for diagnostic were involved in the study. The research design included: 1) collection of anamnesis - via a specially designed questionnaire for collecting the medical history; 2) To clarify the common etiologic factor of gastrointestinal dysfunction, conduction of laboratory examinations including detection of total IgM, IgG titers on Helicobacter pylori; also total IgA, IgM, IgG titers on helminths: Giardia, Ascaris, Toxocara, was scheduled. Based on the analysis of medical history and specific instrumental-laboratory markers in 17 (37%) patients out of 46 with cough, gastrointestinal dysfunction was revealed. Detection of Helicobacter pylori showed an increase in the level of this marker in 6 (35%) patients from 17, established the antibodies in blood on Helicobacter pylori. The laboratory examinations detected an increased level of total IgM in 1(5,8%) case, and IgG titers were increased in 5 (29%) patients on Helicobacter pylori. In addition, the antibodies against all three analyzers on helminths showed: Giardia, Ascaris and Toxocara were revealed. In parallel to the treatment under the Cough State Protocol/Guidelines, the patients were administered antihelminth therapy, resulting in a reliable solution – recovery. Ultimately, the gastroenterologist can play a key role in supporting a systematic, multi-disciplinary approach to refractory cough that judiciously utilizes diagnostic testing and treatment strategies.

Keywords: Chronic Cough, Helicobacter Pylori, GERD, Helminths